IDENTIFYING *IN UTERO* RISK FACTORS ASSOCIATED WITH MALE REPRODUCTIVE MALFORMATION

by

Jack W. Pike

A dissertation submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Biological Sciences

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ABSTRACT

Male reproductive development is mediated by hormone signaling events. A surge of testis testosterone production occurs during a critical window: gestational days 15-18 in the rat and gestational weeks 10-22 in the human. This period of development corresponds with many of the reproductive masculinization events that are required for normal formation. Disruption of steroidogenesis during this time can lead to malformations in the male reproductive system in the forms of hypospadias, cryptorchidism, and decreased anogenital distance.

Steroidogenesis can be disrupted by many factors including environmental chemical exposure, genetic predisposition, or *in utero* conditions. Dibutyl phthalate is a plasticizer used in food packaging, medical devices, and cosmetics. In rats it has been shown to disrupt *in utero* testosterone production and cause reproductive malformations. Human sensitivities to this compound, however, have not been well established.

Another factor that has been linked to fetal testis steroidogenic disruption is *in utero* growth restriction. When a fetus receives insufficient nutrients due to placental insufficiency, genetic predisposition, or maternal nutritional deficits, an increased prevalence of reproductive malformations that are associated with insufficient androgen signaling is observed.

This study has examined the effects of *in utero* dibutyl phthalate exposure on rat foreskin gene expression. Several genes were selected for analysis by qRT-PCR from a pool of significantly altered genes, as identified by microarray analysis. *Marcks, Pum1*, and *Penk* expression were decreased and *Nupr1* expression was increased in rat foreskin of offspring of dibutyl phthalate treated pregnant rats. Following prenatal exposure, gene expression changes persisted several days after birth and as such, could serve as potential markers of chemical exposure and biological response.

Moreover, *in utero* growth restriction was assessed to determine its effects on fetal testis steroidogenesis. Growth restriction was elicited by means of maternal food restriction and caused a significant decrease in testicular gene expression of key genes involved in testosterone steroidogenesis including *Scarb1*, *Star*, *Cyp11a1*, and *Cyp17a1*. Moreover, testosterone production was reduced by 40% following maternal food restriction. We then assessed the potential cooperative effects of dibutyl phthalate with *in utero* growth restriction on gene expression. There was a significant decrease in testis steroidogenic gene expression in the combined growth restriction and dibutyl phthalate group as compared to either individual treatment. The combined treatment resulted in a 70% reduction in testosterone whereas there was only a 40% reduction for either individual treatment. Postnatally, the combined treatment resulted into numerous reproductive abnormalities. Interestingly, however, IUGR seemed to provide a protective effect wherein fetuses with DBP alone expression a growth restriction and restriction and restriction was reduced by the palone expression and to provide a greater

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incidence of reproductive malformation than those in the DBP IUGR combined exposure group.

Collectively, these findings can help in the risk assessment of dibutyl phthalate and *in utero* growth restriction while also demonstrating the potential interaction among these treatments. Prenatal studies indicate a cooperative disruption in steroidogenesis; however, postnatal analysis suggests a protective effect. The effects of IUGR on reproductive masculinization are clearly complicated. This study suggests that an interaction, whether preventative or compounding, may exist between IUGR and *in utero* exposure to the environmental antiandrogen, DBP.

Chapter 1

INTRODUCTION

1.1 Testis Structure and Function

Mammalian reproductive development occurs during a critical period of time, during which even the slightest error can cause permanent malformation. Early development begins with differentiation of male and female gonads with the aid of sex-determining region Y (*Sry*), (Mittowich, et al. 1988). This protein acts as a transcription factor, activating downstream genes that induce differentiation (Kashimada and Koopman, 2010). *Sox9* upregulation in the Sertoli cells of the testis inhibit ovarian formation, leading to gonadal masculinization (Hemendinger, et al., 2002; Jakob, and Lovell-Badge, 2011). This, in turn, drives the differentiation of germ cells towards masculine forms, in particular fetal Leydig cells (Kashimada and Koopman, 2010). It is these cells that produce the key hormone in reproductive masculinization: testosterone.

The testis is an oblate spheroid structure, surrounded by a protective membrane, the tunica albuginea. Within the testis lie the seminiferous tubules where male gonocytic maturation occurs (Amann, 1989; Li, et al., 2005) as shown in Figure 1, red arrows. These tubules carry mature sperm to the epididymis for excretion. The Leydig cells are found in the interstitium between these tubules (Figure 1, green stain).

The testis can contain two different kinds of Leydig cells: fetal and adult (Dong, et al., 2007). The fetal forms are responsible for producing sufficient testosterone for reproductive masculinization, while the adult form, that develops after

birth, aid in pubertal development (Habert, et al., 2001). Fetal Leydig cells appear to undergo a dedifferentiation step followed by apoptosis, but the factors that contribute to loss of fetal cells and production of adult cells is unknown (Kuopio, et al., 1989; Hazra, et al., 2013; Zirkin, 2010).

In humans, fetal testosterone production is initiated by the placental signaling hormone chorionic gonadotropin. The pituitary analog of this, luteinizing hormone, takes over in signaling testosterone production as children approach adulthood (Huhtaniemi, et al., 2006). In rats, it is unknown which factors initiate testosterone production *in utero*, as there is no rodent homolog of chorionic gonadotrophin. In humans, chorionic gonadotrophin signals through the LHCG receptor, a homolog of which is expressed in rodents, but knockout of this receptor in mice does not affect masculinization of pups. As is the case for humans, luteinizing hormone is primarily responsible for LH receptor signaling in adult rodents (Scott, et al., 2009). Nevertheless, fetal androgen production is required for normal male reproductive development.

1.2 Reproductive Masculinization

After gonadal masculinization occurs, reproductive development continues externally with the formation of the cloacal membrane, a region which later forms the urogenital sinus, rectum, and anal canal (Yamada, et al., 2003). The next stage of development requires complex hormonal signaling to differentiate the male and female external genitalia. Human fetal testosterone production begins at gestational week 10 and continues through week 22 (Welsh, et al., 2008). In rats, this masculinization programing window occurs from gestational day (GD) 15 through 18.

During this time, there is a large surge of testicular testosterone production peaking at GD17 (Welsh, et al., 2008; Scott, et al., 2008) as shown in Figure 2.

The resulting androgen signaling cascade allows for the masculinization of the external genitalia. Important testosterone-dependent stages include the testis descent, urethral closure, and enlargement of the anogenital distance (AGD). The testes are formed in the abdominal cavity and bound to the abdominal wall by the gubernacular ligament. Testosterone and INSL3 signaling stimulates this ligament to contract and pull the testes through the inguinal canal and into the scrotum (Feng, et al., 2009; Huang, et al., 2012). Testosterone drives the closure of the urethra proximally to distally along the underside of the phallus towards the meatus. Finally, androgen signaling causes an increase in the distance between the anus and genitals, resulting in males having a greater AGD as compared to females.

1.3 Testosterone Biosynthesis

Testosterone is synthesized from cholesterol in the Leydig cells of the testes (Hou, et al., 1990; Hu, et al., 2010). Cholesterol can either be produced within the Leydig cells through the mevalonate pathway and the rate limiting enzyme 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) or imported into the Leydig cells by scavenger receptor class B, member 1 (SCARB1) (Emanuele and Emanuele, 1998; Shan, et al., 1993). Once inside the cell, cholesterol is imported into the mitochondria by sterol acute regulatory protein (STAR) (Li, et al., 2011). This is the rate-limiting step of the testosterone biosynthesis pathway (Stocco, et al., 2001). Once inside the mitochondria, side chain cleavage by Cytochrome P450, family 11, subfamily A, polypeptide 1 (CYP11A1) processes cholesterol into pregnenolone (Issop, et al., 2012). Pregnenolone is transported to the endoplasmic reticulum, where cytochrome

P450 17A1 (CYP17A1) converts it into 17α -Hydroxypregnenolone and further to androstenedione (Habert, et al., 2001; Shima, et al., 2013). Finally, androstenedione is converted into testosterone by 17β -hydroxysteroid dehydrogenase. These steps are summarized in Figure 3, adapted from Emanuele and Emanuele, 1998.

Testosterone exits the Leydig cells and enters the bloodstream where it can travel to androgen-responsive tissues. Here it can either directly activate the androgen receptor or be transformed by 5- α reductase into the more potent androgen receptor agonist, dihydrotestosterone. While both maternal circulating testosterone and fetal adrenal gland testosterone production can enter the fetal bloodstream, these levels are far too low to contribute to masculinization in any significant way (Veyssiere, et al., 1976; Thompson, et al., 2005). As such, if any stage of the testis testosterone biosynthetic pathway is disrupted in the fetus, it can have severe consequences on masculinization.

1.4 Causes of Reproductive Malformation

Disruption of fetal testis testosterone production can prevent many of the androgen-dependent developmental steps required for normal reproductive masculinization. One of the more sensitive endpoints is the lengthening of the male AGD. Without sufficient testosterone signaling, this metric is feminized, causing a shorter distance between the anus and genitals. Another reproductive malformation that can occur from insufficient androgen signaling is the incomplete closure of the urethra. This condition, hypospadias, consists of the urethral opening forming on the bottom of the phallus (Figure 4). In more severe cases, the opening can be as far back as the scrotum or perenium. Finally, without adequate androgen signaling, the gubernacular ligament can fail to contract and pull the testes into the scrotum, causing

cryptorchidism (Figure 5, adapted from Feng, et al., 2009). Hypospadias and cryptorchidism occur in approximately 0.5% and 2-9% of male births in humans, respectively (Bay, et al., 2011; Hsieh, et al., 2008; Bryan and Hindmarsh, 2006).

Insufficient testosterone production can be caused by numerous factors. The two main categories of endocrine disruptors are environmental and genetic. Genetic causes include defects of the key proteins of the steroidogenic pathway, as previously described. Environmental factors can include exposures to antiandrogenic compounds as well as adverse maternal conditions contributing to a decrease in testosterone production.

1.5 In Utero Growth Restriction

One factor associated with reproductive malformation in humans is being born small for gestational age (SGA) (Jensen, et al., 2012). SGA is typically defined as falling below the 10th percentile of birthweight for gestational age. Being SGA is often brought on by *in utero* growth restriction (IUGR), wherein the fetus does not receive sufficient nutrients for normal growth (Wu, et al., 2004). IUGR occurs in 1-3% of human pregnancies (Bryan and Hindmarsh, 2006). Often times, IUGR occurs due to placental insufficiency, caused by the placenta lacking adequate vasculature, having poor transport of proteins, or having a structure that does not supply a fetus with adequate nutrients (Usha and Sarita, 2011). Incidence of malformations correlates with severity of SGA, resulting in neonates in the 1st percentile of birthweights having a 20-30% incidence rate for reproductive malformations (Gatti, et al., 2001; Damgaard, et al., 2008). Much of the current research on IUGR is dedicated to the Barker hypothesis which states that the conditions experienced by a fetus *in utero* predict the conditions it will face in life after birth (Barker, 1990). This means

that should a fetus receive insufficient nutrients *in utero*, it will be genetically programed for a life of scarcity, even if food and nutrition is abundant. This can lead to numerous problems including obesity, diabetes, and cardiovascular problems in life (Hanson and Gluckman, 2005; Barker, et al., 1990). No research, however, has investigated why IUGR babies have a higher incidence rate of male reproductive malformations.

1.6 Dibutyl Phthalate

An important class of environmental compound that has been shown to have antiandrogenic effects in *in utero* rat studies is phthalates. Dibutyl phthalate (DBP) is a phthalate commonly used in food packaging, medical devices, cosmetics, and perfumes. It can be used to bind fragrances or as a plasticizer to make plastics more pliable and durable (Schettler, 2005). Because it is not covalently bonded, however, it is free to leach into the environment where it can affect organisms exposed to it. Human exposures can reach the tens of mg/kg body weight per day (Swan, et al., 2005; Silva, et al., 2004; Schettler, 2005). In rats, this compound has been shown to disrupt testosterone production by means of decreasing steroidogenic gene expression in a dose-dependent manner (Thompson, et al., 2005; Sharpe, et al., 2008; Zhu, et al., 2009). The minimal *in utero* DBP dose level required to reduce testiticular steroidogenic gene expression has been shown to be between 50-100 mg/kg, if administered during the reproductive masculinization window. Higher doses have a greater effect on gene expression (Lehmann, et al., 2004). DBP is rapidly metabolized and cleared from the rat in approximately 2 hours, though its effects on steroidogenesis may persist for longer (Chang, et al., 2013). This reduction in gene expression is accompanied with a significant reduction in testis testosterone

production. Interestingly, DBP has been shown to act cooperatively if administered with other phthalate compounds, allowing a smaller dose level to have a statistically significant effect (Sharpe, 2008). Studies have also indicated that as a result of *in utero* DBP exposure, rats experience infertility in adult life, with the potential for transgenerational effects (Mahood, et al., 2007; Foster, et al., 2001).

Human studies investigating the toxicity of DBP have not been as conclusive. Studies have suggested a correlation between maternal urinary concentrations of monobutyl phthalate, the active metabolite of DBP, and male reproductive abnormalities (Blount, et al., 2000; Chang, et al., 2013) and decreases in anogenital distance (Suzuki, et al., 2011). However in xenograft models in which human fetal testes were implanted in rats, DBP treatment only affected rat tissues, suggesting that DBP does not affect human steroidogenesis in the same way (Heger, et al., 2012; Mitchell, et al., 2012). More studies are required to determine whether phthalates can have toxic effects in humans.

One of the major difficulties in assessing human risk is lack of an accurate marker of exposure. Commonly, urinary metabolites are examined to determine maternal exposure (Blount, et al., 2000; Chang, et al., 2013), however this does not accurately represent the exposure of the fetus to the active metabolite and does not indicate whether the metabolite had any effect. In a pilot study, Adibi, et al., (2009) examined expression levels of four genes in the steroidogensis pathway in placental tissue and showed that their expression was lower in subjects that had higher levels of urinary phthalate metabolites. However, they were not able to show a direct correlation between levels of phthalate and reduced gene expression. Placenta tissue is readily available at birth, but may not be an ideal source of tissue to measure effects

of phthalates on male reproductive development. Foreskin may be a better surrogate tissue for such research studies because it expresses the androgen receptor and can be easily obtained after birth (Fichman, et al., 1981). In the rat, preputial separation, defined as the separation of the foreskin from the glans penis serves as a pubertal milestone (Korenbrot, et al., 1977; Sengupta, 2013). Disruption of testosterone signaling due to exposure to an anti-androgen compound or castration causes a delay in preputial separation (Korenbrot, et al., 1977; Andrade, et al., 2006; Ge, et al., 2007). This indicates that this step in reproductive development is androgen responsive.

1.7 **Project Goals**

At present, research has not established the toxic risk of DBP in humans. Additionally, studies have shown that environmental anti-androgens can have compounding effects, allowing lower exposures to multiple chemicals to have a significant effect on steroidogenesis collectively. As such, our first goal is to identify a gene expression biomarker of *in utero* DBP exposure that can ultimately be used to assess the toxicity of this compound in humans. We will then examine the effects of IUGR on steroidogenesis to help understand the causes of an increased incidence rate of male reproductive malformations in SGA babies revealed by human epidemiological studies. Finally, we will determine whether DBP and IUGR can cooperatively disrupt steroidogenesis. We hypothesize that since both IUGR and DBP exposures are associated with the same reproductive malformations, a combined treatment of both will show a synergistic reduction in steroidogenic gene expression and, subsequently, testosterone production.



Figure 1 – Immunostaining of GD17 Rat Testis. Rat testes were sectioned and immunostained at GD17 for HSD3B1, a Leydig cell marker, and DAPI for nuclear staining. Seminiferous cords are indicated by red arrows. Cords are interspersed with fetal Leydig cells.







Figure 3 – Testosterone biosynthesis pathway. The testis testosterone pathway occurs in the fetal rat from GD15-18 and in the human from gestational weeks 10-22. These steps begin with cholesterol import into the Leydig cell through the action of *Scarb1*. Testostosterone is ultimately exported where it can be converted into dihydrotestosterone and bind to the androgen receptor to activate downstream pathways.



Figure 4 – Hypospadias in the mammalian phallus. Hypospadias occurs when the urethra fails to close properly. This causes the urethral meatus to form on the underside of the phallus. In more severe cases, this occurs more proximally, with extreme cases as far as the perineum.



Figure 5 – Gubernacular ligament aids in testis descent. The gubernacular ligament connects the testis to the body wall that will ultimately form the scrotum. Through hormone signaling this ligament shortens as the body grows. Together, these actions pull the testis from the abdomen, through the inguinal canal, and into the scrotum.

Chapter 2

MATERIALS AND METHODS

2.1 Animal Care

Animals were purchased from Charles River Laboratories (Raleigh, NC). The day of sperm detection was denoted GD0 and the date of parturition was considered postnatal day (PND) 1. All animal protocols were reviewed and approved by the Institutional Animal Care and Use Committee at Alfred I. duPont Hospital for Children. Rats were housed in a climate-controlled room with 12 hour light-dark cycles in an on-site facility accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International. A single dam was housed per polycarbonate cage with pine shaving bedding, fed Lab Diet Rat Chow 5012 (PMI Nutrition International, Brentwood, MO) and provided tap water *ad libitum*. Once received, animals were allowed to acclimate for six days prior to the start of any treatment.

To identify biomarkers of *in utero* DBP exposure and subsequent androgen signaling disruption, Sprague Dawley rats were used as a model. Timed-pregnant Sprague Dawley rats (strain code 001) were purchased from Charles River Laboratories (Raleigh, NC), arriving on GD 10. Upon arrival of timed-pregnant animals, maternal body weights were measured and dams were distributed evenly by weight between control and treated groups.

IUGR studies were performed on female Wistar rats (strain code 003) aged between 13 and 15 weeks of age. Animals were mated one male and three females to

a cage. Females were checked for the presence of sperm each morning by vaginal lavage. At sperm detection, dams were singly housed to accurately measure and regulate food consumption. Animals were divided evenly into treatment groups based on body weight at time of pregnancy.

In prenatal studies, dams were euthanized on GD17 or 20 by carbon dioxide asphyxiation six hours after their final DBP or flutamide exposure. In postnatal studies, PND1 and 5 pups were euthanized by decapitation, while PND14 and 28 pups were euthanized by carbon dioxide asphyxiation. Carbon dioxide asphyxiation was performed for two minutes. Once dams were opened for pup removal, the diaphragm was punctured to ensure death.

2.2 Vaginal Lavage

A standard eye-dropper was used to rinse the vagina with 200-500 uL physiological (0.9%) saline solution. The collected solution was observed under a light microscope for the presence of sperm. Droppers were rinsed several times with water and 70% ethanol to sterilize for reuse.

2.3 Maternal Food Restriction

Dams were food restricted from GD3-17 for prenatal studies and from GD3-18 for postnatal studies. GD3 was selected as a starting point as beginning earlier can result in pup or litter loss (Berg, 1965). GD17 was chosen as a stopping point for prenatal studies. This timepoint is during the masculinization programing window when testosterone production is the highest. Examining steroidogenic endpoints at this time provides a better look at the severity of disruption since there is more potential for decreased testosterone production. GD18 was selected for postnatal trials

to cover the entire masculinization programing window as well as to provide the dam with sufficient time to recover from food restriction prior to giving birth (GD21). Food restriction levels were either 50% (FR50) or 70% (FR70) of *ad libitum* controls. These levels were selected as a moderate and severe reduction in food in order to minimize litter loss while still inducing IUGR (Berg, 1965).

The first five dams identified as sperm positive were placed in the *ad libitum* control group. These animals were singly housed and given 250 g of food on GD0. Food was weighed and recorded each morning before being topped off to 250 g. The average weight of food consumption was determined for each gestational day. Dams in the FR50 and FR70 groups were allotted 50% or 70% less food than eaten by the *ad libitum* group of rats. This was continued until GD17 for prenatal trials, at which point dams were euthanized for dissection, or through the morning of GD18 for postnatal trials. Beginning on GD19, these dams were given food *ad libitum*.

2.4 Oral Gavage

To identify a foreskin biomarker of *in utero* DBP exposure and androgen signaling disruption, dams were administered DBP (100 or 500 mg/kg body weight), flutamide (5 mg/kg body weight), or corn oil vehicle by oral gavage once each morning between 8:00 and 10:00AM beginning on GD16 and continuing through GD20. Corn oil vehicle (C8267), DBP (524980) and flutamide (F9397) were purchased from Sigma (St. Louis, MO).

In combined IUGR and DBP studies, Wistar rats were administered DBP (150 or 500 mg/kg body weight) or corn oil vehicle once each morning between 8:00 and 10:00AM from GD15-17 (prenatal studies) or GD15-18 (postnatal studies).

Rats were restrained by hand using protective gloves (TurtleSkin) and gavaged using a rat-grade oral gavage needle (Cadence, Staunton, VA) attached to a 1 mL insulin syringe (Becton Dickinson, Franklin Lakes, NJ).

2.5 AGD Measurement

AGD was defined as the distance from the anterior wall of the anus to the posterior edge of the genitals in both prenatal and postnatal studies. In prenatal and PND1 rats, AGD was measured using a 1 mm ocular micrometer with increments of 0.1 mm. Rats were held supine in focus of the microscope with the anal wall positioned at the edge of the micrometer. In postnatal analyses, AGD was measured using a digital micrometer (Fisher).

2.6 Determining the Presence of Hypospadias

Pups and fetuses were examined for presence of hypospadias *post mortem* by gently pressing on the bladder and observing the location of the urethral opening on the phallus. Hypospadias was graded from mild to severe based on the location of the urethral meatus on the underside of the phallus. A urethral opening on the underside of the distal end of the phallus was defined as mild with severity increasing the more proximally it was located.

2.7 Determining the Presence of Cryptorchidism

On PND28, rats were checked for the presence of cryptorchidism. Rats were restrained in the supine position using protective gloves. With a free hand, the testes were palpated to determine whether they had descended into the scrotum.

2.8 Testis Sample Collection

Foreskin samples were collected from male rats at GD20 or PND5. Figure 6 demonstrates foreskin collection at PND5. Two foreskin samples were pooled per litter. Prenatal foreskin was flash frozen in dry ice and stored at -80°C. Postnatal foreskin was stored in RNAlater (Invitrogen, Carlsbad, CA).

Both prenatal and postnatal testis samples for RNA analysis were collected and flash frozen in dry ice and stored at -80°C until further processing. Two testes per litter from separate pups were pooled in each collection tube. Prenatal testes selected for immunostaining were placed in Bouin's fixative for 1 hour, and then in 70% ethanol overnight for dehydration. They were then paraffin embedded for later processing.



Figure 6 – Postnatal rat foreskin collection. Rat foreskin was collected on PND5. Foreskin was cut as shown.

2.9 Fetal Testis Histology

Testes were fixed in modified Davidson's solution overnight, dehydrated in 70% ethanol, and embedded in paraffin, and sectioned 5 μ m thick. These sections were stained with hemotoxylin and eosin. Testes were observed at 40X using an

Axiostar plus microscope (Carl Zeiss, Inc., Thornwood, NY) and the seminiferous cords that contained multinucleated germ cells were counted.

2.10 Testosterone Radioimmunoassay

For foreskin biomarker studies, two GD20 testes from different pups per litter were homogenized in 100 µL PBS (Sigma) for 1 minute using a PowerGen125 Homogenizer (Fisher-Scientific, Pittsburgh, PA). Samples were centrifuged, and supernatant testosterone levels were measured in duplicate by radioimmunoassay (Catalog #TKTT2, Siemens Medical Solutions Diagnostics, Los Angeles, CA; intraassay sensitivity – 0.1 ng/ml) at the University of Virginia Ligand Assay and Analysis Core Laboratory, supported by the Eunice Kennedy Shriver NICHD/NIH (SCCPIR) Grant U54-HD28934.

Testes from the IUGR or IUGR with DBP studies were collected on GD17 for radioimmunoassay (RIA). Three testes from different pups per litter were pooled in M199 culture medium (Life Technologies) and incubated for 3 hours at 37°C with agitation. Medium was then collected and sent for testosterone quantification by RIA at the University of Virginia Ligand Assay and Analysis Core Laboratory.

2.11 RNA Extraction and Processing

Foreskin RNA was extracted using RNeasy Fibrous Tissue Mini Kits (Qiagen, Valencia, CA) as per the manufacturer's protocol. RNA quantification was performed using a ND-1000 Spectrophotometer (NanoDrop Technologies, Wilmington DE). An Agilent 2100 Bioanalyzer (Agilent Technologies, Santa Clara, CA) was used to examine the integrity of RNA samples, and an RNA Integrity Number above seven was used as a cutoff for use in microarray analyses.

To examine testes from IUGR and combined exposure studies, GD17 rat testes were collected 6 hour following the final dose of DBP. Two testes from different pups per litter were pooled, flash frozen, and stored at -80°C. RNA was extracted using RNeasy Mini Kits (Qiagen, Valencia, CA) as per the manufacturer's protocol. RNA quantification was performed using the ND-1000 Spectrophotometer (NanoDrop Technologies, Wilmington, DE).

2.12 Microarray Processing

For DBP studies, gene expression microarray was performed using the RatRef-12 Expression BeadChip Kit (Illumina, San Diego, CA) at the Northwestern University Genomics Core Facility. Labeling was performed using Illumina TotalPrep RNA Amplification Kits (Ambion, Carlsbad, CA), and arrays were scanned using iScan (Illumina). Quality control was performed using lumi, a Bioconductor package (Du, et al, 2008). Because RatRef-12 arrays were discontinued by the manufacturer, arrays used for the flutamide study were GeneChip Rat Gene 1.0 ST Arrays (Affymetrix, Santa Clara, CA). Foreskin RNA samples from the flutamide study were labeled using the Applause WT-Amp ST System (Nugen, San Carlos, CA) with 50 ng total RNA. After hybridization and washing, Affymetrix microarray chips were scanned using the GeneChip Scanner 3000 (Affymetrix). Quality control was determined with the GeneChip Poly-A RNA Control Kit and the GeneChip Hybridization Control Kit (Affymetrix). Although two different microarray platforms were used, both platforms provide similar microarray data (Shi, et al., 2006; Maouche, et al., 2008; Barnes, et al., 2005).

2.13 Microarray Analysis

Illumina microarray data were log2 transformed and quantile normalized using lumi, a Bioconductor package. Affymetrix microarray data were normalized by Robust Multiarray Analysis (RMA) within the affylmGUI (Wettenhall, et al., 2006) package using R software. The R package ComBat (Johnson, et al., 2007) was used to ameliorate batch effects detected by principal component analysis. Data were analyzed statistically by Linear Models for Microarray Data (LIMMA) and Significance Analysis of Microarray (SAM) using R software (R Development Core Team, 2011) and MultiExperiment Viewer, a part of the TM4 Microarray Software Suite (Saeed, et al., 2006; Saeed et al., 2003), respectively. Bioconductor packages for LIMMA analyses included limma (Smyth, at al., 2005) as well as supporting packages affy (Gautier, et al., 2004) and Biobase (Gentleman, et al., 2004). Quality control analyses including principle component analysis and hierarchical clustering were performed using MultiExperiment Viewer (Saeed, et al., 2006; Saeed et al., 2003). Data were false discovery rate (FDR) corrected for multiple testing with a p-value of < 0.05 considered significant.

Microarray data are available through Gene Expression Omnibus accession number GSE48803.

2.14 Filtering of Microarray Results

Microarray results were filtered and genes were selected for subsequent qRT-PCR analysis. The first cutoff separated genes that were significantly (p<0.05) different to the control group. Gene lists were then examined by Ingenuity Pathway Analysis (IPA) (Ingenuity Systems, Redwood City, CA). This was used to determine which genes had significantly altered expression levels interacted, either directly or
indirectly, with either the androgen receptor or the steroidogenic pathway. These lists were then compared to determine which gene expression changes persisted from the prenatal study to the postnatal study, which genes were identified by both LIMMA and SAM analyses, and which gene expression changes were enhanced at a higher level of DBP. Finally, the fold changes and p-values of the remaining lists were examined to select genes for further analysis by qRT-PCR.

2.15 qRT-PCR

Complementary DNA was synthesized from total RNA using High-Capacity cDNA Archive Kits (Applied Biosystems). Real time qRT-PCR was performed using TaqMan Gene Expression Assays (Table 1) and TaqMan Gene Expression Master Mix (Applied Biosystems) in an ABI Prism 7900HT. Relative quantification was measured as compared to TATA-binding protein (TBP) and analyzed using the 2⁻ ^{AACT} method (Livak and Schmittgen, 2001). Microarray analysis revealed that DBP exposure may alter GAPDH expression (Appendix B). Because of this, we selected TBP as our housekeeping control. For foreskin biomarker studies, genes were selected for qRT-PCR analysis based on microarray results, while in IUGR studies, key steroidogenic genes including *Star*, *Scarb1*, *Cyp11a1*, and *Cyp17a1* were examined.

2.16 Statistical Analysis

Statistical analysis of all non-microarray data was performed using GraphPad Prism 5.0 (GraphPad Software, San Diego CA). Analysis consisted of t-tests, oneway ANOVAs with Dunnett's post test, two-way ANOVAs with Bonferroni post test, or Fisher's exact test. In all cases, the statistical unit was pooled tissue from a single

litter. Data are presented as the mean \pm standard deviation (SD). For all nonmicroarray data, a p-value less than 0.05 was considered significant.

Chapter 3

IDENTIFICATION OF GENE EXPRESSION CHANGES IN THE RAT FORESKIN FOLLOWING *IN UTERO* DBP EXPOSURE

3.1 Introduction

There is countless research demonstrating that DBP has toxic effects on *in utero* steroidogenesis in the rat, however its toxicity in humans has not been established. There have been association studies suggesting that higher concentrations of urinary metabolites are linked to an increased prevalence of male reproductive abnormalities. Meanwhile, xenograft models of human testis development suggest that they are not responsive to DBP or its metabolites. Because of these inconsistencies, we aimed to identify a biomarker of DBP exposure and androgen disruption in the rat foreskin.

To do this, we examined gene expression changes by microarray analysis in the rat foreskin both prenatally (GD20) and postnatally (PND5) to determine both the immediate and lasting effects of DBP exposure. We utilized both a low, 100 mg/kg (DBP100), and high, 500 mg/kg (DBP500) dose level in each study. Finally, to establish which effects were due to the disruption of androgen signaling and which were from chemical exposure, we examined gene expression changes with an additional compound, flutamide.

Flutamide is an anti-androgenic drug used in the treatment of prostate cancer. This compound works by competitively inhibiting the androgen receptor, preventing testosterone and dihydrotestosterone from binding (Brogden and Clissold, 1989). Rat

studies have shown that *in utero* exposure to this compound results in similar reproductive malformations as DBP, though dose levels are much smaller due to the increased potency of the compound (Imperato-McGinley, et al., 1992; Foster, et al., 2005; Macleod, et al., 2010).

3.2 Results

3.2.1 Prenatal Phenotypic Anchoring

There was no significant difference in GD20 maternal body weight between corn oil control, DBP100, and DBP500 treated dams (Table 2). Additionally, there were no significant differences in average litter size, maternal, or fetal weight between groups (Table 2). Fetuses exposed to *in utero* DBP had a significantly higher percentage of seminiferous cords with MNGs than corn oil controls (Figures 7A, B). Following a DBP100 exposure, there was no significant difference in testis testosterone (Figure 8A) or male pup AGD (Table 2). DBP500 exposure significantly decreased both GD20 testis testosterone levels (Figure 8B) and male AGD (Table 2). There was no change in female AGD following DBP exposure (Table 2).

3.2.2 Postnatal Phenotypic Anchoring.

Following GD16 to 20 DBP exposures to DBP100 or DBP500, postnatal phenotypic anchoring endpoints were examined on PND5. There was no significant difference in average litter size between corn oil control, DBP100, or DBP500 exposure groups (Table 2). Additionally, no difference in average pup or maternal weight was observed (Table 2). There was a significant decrease in male AGD following DBP500 treatment, but no significant difference after DBP100 exposure. Female AGD was not affected (Table 2). Of the DBP500 treated animals, five of the seven (71%) litters (five out of 25 total male pups examined) contained male pups with retained thoracic nipples, while none of the DBP100 litters contained pups with nipple retention. One of seven (14%) corn oil control litters contained two pups with retained thoracic nipples out of twenty-one total males. Hypospadias was not evident in any control litters.

GD16 to 20 flutamide exposure significantly decreased male but not female AGD at PND5 (Table 2). Flutamide exposure did not affect pup weight or litter size; male nipple retention was not examined. Six of the seven litters (eight out of 17 total male pups examined) exposed to flutamide contained male pups with hypospadias ranging from mild to severe, depending on where the urethral meatus appeared on the phallus. A subset of pups was allowed to develop through PND14 when they were examined for retained thoracic nipples. All of the litters exposed to flutamide *in utero* contained pups with retained nipples (Table 2). No reproductive malformations were noted in control groups.

3.2.3 Microarray Results

A complete list of significantly altered genes is included in Appendix B.

3.2.4 GD20 Microarray Analysis

LIMMA analysis of GD20 foreskin samples treated with DBP100 showed no significant gene expression changes compared to controls but SAM analysis identified three genes with significantly reduced expression levels. For samples exposed to DBP500, LIMMA analysis revealed 216 genes with significantly altered expression levels, while SAM analysis identified 117 significantly altered genes. 85 genes were identified by both LIMMA and SAM analyses of GD20 results, as shown in Appendix C. Of the LIMMA-identified genes, 131 were downregulated and the remaining 85 were upregulated. The three genes significantly altered after DBP100 exposure were not differentially expressed after DBP500 exposure.

3.2.5 PND5 Microarray Analysis

LIMMA analysis also failed to predict any gene expression changes at PND5 after treatment with DBP100 whereas SAM analysis indicated that expression of 35 genes were significantly altered at this time point. At PND5 after treatment with DBP500, LIMMA analysis revealed 233 genes with significantly altered expression levels and SAM analysis revealed 265 genes. 141 genes were found by both LIMMA and SAM analytical methods of DBP500 data at PND5 (Appendix D). Of the 35 genes found to be differentially expressed at DBP100 by SAM analysis, only 17 were also differentially expressed at DBP500 using LIMMA (Appendix E), and 20 using SAM (Appendix F).

LIMMA analysis of PND5 pups born to mothers exposed to flutamide showed only one gene, *Snrpf*, whose expression was significantly altered by treatment. SAM analysis of these data revealed 68 genes with significantly altered expression values, including *Snrpf*.

3.2.6 Real Time qRT-PCR

Genes identified by microarray analysis that might serve as biomarkers of *in utero* DBP exposure/responsivity or androgen signaling disruption were selected for validation by qRT-PCR. The significant decrease in *Penk* expression at GD20 following *in utero* DBP500 treatment was confirmed by qRT-PCR (Figure 9A). The

significant increase in *Nupr1* expression was also confirmed by qRT-PCR at both the GD20 DBP500 and PND5 DBP500 exposure levels (Figure 9B).

Microarray analysis showed that *Marcks* and *Pum1* were downregulated both at GD20 and PND5 after DBP500 treatment. qRT-PCR analysis confirmed these effects for *Marcks* at PND5 and also showed reduced expression of this gene at PND5 after DBP100 treatment (Figure 9C). Decreased expression of *Pum1* by DBP500 at PND5 was also confirmed by qRT-PCR, although the difference at GD20 was not significant (Figure 9D).

Snrpf and *Higd1b*, two genes identified as being down regulated by flutamide in the microarray analysis, were not found to be significantly reduced by qRT-PCR (Figure 9E,F).

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Figure 7 – Multinucleated gonocytes in fetal testis seminiferous cords. Fetal rat testes were examined on GD20 for presence of multinucleated gonocytes within the seminiferous cords. Data was examined by Fisher's exact test, and is reported as percentage of total cords with multinucleated gonocytes present. *A*) Fetal rat testes had a significantly higher percentage of multinucleated gonocytes following exposure to DBP100 compared to control animals (p=0.0097). *B*) Similarly, after exposure to DBP500, GD20 rat fetal testes had significantly higher amount of multinucleated gonocytes than controls (p<0.0001).



Figure 8 – GD20 testis testosterone production following *in utero* **DBP exposure.** Gestational day 20 testes were homogenized and intratesticular testosterone was measured by radioimmunoassay following *A*) DBP100 or *B*) DBP500 exposure *in utero*. A statistically significant decrease was detected at the DBP500 exposure level (p < 0.0001).











PND5 Pum1 Expression



PND5 Higd1b Expression





Figure 9 – Real time qRT-PCR results for confirmation of foreskin gene expression changes. A) Penk expression levels in the GD20 foreskin were decreased at the DBP500 exposure level as identified by both LIMMA and SAM analyses of microarray data. When examined by qRT-PCR, expression was significantly reduced at the GD20 and PND5 with DBP500 (p<0.01). No significant change was observed in animals exposed to flutamide. B) Nuprl expression following prenatal exposure to DBP500 was found to be significantly upregulated at GD20 by microarray analysis. qRT-PCR revealed a significant increase in Nupr1 expression at both GD20 and PND5 following DBP500 exposure (p<0.001, p<0.01). Additionally, following flutamide exposure, PND5 Nupr1 expression was reduced significantly (p < 0.05). C) Marcks expression was reduced at both the GD20 and PND5 DBP500 exposure levels in microarray analyses. Additional analyses by qRT-PCR revealed significant downregulation at PND5 following both DBP100 and DBP500 exposures (p<0.05, p<0.01). D) Microarray analysis showed Pum1 expression was downregulated at both GD20 and PND5 after *in utero* exposure to DBP500. gRT-PCR analysis revealed a significant decrease in *Pum1* expression at PND5 after DBP500 exposure (p<0.01). E) Following flutamide exposure, *Higd1b* levels were decreased as identified by microarray, though did not reach significance. qRT-PCR analysis revealed no significant changes at any exposure level or gestational age. F) Snrpf was shown by microarray analysis to be significantly downregulated at PND5 following in utero exposure to flutamide. There were no significant changes revealed by qRT-PCR.

Gene	
Symbol	Catalog Number
Snrpf	Rn01502828_g1
Penk	Rn00567566_m1
Nupr1	Rn00586046_m1
Marcks	Rn02102492_s1
Pum1	Rn00982780_m1
Higd1b	Rn01463844_g1

 Table 1: Taqman gene expression assays for qRT-PCR.

Table 2: Phenotypic anchoring data following *in utero* DBP or flutamide exposure. This table summarizes the phenotypic changes from prenatal and postnatal DBP studies as well as the flutamide study.

	GD20 - Dibutyl Phthalate					PND5 - Dibutyl Phthalate			PND5 - Flutamide	
	Control (DBP100)	Control (DBP500)	Combined Controls	DBP100	DBP500	Control	DBP100	DBP500	Control	Flutamide
Maternal Weight (g)	350.8 ± 10.6	354.3 ± 28.8	352.6 ± 20.8	333.0 ± 19.5	362.9 ± 23.5	351 ± 19.18	355 ± 13	362.43 ± 21.55	_a	_a
Male and Female Pup Weight (g)	4.58 ± 0.28	4.11 ± 0.17	4.34 ± 0.33	4.8 ± 0.16	4.08 ± 0.27	10.83 ± 1.30	11.68 ± 0.92	11.11 ± 1.37	11.21 ± 0.56	11.73 ± 1.35
Litter Size (fetuses/pups)	10.7 ± 2	12.5 ± 2.2	11.6 ± 2.2	7.8 ± 3.1	12.7 ± 1.1	12.1 ± 1.9	11.7 ± 1.3	11.9 ± 2.3	10.43±2.8 ^b	10.1±1.6 ^b
Male AGD (mm)	2.7 ± 0.14	2.69 ± 0.17	2.70 ± 0.15	2.64 ± 0.06	2.19 ± 0.14 *	4.73 ± 0.29	4.74 ± 0.20	4.29 ± 0.27 *	4.62 ± 0.26	3.33 ± 0.44 *
Female AGD (mm)	1.3 ± 0.08	1.3 ± 0.06	1.3 ± 0.08	1.2 ± 0.05	1.2 ± 0.04	2.3 ± 0.25	2.4 ± 0.25	2.4 ± 0.17	2.2 ± 0.08	2.1 ± 0.16
Litters with Hypospadias (%)	_a	_a	_a	_a	_a	_ a	_ a	_ a	0	86*
Litters with Nipple Retention (%)	_a	_a	_a	_a	_a	14 ^c	0 ^c	71 *c	0 ^c	100 *c

-a = Data not collected

-^b = Litters culled

-c = Measurement taken at PND14

Table 3: Effect of increased dose of DBP on reduction in gene expression. This table shows genes that were expressed at lower levels as dose of DBP was increased. All genes included were significantly lower than corn oil control according to LIMMA and/or SAM analyses.

Cone ID	Cono Namo	Gene	DPP100	DPBCOO
Gene in	Gene Name	Symbol	DBF100	DBF300
ILMN_1350792	Phd Finger Protein 20-Like 1	Phf20L1	0.83	0.74
ILMN_1351226	Cbl Proto-Oncogene, E3 Ubiquitin Protein Ligase B	Cblb	0.79	0.78
ILMN_1351553	Similar To Acyl-Coenzyme A Binding Domain Containing 5	Loc682593	1.01	0.77
ILMN_1354105	Similar To Riken Cdna 2810403A07	Rgd1565775	0.74	0.68
ILMN_1354288	Kinesin Family Member 5B	Kif5B	0.82	0.75
ILMN_1355423	Prp39 Pre-Mrna Processing Factor 39 Homolog	Prpf39	0.77	0.73
ILMN_1355694	Similar To Ac1262	Loc363492	0.66	0.59
ILMN_1359410	Krit1, Ankyrin Repeat Containing	Krit1	0.76	0.75
ILMN_1361017	Similar To Lrrgt00082	Loc500398	0.80	0.75
ILMN_1363227	Similar To Orf2 Consensus Sequence Encoding Endonuclease And Reverse Transcriptase Minus Rnaseh	Loc499554	0.69	0.61
ILMN_1363928	Polypyrimidine Tract Binding Protein 2	Ptbp2	0.66	0.65
ILMN_1364779	Zinc Finger Ccch-Type Containing 7A	Zc3H7A	0.81	0.68
ILMN_1366649	Similar To Lrrgt00057	Rgd1562999	0.66	0.58
ILMN_1369444	Similar To Orf4	Loc361942	0.70	0.60
ILMN_1370492	Tetraspanin 2	Tspan2	0.82	0.74
ILMN_1371063	Similar To Orf4	Loc498048	0.69	0.58
ILMN_1371120	Similar To Lrrg00135	Loc501637	0.48	0.38
ILMN_1376515	Origin Recognition Complex, Subunit 2	Orc2L	0.79	0.79
ILMN_1650840	Cyclin L2	Ccnl2	0.73	0.66

3.3 Discussion

For translation of experimental findings to human biomarker studies, it is essential to utilize tissues that are clinically relevant and readily available. Biomarkers are often examined in blood or urine, but these bodily fluids are not particularly relevant sources of expressed genes for reproductive development. We chose foreskin for two reasons: it expresses AR and therefore may be responsive to altered androgen signaling; and it can be obtained postnatally from humans in routine circumcisions. Another possible surrogate tissue readily available from humans is the placenta. In a human study, an association between expression of steroidogenesis pathway genes and environmental phthalate exposure has been reported, but this study only examined expression of four such genes and an association was only seen for one of four phthalate metabolites (Adibi, et al., 2009). We began our studies with placental tissues, as these are readily available at birth but only found 2 genes (RGD1563748 and Prl3a1) that showed significant changes in expression changes by microarray analysis of GD20 rat placenta following *in utero* DBP500 exposure. Neither of these genes are obviously related to testosterone production and consequently we concluded that this tissue is not likely to be a good source of biomarkers of DBP exposure.

For DBP exposure in the rat, both GD20 and PND5 were examined because these time points would capture responses observed when phthalate metabolites were present in the system (GD20) and several days after metabolites were cleared from the system (PND5). The half-life of the phthalate monoester metabolite in the rat fetus is two to three hours (Fennell et al., 2004). Thus, our experimental design allows a

measurement of potential immediate phthalate effects at GD20 as well as sustained changes in biology at PND5, well after phthalate metabolites are excreted. Additionally, rat PND5 roughly corresponds with an age at which circumcision is performed in the human male. Foreskin tissue collection in humans is only feasible after birth, so expression changes observed at this time point may be examined as potential biomarkers in human studies.

It is important to identify phenotypic anchors when examining and rogen signaling disruptors to indicate successful exposure and adequate disruption has taken place. Exposure to phthalates *in utero* reduces fetal testis testosterone production and induces the appearance of seminiferous cord MNGs. The significantly higher incidence of MNGs observed in animals exposed *in utero* to DBP100 or DBP500 recapitulates previous observations (Scott, et al., 2007). Compared to females, AGD is longer in males due to androgen signaling *in utero*. As such, we measured the AGD of both male and female pups following DBP treatment at GD20 and PND5 and of flutamide treated animals at PND5. As expected, significant decreases in male AGD were observed following both DBP500 and flutamide exposures (Table 2). Testicular testosterone levels measured at GD20 were only slightly decreased following in utero DBP100 exposure. After DBP500 exposure, testosterone levels were decreased almost 85% compared to controls. Having established that testosterone production was diminished to levels that cause reproductive malformations, experiments were conducted to identify potential gene expression markers of androgen signaling disruption in the foreskin.

To determine changes in gene expression that take place immediately after DBP exposure, prenatal foreskin was examined. Expression microarray analysis was

utilized to investigate expression changes throughout the transcriptome. Data were examined statistically by both LIMMA and SAM analyses to establish lists of genes whose expression levels were significantly altered by exposure. Both of these methods of microarray analysis are suitable for the small sample sizes used in this study (Breitling and Herzyk, 2005). These data indicate that DBP100 exposure was sufficient to induce prenatal foreskin gene expression changes, though more changes were detected following DBP500 exposure.

Changes in gene expression were examined in postnatal samples to determine if prenatal gene expression changes persisted after parturition. Postnatal analysis of rat foreskin gene expression following in utero DBP exposure was performed at PND5. Analysis of the DBP500 exposure group yielded numerous genes by both LIMMA and SAM analyses. LIMMA analysis did not identify any gene expression changes after DBP100 treatment, and only 35 gene changes were identified by SAM. Of note, 23 of these were also identified in the DBP500 treatment group by SAM analysis, and all 23 genes were downregulated in DBP exposure groups as compared to controls (Appendix G). Furthermore, LIMMA analysis showed that 19 of these genes were reduced more by the higher concentration of DBP, implying a dosedependent effect (Appendix H). These results show that there were persistent significant gene expression changes after birth induced by DBP exposure in utero. Moreover, three genes identified in the prenatal study persisted to postnatal analysis at the DBP500 exposure level using LIMMA: *Marcks*, *Pum1*, and *Slc7a1*, as identified by microarray analysis. Comparing DBP500 SAM analyses from GD20 to PND5, 20 genes were conserved (Appendix I). The identification of postnatal foreskin gene expression changes in the rat could eventually aid in development of translational

biomarkers in human foreskin collected after birth. Gene expression changes detectable both prenatally and postnatally would be ideal candidates. Not only do they represent immediate effects of DBP exposure at GD20, but they persist at PND5, allowing for potential detection in human tissues.

Although phthalates produce a variety of molecular changes in the rat reproductive system, phthalate-induced reproductive malformations are caused primarily by a reduction in fetal testis hormone production (Johnson et al., 2012). Evidence from phthalate-exposed mice shows that changes can occur in fetal testis histopathology (MNG induction) and gene expression without concurrent alterations in testosterone production (Gaido et al., 2007). Thus, not all phthalate biological effects are downstream of altered androgen signaling. To determine if DBP-induced gene expression changes in PND5 foreskin might be linked to reduced androgen signaling or another mechanism of phthalate action, we compared the DBP results with those obtained at PND5 after in utero exposure to flutamide, a specific inhibitor of AR signaling. Like DBP, flutamide has a short halflife in the rat (Xu and Li, 1998). Compared to the DBP study, a 5 mg/kg flutamide exposure from GD16 to GD20 induced far fewer gene expression changes in PND5 foreskin. Only one significant gene was identified by LIMMA, *Snrpf*, while SAM analysis resulted in 47 significant genes. None of the genes from the flutamide exposure study identified by either LIMMA or SAM were present in DBP trial gene lists. This suggests that the differentially expressed genes are likely specific for each compound and that the changes seen in the DBP study are not a direct consequence of endocrine disruption. Both flutamide and DBP act on the androgen signaling pathway, with flutamide competitively inhibiting the AR and DBP limiting testosterone production. Had the

differentially expressed genes been the direct result of disrupted androgen signaling, we would expect the same genes to be altered in both flutamide and DBP treated animals. Instead, gene expression changes were dependent on treatment group, indicating that those detected were not the result of disrupted androgen signaling. Thus, the identified gene expression changes may be valuable for examining phthalate exposure but not phthalate-induced endocrine disruption.

Our data indicate that genes such as *Marcks, Pum1, Penk*, and *Nupr1* may be useful in identifying prenatal exposures to DBP. However in our studies, significant changes were only seen in rats dosed with levels of DBP that are not likely to occur in human populations. Whether lower doses over prolonged periods of time has the same effect on gene expression in humans is not known and is not easily determined in rodent studies. Furthermore, it would be of interest to determine whether other phthalates, including nontoxic variants, result in similar gene expression changes. This study has shown that the foreskin may be a useful tissue to identify prenatal exposure to DBP using gene expression biomarkers.

Chapter 4

IDENTIFICATION OF THE EFFECTS OF IUGR ON MALE REPRODUCTIVE DEVELOPMENT

4.1 Introduction

IUGR has been associated with a higher prevalence of male reproductive malformations including hypospadias and cryptorchidism in human epidemiological studies but there are few studies that directly examine the effects of IUGR on the reproductive system. The goal of this study is to identify the underlying cause of these associations utilizing an animal model. Wistar rats were used due to their increased sensitivity to the effects of testosterone disruption (Berg, 1965; Hannas, et al., 2011). The baseline testosterone level of Wistar rats is higher than in Sprague Dawley and other strains of rats, although after steroidogenic disruption by DBP exposure testosterone levels decrease to the same minimum level in all treated strains of rats. Thus the overall decrease in testosterone production by the Wistar rats is a greater percentage of baseline testosterone levels, making this strain a more sensitive model.

To determine both the immediate effects of IUGR on steroidogenesis and subsequent developmental consequences, two separate studies were performed. First, a prenatal study examined steroidogenic gene expression in testis at GD17. This timepoint occurs at the peak of prenatal testosterone production, providing information of the effects of IUGR when the fetus both requires and produces the most testosterone and when effects are likely to be most apparent. A post-natal study at PND1, 14, and 28 was performed to examine reproductive malformations that may be

associated with insufficient *in utero* testosterone signaling due to IUGR. PND1 measurements were taken the day of birth and provided the most accurate information as to whether our IUGR protocol had a direct effect on fetal growth. The PND14 timepoint takes place after initial postnatal maturation and provides a more accurate measurement of AGD, better visualization of thoracic nipple retention, and evidence of hypospadias. In normal rat development, testis descent occurs just before PND28, allowing us to determine the effect of IUGR on this developmental milestone.

4.2 Results

4.2.1 Prenatal IUGR Model

Since IUGR has been linked to malformations typically associated with insufficient androgen signaling, we first aimed to identify its effects on prenatal steroidogenesis. After maternal food restriction from GD3-GD17, fetuses were removed and weighed prior to tissue collection. Fetal rat testes were collected and flash frozen for gene expression analysis or cultured for testosterone quantification.

Fetuses from dams restricted to diets that were 50 and 70% lower than the amount of food consumed by control dams on an *ad libitum* diet (FR50 and FR70) weighed significantly less than controls (Figure 10). Some dams in the FR70 group lost their entire litters and are not included in these numbers. The pups in the FR70 group appeared to be less healthy than those in the FR50 group based on examination of body condition. qRT-PCR of selected genes of the Leydig cell steroidogenic pathway showed that expression levels of *Scarb1*, *Cyp11a1*, and *Cyp17a1* were significantly reduced by both FR50 and FR70 and that *Star* was significantly reduced

at the FR70 level (Figure 11). Testosterone levels in tissue culture media from GD17 testes were significantly lower in both FR50 and FR70 samples than *ad libitum* control samples (Figure 12).

4.2.2 Postnatal IUGR Model

Maternal food restriction was maintained from GD3-18 at the FR50 level to examine pups for postnatal reproductive malformations including reduced male AGD, hypospadias, and cryptorchidism. PND1 measurements indicated that there was a significant decrease in pup bodyweight in the FR50 group (Figure 13). There was no difference in body weight by the PND14 timepoint, as expected (Shahkhalili, et al., 2009) (data not shown). A small decrease in AGD at PND1; 3.02±0.19 mm (n=11) in FR50, as compared to *ad libitum* control animals, 3.17±0.23 mm (n=9) was not significant. Moreover, no reproductive abnormalities, including hypospadias and cryptorchidism, were detected in any pups at any time point (data not shown).



Figure 10 – Fetal pup weights following maternal food restriction. GD17 fetal weights were found to be significantly smaller following maternal food restriction of 50 and 70% from GD3-17 as compared to *ad libitum* controls. * significantly less than controls, p<0.05.



Figure 11 – Fetal testis steroidogenic gene expression following maternal food restriction. Testis steroidogenic gene expression was examined at GD17. *Cyp11a1*, *Cyp17a1*, and *Scarb1* expression was significantly reduced in both FR50 and FR70 groups as compared to *ad libitum* control. *Star* expression reached significance at the FR70 level.



Figure 12 – Fetal testis testosterone production following maternal food restriction. Fetal testis testosterone levels were significantly reduced at both the FR50 and FR70 levels as compared to *ad libitum* controls.



Figure 13 – Postnatal day 1 pup weight following IUGR. Following 50% maternal food restriction from GD3-18, PND1 pup weights were significantly reduced as compared to *ad libitum* controls.

4.3 Discussion

4.3.1 IUGR Causes Disruption of Fetal Testis Steroidogenesis

Initial analyses examined the effects of IUGR on fetal androgen signaling and subsequent male reproductive development. Our food restriction model was first used to determine the steroidogenic disruption stemming from IUGR at the point when developing males require the most testosterone: i.e. GD17. Initial analysis indicated that GD17 pups exposed to maternal food restriction had significantly smaller weights than control fetuses (Figure 10). This confirmed that our food restriction model successfully induced IUGR at both the 50 and 70% restriction levels, justifying subsequent analyses. GD17 expression analysis was performed by qRT-PCR on selected genes of the testicular steroidogenic pathway; *Cyp11a1*, *Cyp17a1*, *Scarb1*, and *Star*. Expression of all four genes was reduced at both the FR50 and FR70 levels, although the reduced level of *Star* at the FR50 level was not significant. Furthermore, GD17 testosterone production was significantly reduced in both FR50 and FR70 groups as compared to *ad libitum* controls. These data show that restricting maternal nutrition can reduce fetal androgen signaling by means of disrupting the expression of steroidogenic genes in the testis.

Although the FR70 pups weighed less than pups in the FR50 group, there was no significant further decrease in expression of the steroidogenic genes or testosterone production in the FR70 pups. This, in combination with litter loss and poorer body condition scores for pups in the FR70 group led us to restrict subsequent experiments to the FR50 treatment group.

4.3.2 IUGR Does Not Lead to Reproductive Malformations Postnatally

For post-natal analysis of the effects of IUGR, food restriction was continued through GD18, and postnatal endpoint measures included AGD, thoracic nipple retention, hypospadias, and cryptorchidism. Continuing maternal food restriction for an additional day maintained food restriction through the entire masculinization programing window while still allowing sufficient time for recovery of nutrition of the dam before parturition to enable it to give birth. Following 50% maternal food restriction, we observed no evidence of androgen-dependent reproductive malformations at any timepoint. Other studies have shown that a 50% reduction of *in utero* testosterone production can induce male reproductive malformations (Mylchreest, et al., 2000; Lehmann, et al., 2004; Blystone, et al., 2007). In our study testosterone production was reduced by less than 40% in FR50 and FR70 fetuses as compared to the *ad libitum* control group and consequently appears not to be sufficient to cause reproductive malformations (Figure 12).

Epidemiological studies have shown a higher incidence of androgen-dependent male reproductive abnormalities in IUGR babies (Yinon, et al., 2009; Fujimoto, et al., 2008). Our data show that in carefully controlled conditions with no known exposure to additional endocrine disrupting compounds, IUGR does decrease steroidogenesis but that it is not sufficient to induce malformations in rats. Our data indicate that IUGR alone may not be sufficient to cause an increased incidence of reproductive malformations in newborns. We have shown that DBP alone can reduce steroidogenesis and cause reproductive malformations and consequently we

hypothesize that environmental factors, such as DBP, may contribute to the increasesd reproductive abnormalities in IUGR babies.

Chapter 5

EVALUATING THE POTENTIAL COOPERATIVE EFFECTS OF IUGR AND DBP ON FETAL STEROIDOGENESIS

5.1 Introduction

We and others have shown that prenatal exposure of pregnant rats to DBP during the male reproductive programing window leads to decreased steroidogenic gene expression and reduced testis testosterone production (Thompson, et al., 2005; Jiang, et al., 2007). Moreover, we have shown that high doses of DBP induce reproductive malformations in rats. Although there are concerns about potential toxicity of phthalates in humans, it is not clear that the low level of environmental exposure to these compounds would be sufficient to directly affect human development. We hypothesize that combinations of environmental effects may be required to cause defects in human development. We propose a rat model combining treatment with DBP with IUGR to determine whether these two environmental factors can work cooperatively to enhance inhibition of fetal steroidogenesis and cause reproductive malformations. We already showed that treatment of pregnant rats with 500 mg/kg DBP reduced fetal testosterone levels by over 80%, so in an attempt to be able to measure cooperative effects of DBP and IUGR on testorsterone production, we chose a lower level of DBP of 150 mg/kg for the prenatal analysis. For the postnatal analysis we chose the higher dose of 500 mg/kg to ensure that we would see reproductive malformations. For this study, four treatment groups were used. Animals in a control group were given food *ad libitum* and gavaged with corn oil

vehicle (ALCO). There were two individual treatment groups: one was given 50% restricted food and gavaged with corn oil vehicle (FR5O), and the other was given food *ad libitum* and gavaged with DBP in corn oil (150 mg/kg for prenatal analysis, or 500 mg/kg for postnatal analysis, ALDBP). Finally, the combined treatment group was food restricted 50% and gavaged with DBP in corn oil (150 or 500 mg/kg, FRDBP).

5.2 Results

5.2.1 Prenatal analysis of *in utero* DBP Exposure (150 mg/kg) with IUGR

On GD17, dams were euthanized and fetuses were removed for measurement and tissue collection. Testes were collected for both gene expression and testosterone RIA analyses.

Fetuses of FR50 dams had significantly reduced body weights as compared to *ad libitum* controls (Figure 14), regardless of whether they were administered DBP or corn oil vehicle. DBP treatment did not result in any further reduction of body weight.

Two-way ANOVA indicated that *Cyp11a1*, *Cyp17a1*, and *Scarb1* gene expression levels determined by qRT-PCR were significantly reduced by either diet restriction or DBP treatment. Together, effects appeared to be synergistic and twoway ANOVA showed a significant interaction between the two effectors for *Scarb1*. Followup t-tests were performed to further investigate this potential interaction. In comparing *ad libitum* with corn oil against *ad libitum* DBP-exposed, the DBP resulted in a significant decrease. Similarly, this was observed in food restricted with corn oil compared to food restricted with DBP as well as *ad libitum* with corn oil compared to food restricted with corn oil. Expression of the *Star* gene expression was also decreased by reduced diet or by DBP but only the latter was statistically significant (Figure 15).

Both DBP and reduced diet caused a statistically significant reduction on fetal testosterone production and although the combined treatment appeared to be synergistic, a direct interaction was not proven by two-way ANOVA (Figure 16).

5.2.2 Postnatal Analysis of *in utero* DBP Exposure with IUGR

The combined exposure study was repeated using a higher maternal dose of DBP, at 500 mg/kg bw/day, in conjunction with 50% food restriction through GD18. Postnatal endpoints were examined to determine if the combined treatment was sufficient to disrupt fetal testosterone production to the point of reproductive malformation. As found in the pre-natal study, pre-natal diet restriction in the presence or absence of DBP caused a significant reduction in pup weight but DBP alone had no effect on weight (Figure 17). At PND14 control and treated pups had similar masses, indicating that the treated animals recover from *in utero* weight loss, as seen in other studies (Shahkhalili, et al., 2009) (data not shown).

Reduction of AGD is a measure of androgen signaling disruption. On PND1, male AGD was found to be significantly reduced by DBP500 treatment alone but not by IUGR (Figure 18). Female AGD was not reduced significantly by any treatment (data not shown). At PND14, AGD remained significantly reduced in male pups that had been treated with DBP500 *in utero*. IUGR alone did not significantly reduce male AGD at PND14, but two-way ANOVA indicated that IUGR interacted negatively with DBP500 to diminish its effect on AGD (Figure 19). In *ad libitum* pups, DBP had a significant effect as detected by t-test, but there was no effect observed in food restricted animals. Additionally, there was no significant effect of food restriction detected by t-test in either corn oil or DBP groups. The DBP500 negative interaction with IUGR was maintained at PND28 in the male pups (Figure 20). Follow-up t-tests revealed a significant effect of DBP-treatment on *ad libitum* pup AGD as compared to those exposed to corn oil, however no statistical effect of IUGR was shown.

At PND28, males were checked for cryptorchidism. Undescended testes were found in both the ALDBP (26 pups) and FRDBP (7 pups) groups. Ten of the 13 litters in the ALDBP group had cryptorchidism, while five of 13 FRDBP litters exhibited this malformation. There was no significant difference detected when comparing the number of litters with undescended testes by Fisher's exact test, however comparing the number of pups with these malformations reached significance. The lower incidence of cryptorchidism in the FRDBP pups compared to the ALDBP pups is consistent with a negative cooperative effect of IUGR on DBP, as seen in AGD data.

Testis weights were compared within each treatment group to examine the effect of maldescent. Undescended testes from the FRDBP pups were significantly smaller than those that descended, but there was no statistically significant difference between the descended and undescended testes in ALDBP samples (Figure 21).



Figure 14 – Fetal pup weight following combined IUGR and *in utero* **DBP exposure.** After *in utero* DBP150 exposure and maternal food restriction from GD3-17, food restriction was shown to have a significant effect on fetal pup weight. This was evident regardless of DBP exposure.



Figure 15 – Fetal testis steroidogenic gene expression following maternal food restriction and *in utero* **DBP150 exposure.** Fetal testes were examined for steroidogenic gene expression after 50% maternal food restriction and DBP150 exposure. Analyses of *Cyp11a1*, *Cyp17a1*, and *Scarb1* expression levels indicated that both food restriction and DBP exposure had statistically significant effects on gene expression. Additionally, analysis of *Scarb1* expression indicated a significant interaction between these treatments. *Star* analysis suggested that only DBP exposure had a significant effect.



Figure 16 – Fetal testis testosterone production following maternal growth restriction and *in utero* **DBP exposure.** GD17 testes were examined for testosterone production after 50% maternal food restriction from GD3-17 and DBP150 exposure from GD15-17. Two-way ANOVA revealed that both food restriction and DBP exposure had significant effects on fetal testosterone production.



Figure 17 – PND1 pup weight following maternal food restriction and *in utero* **DBP exposure.** After maternal food restriction from GD3-18 and *in utero* DBP500 exposure from GD5-18, two-way ANOVA identified that maternal food restriction had a significant effect on pup weight. There was no significant effect by DBP exposure, though the interaction term neared significance.



Figure 18 – PND1 AGD after 50% maternal food restriction and DBP500. After IUGR and DBP500 exposure, two-way ANOVA indicated that DBP exposure had a significant effect on AGD at PND1, though food restriction did not. There was a significant interaction between DBP exposure and IUGR.



Figure 19 – PND14 AGD after 50% maternal food restriction and DBP500. After IUGR and DBP500 exposure, two-way ANOVA indicated that DBP exposure had a significant effect on AGD at PND14, though food restriction did not. There was a significant interaction between DBP exposure and IUGR.



Figure 20 – PND28 AGD after 50% maternal food restriction and DBP500. After IUGR and DBP500 exposure, two-way ANOVA indicated that DBP exposure had a significant effect on AGD at PND28, though food restriction did not. There was a significant interaction between DBP exposure and IUGR.


Figure 21 – Weight of descended and undescended testes at PND28. In animals of the FRDBP group, testis weight was significantly smaller in undescended testes than descended. There was no statistically significant difference in testes of the ALDBP group.

5.3 Discussion

5.3.1 Combined IUGR and DBP Exposure Cooperatively Disrupts Fetal Testis Steroidogenesis in the Rat

Much of the current research on human IUGR is associated with the Barker Hypothesis, which explores the correlation between intrauterine environment and postnatal disease (Barker, 1990). These studies predominantly focus on cardiovascular disease and adult degenerative disease (Vuguin, 2007; Mandruzzato, et al., 2008), and, except for epidemiological correlations, none have explored the consequences of the intrauterine environment on reproductive masculinization. Babies born SGA (but not necessarily due to IUGR) have been linked to a higher incidence of male reproductive malformations typically associated with insufficient androgen signaling (Mandruzzato, et al., 2008; Hanson and Gluckman, 2005). My work focuses on exploring the mechanism behind this signaling by utilizing a rat model of IUGR.

Wistar rats were selected for our studies based on previous work showing that this strain has a higher prevalence of androgen-dependent male reproductive abnormalities (Berg, 1965; Hannas, et al., 2011). Maternal food restriction began on GD3 to provide enough time to deplete maternal nutrient stores to cause IUGR. Beginning food restriction earlier in gestation has been shown to cause pup or litter loss (Berg, 1965). Maternal food restriction was continued in prenatal studies through GD17 to establish effects on steroidogenesis at the point when fetal testes produce the most testosterone (Welsh, 2008; Thompson, et al., 2005), or GD18 for postnatal studies to cover the entire masculinization programing window.

Epidemiological studies show a higher incidence of androgen-dependent male reproductive abnormalities in IUGR babies (Yinon, et al., 2009; Fujimoto, et al., 2008), and we proposed that environmental factors may contribute to the decrease in *in utero* testosterone production and work cooperatively with IUGR. To test this hypothesis, we used the known endocrine disrupting compound DBP in conjunction with IUGR. We and others have shown that prenatal exposure to DBP during the male reproductive programing window leads to decreased steroidogenic gene expression as well as reduced testis testosterone production (Thompson, et al., 2005; Jiang, et al., 2007). Moreover, DBP, at high enough doses, induces reproductive malformations in rats.

We first examined the combined effects of DBP and maternal food restriction at GD17. We confirmed our earlier observation that 50% food reduction decreased pup weight at GD17. *In utero* exposure to DBP alone did not affect pup growth and when combined with food restriction did not reduce pup weight more than food restriction alone.

Expression of genes involved in steroidogenesis (i.e. *Scarb1*, *Cyp11a1*, *Cyp17a1* and *Star*) was reduced by either food restriction or DBP treatment (150 mg/kg). When food restriction and DBP were combined, expression of these genes was reduced further. Two-way ANOVA only showed the interaction to be significant for *Scarb1* expression as the synergistic effects were only small and sample size not sufficient to show any statistical significant differences for the cominbed effects of IUGR and DBP for the other genes. Followup t-tests were used to investigate the significant interaction term identified in *Scarb1* analysis. It was demonstrated that individually, both DBP and food restriction led to significant decreases in gene expression at GD17. Since both expression changes are reductions, it can be concluded that the significant interaction is responsible for the further reduction

observed by ANOVA. While the rate limiting step in testis steroidogenesis is the action of *Star*, under the influence of DBP and IUGR, this may be shifted to the role of *Scarb1* given its dramatically reduced expression. This, in turn, may yield postnatal reproductive malformations associated with poor androgen signaling.

Consistent with these reductions in gene expression, testosterone production was reduced by either food restriction or DBP treatment. In fetuses from dams with both food restriction and DBP treatment, average levels of testosterone were lower than either treatment alone, but the difference was small and did not reach statistical significance. Despite this limitation, the reduced levels of testosterone are conssistent with the reduced levels of steroidogenic genes that are needed to produce testosterone, supporting a cooperative effect of IUGR and DBP exposure on testosterone exposure.

Previous studies have shown that a reduction of 50% testosterone production during the male reproductive programing window is required to induce reproductive malformation in rats (Mylchreest, et al., 2000; Lehmann, et al., 2004; Blystone, et al., 2007). IUGR and DBP150 alone did not reduce testosterone levels by more than 40% and we have already shown that IUGR and low levels of DBP do not induce reproductive malformations. However the combination of IUGR and DBP did reduce testosterone levels by more than 50%, indicating that synergistic effects of IUGR and environmental factors could cause such malformations. Postnatal analysis is required to determine the significance of these combined effects.

5.3.2 Combined IUGR and DBP Exposure Causes Reproductive Malformation in the Rat

To ensure that reproductive malformations would be produced, we increased DBP concentrations to 500 mg/kg in our postnatal study of the effect of DBP in

combination with 50% maternal food restriction. A DBP500 dose is known to induce malformation without the aid of IUGR (Thompson, 2005). Even higher levels of DBP are required for maximal inhibition of testosterone production (Jiang, 2007) and consequently IUGR could enhance the reduction of testosterone caused by DBP500 treatment and consequently enhance reproductive malformations.

The effect of maternal food restriction on growth of pups at PND1 was again confirmed and DBP was shown to have no effect on pup weight. As seen in the prenatal analysis, DBP did not cause any additional reduction in pup weight when combined with IUGR.

AGD was significantly reduced by DBP500 at PND1, 14, and 28. A small reduction in AGD was also noted in the IUGR rats, but the small difference was not significant. Surprisingly, there were no synergistic effects of IUGR and DBP500 and at both PND14 and PND28, there was a statistically significant negative interaction between DBP500 and IUGR. This contrasts with the weak but consistent synergistic effects of DBP150 and IUGR on reduced expression of genes involve in testosterone biosynthesis and reduced testosterone production at GD17. To investigate the significant interactions, follow-up t-tests were performed on both PND14 and PND28 AGD data. In both cases, it was found that DBP had a significant effect on its own, though IUGR did not. This suggests that the effect of DBP is being influenced by the addition of IUGR, however its effect is insignificant. Had both IUGR and DBP reached significance by t-test analysis, we could then examine the direction of change to predict whether these conditions play a cooperative role in steroidogenic disruption, or support a protective role wherein one treatment reduces the effects of the other.

At PND28, we examined pups for cryptorchidism. There were significantly more pups with this malformation in the ALDBP group than the FRDBP treatment group, further supporting a protective effect of IUGR on the developmental defects caused by DBP. The number of litters with reproductive malformation, however, did not reach significance. Together, these findings suggest that while there may be some underlying effects of IUGR on DBP exposure within individual pups, there is no significant effect between litters. Overall, the addition of IUGR did not alter the incidence rate of cryptorchidism in DBP-exposed pups. Since the role of IUGR has not been studied in terms of reproductive development, there are many possibilities as to why we observed this effect. One possibility is that IUGR may shift the reproductive masculinization window to prioritize nutrient allocation during development. This would cause DBP exposure to miss the middle of the programming window when the greatest testosterone production occurs. If this happens, it would appear as though the addition of IUGR has no effect on DBP exposure.

Moreover, the average weight of the undescended testes in the affected pups treated with DBP alone did not differ from that of the descended testes. Although there were fewer undescended testes in the pups with IUGR and DBP treatment, they weighed significantly less than the descended testes. As IUGR alone did not result in any undescended testes, this indicates that IUGR may alter the maturation of the testis in conjunction with DBP. The cause of this alteration is not clear, but the combination of a smaller testis with a reduced pup weight poses some interesting possibilities. A smaller pup may require the reduced testosterone production that we detected. This is shown as both significantly reduced testosterone production and smaller pup weight,

however a more useful metric may be the relative levels of circulating testosterone within each pup. Future analysis of fetal trunk blood is important to determine whether these effects are synergistic.

When examining the cooperative effects of IUGR and DBP on male reproductive development, it can be concluded from these data that despite the synergistic effects on both steroidogenic gene expression and testis testosterone production, this does not carry over to postnatal reproductive malformations. Despite the significantly lower incidence of reproductive malformations in the combined exposure group when compared on a pup level, it is important to compare using the litter as the statistical unit to counter any influential effects of uterine position or maternal sensitivities.

CONCLUSIONS AND FUTURE DIRECTIONS

Reproductive masculinization is an intricate and sensitive developmental process. Despite several differences in human and lower order mammalian masculinization, the core signaling process is essentially the same. This process is largely dependent on androgen signaling wherein testis testosterone production drives masculinization events including testis descent, urethral closure, as well as the lengthening of the male AGD. Disruption of this signaling during a critical window of mammalian development can result in lasting reproductive abnormalities. This steroidogenic interference can be brought on by genetic predisposition, exposure to anti-androgenic compounds, or other environmental conditions. This investigation identified the risk factors associated with a particular environmental anti-androgen, DBP, as well as a poor fetal growth condition in which the fetus receives insufficient nutrition and are born small for gestational age.

Initially, we examined the effects of DBP on gene expression in the rat foreskin, since evidence suggests that this tissue is androgen-responsive. Moreover, we used an additional anti-androgenic compound, flutamide, to determine whether observed expression changes were due to disruption of androgen signaling or specific to individual chemical exposure. Our findings identified several gene expression changes resulting from DBP exposure both prenatally and postnatally, with many genes conserved between timepoints. These genes, including *Marcks, Pum1, Penk*, and *Nupr1*, may be useful biomarkers for identifying *in utero* exposures to DBP in humans. This would allow a better understanding of human DBP exposure levels which could then be used to better assess risk.

At present, the human sensitivity to DBP is not well established. By combining a useful biomarker assessment of DBP exposure level with downstream reproductive endpoints, human sensitivity could be determined and subsequent risk prevention steps could be taken. One major factor to consider when examining translational biomarker studies is the effect of multiple births. A typical human birth consists of one developing fetus, which receives all of the nutrients, and is exposed to all of the toxins that cross the placental barrier. Rats, in contrast, have numerous pups per litter. Each fetus may receive a different dose of both nutrients and toxins, skewing the results. For this reason, it is important to validate these findings in human tissue.

Future studies should investigate these and other gene expression changes in human foreskin samples of patients with reproductive malformations associated with insufficient testosterone signaling including hypospadias and cryptorchidism. Human studies would demonstrate potential biomarkers of insufficient androgen signaling, whether brought on by environmental anti-androgen exposure or genetic predisposition. As such, this study should be coupled with dose response studies in the rat designed to study foreskin gene expression changes brought on by low-dose DBP exposure. While our work has demonstrated that the foreskin is susceptible to DBP-induced gene expression changes, the dose-levels used were much higher than that of estimated daily human exposures. Similarly, human daily exposures may be to multiple toxic phthalates, whereas the present study was performed in a carefully controlled environment to assess the effects of only DBP. Rat studies should examine the foreskin expression changes brought on by several toxic phthalates at low dose level exposures to more accurately mimic human exposures.

With potential biomarkers of DBP established, we were able to investigate the effects of IUGR on masculinization. Given the present limited knowledge of IUGR, the results of this study have revealed just how widespread its effects on fetal development are. Prenatally, IUGR significantly reduced both steroidogenic gene expression and testosterone production and hinted at a synergistic effect with the addition of DBP. Postnatally, however, it had little to no additional effect. While we observed reproductive malformations in both the food restriction DBP group and the *ad libitum* DBP group, there was no statistically significant difference between them. It seems that while IUGR may have a prenatal effect on steroidogenesis in the rat, these changes are not sufficient to induce the reproductive malformations observed in human epidemiological studies.

Again, the issue of multiple births may play a role in the effects of maternal food restriction on the rat. Human fetuses may be more susceptible to the effects of maternal food restriction. Humans have evolved to consume a certain amount of nutrients to properly support a fetus. Any deficit in nutrition affects that one fetus directly. Conversely, a rat can support upwards of 12 fetuses in a single litter. A reduction in nutrition may be divided among the fetuses, affecting each one less. Additionally, if a male is next to additional males in the uterine horn, they may indirectly share their produced testosterone, minimizing the steroidogenic effects of IUGR. This could begin to explain the higher incidence of male reproductive malformations seen in IUGR babies in human epidemiological studies compared to the lack of effect in our rat studies. Future work should investigate the effects of IUGR in single-birth animal studies to better mimic human embryonic conditions. This could

be accomplished using a different animal model, or by surgically reducing the number of pups in a rat litter to a single birth.

We next investigated the cooperation of IUGR with DBP exposure in a rat model. Prenatally, we observed a 70% reduction in testosterone production by combined IUGR and DBP treatment, with only a 30-40% reduction occurred from individual treatments. Postnatally, however, there was no significant effect of IUGR detected on AGD. There were significantly fewer reproductive malformations in the DBP group with the addition of maternal food restriction when comparing pups, however when using the litter as the statistical unit, this metric did not reach significance. This suggests that both food restricted, DBP-exposed rats and food restricted, corn oil-exposed rats had the same incidence rate of reproductive malformation. The pup-level analysis, however, indicates that food restriction may offer a protective effect from DBP exposure, as there were significantly fewer malformations in this group. This interesting finding warrants further investigation.

Given the significantly decreased testis testosterone production at GD17 in the combined exposure group compared to each individual group, and the significantly decreased body weight in food restricted pups, a future analysis should investigate circulating testosterone levels of pups. Exposure groups should include DBP, IUGR, and a combination of both. The relative levels of circulating testosterone may be the same in food restricted DBP groups as compared to other treatment groups, with the smaller body size induced by IUGR requiring a decreased testosterone production level, achieved by DBP exposure. If relative levels are different, however, this would point to a seemingly protective effect of IUGR on DBP exposure. Postnatal analysis of reproductive malformation should then be repeated using a greater sample size.

Analyzing data using the litter as the statistical unit is a more accurate representation of human exposures, however with the conflicting data between pup-level and litterlevel analyses, a larger sample size will achieve more accurate results.

Another possible explanation for the lack of reproductive malformation is a potential effect of IUGR on the timing of masculinization. The period of reproductive masculinization corresponds with a surge of fetal testis testosterone production. Growth restriction may alter this window, either delaying it or advancing it in the gestational period. The developing fetus may recognize that it is receiving insufficient nutrients and prioritize development differently to achieve proper growth. If this is the case, then our gestational timepoint may not demonstrate a reduction in testosterone production; rather it would show only the beginning or end of the masculinization window, rather than its peak. To investigate if this is occurring, future work requires a timecourse study to map out the masculinization programming window in IUGR rats. If this shift in masculinization is truly occurring, follow-up investigations could introduce DBP at an appropriate time to accurately assess potential interactions.

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Appendix A

IACUC APPROVAL

	ANIMAL CARE PROTOCOL
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	Erin McDowell
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Institutional Animal Care and Use Committee

MEMORANDUM

DATE:	July 23, 2009
TO:	Kamin Johnson, Ph.D.
FROM:	Paul T. Fawcett, Ph.D., Chair
SUBJECT:	"Mechanistic Biomarkers of Endocrine Disruption" NBR-2009-006

The Institutional Animal Care and Use Committee (IACUC) have reviewed the above referenced protocol for approval, and the following decision has been made:

Action: Approved

Date of Action: July 23, 2009

Approval Period: July 23, 2009 - July 22, 2010

Protocol Approval Number: NBR-2009-006

Approved Number of Animals: 40

Rat: Sprague Dawley

Please maintain this approval with your project records. A tally of the number of animals approved and the number ordered for the project will be maintained in the Life Science Center. If changes occur in your protocol or if you require more animals than approved, and amendment to your protocol will need to be submitted for consideration

If you have any questions regarding this memorandum, please contact Paul T. Fawcett, Ph.D. at x 6776 or email: pfawcett@nemours.org.



Institutional Animal Care and Use Committee

MEMORANDUM

DATE:	July 28, 2010
TO:	Kamin Johnson, Ph.D.
FROM:	Paul T. Fawcett, Ph.D.

SUBJECT: "Mechanistic Biomarkers of Endocrine Disruption" NBR-2009-006

The Institutional Animal Care and Use Committee (IACUC) have reviewed the above referenced protocol for approval, and the following decision has been made:

Action: Amendment approved (dated June 14, 2010)

Date of Action: July 22, 2010

Approval Period: July 28, 2010 - July 21, 2011

Protocol Approval Number: NBR-2009-006

Approved Number of Animals:

96 Rats: Sprague Dawley and 28 pregnant CD-1 mice.

Please submit your Biosafety Classification form electronically to the Alfred I. duPont Hospital for Children Institutional Biosafety Committee via the link:

http://www.nemours.org/research/biomedical/committee/ibc.html

Please note that the study cannot begin until the Office of Regulatory Compliance in Research Administration has received all approvals.

Please maintain this approval with your project records. A tally of the number of animals approved and the number ordered for the project will be maintained in the Life Science Center. If changes occur in your protocol or if you require more animals than approved, and amendment to your protocol will need to be submitted for consideration

If you have any questions regarding this memorandum, please contact Paul T. Fawcett, Ph.D. at x 6776 or email: pfawcett@nemours.org.



Institutional Animal Care and Use Committee

MEMORANDUM

DATE:	January 28, 2011					
TO:	Kamin Johnson, Ph.D.					
FROM:	Paul T. Fawcett, Ph.D.					
SUBJECT:	"Mechanism of Environmental Chemical Disruption" NBR-2009-001					
The Institutional Animal Care and Use Committee (IACUC) have reviewed the above referenced protocol for approval, and the following decision has been made:						

Action: Renewal approved

Date of Action: January 28, 2011

Approval Period: January 28, 2011 - January 27, 2012

Protocol Approval Number: NBR-2009-001

Approved Number of Animals: 67

Please submit your Biosafety Classification form electronically to the Alfred I. duPont Hospital for Children Institutional Biosafety Committee via the link:

http://www.nemours.org/research/committee/ibc.html

Please note that the study cannot begin until the Office of Regulatory Compliance in Research Administration has received all approvals.

Please maintain this approval with your project records. A tally of the number of animals approved and the number ordered for the project will be maintained in the Life Science Center. If changes occur in your protocol or if you require more animals than approved, and amendment to your protocol will need to be submitted for consideration

If you have any questions regarding this memorandum, please contact Paul T. Fawcett, Ph.D. at x 6776 or email: pfawcett@nemours.org.



Institutional Animal Care and Use Committee

MEMORANDUM

DATE:	April 27, 2012
TO:	Kamin Johnson, Ph.D.
FROM:	Paul T. Fawcett, Ph.D.

SUBJECT: "Male Perinatal Reproductive Malformations" NBR-2012-001

The Institutional Animal Care and Use Committee (IACUC) have reviewed the above referenced protocol for approval, and the following decision has been made:

Action: Amendment approved

Date of Action: April 27, 2012

Approval Period: April 27, 2012 - April 26, 2013

Protocol Approval Number: NBR-2012-001

Approved Number of Animals:

Wistar Rat Yearly No. 568 (including 500 pups); Project Total: 568 Mouse C57B1/6 Yearly No. 299 (including 200 pups); Project Total: 598

Please submit your Biosafety Classification form electronically to the Alfred I. duPont Hospital for Children Institutional Biosafety Committee via the link:

http://www.nemours.org/research/committee/ibc.html

Please note that the study cannot begin until the Office of Regulatory Compliance in Research Administration has received all approvals.

Please maintain this approval with your project records. A tally of the number of animals approved and the number ordered for the project will be maintained in the Life Science Center. If changes occur in your protocol or if you require more animals than approved, and amendment to your protocol will need to be submitted for consideration

If you have any questions regarding this memorandum, please contact Paul T. Fawcett, Ph.D. at x 6776 or email: pfawcett@nemours.org.

Nemours.

Institutional Animal Care and Use Committee 1600 Rockland Road Wilmington, DE 19803 p (302) 651-6776 f (302)-651-6881 IACUC@nemours.org

MEMORANDUM

DATE:	March 6, 2013
TO:	Kamin Johnson, PhD
FROM:	Paul T. Fawcett, Ph.D., Chair
SUBJECT:	Male Perinatal Reproductive Malformations

The Institutional Animal Care and Use Committee (IACUC) have reviewed the above referenced protocol for approval, and the following decision has been made:

Action: Renewal Approved

Date of Action: February 28, 2013

Approval Period: February 28, 2013 - February 28, 2014

Protocol Approval Number: NBR-2012-003

Approved Number of Animals:

Wistar Rate Yearly Number: 568 (including 500 pups); Project Total: 568 Mouse C57B1/6 Yearly Number: 299 (including 200 pups); Project Total 598

Please note: The approved protocol number for your project is "NBR-2012-003". Any paperwork previously submitted with a different number will be manually changed.

Please maintain this approval with your project records. A tally of the number of animals approved and the number ordered for the project will be maintained in the Life Science Center. If changes occur in your protocol or if you require more animals than approved, an amendment to your protocol will need to be submitted for consideration.

If you have questions regarding this memorandum, please contact Paul T. Fawcett, Ph.D. at x 6776 or email: pfawcett@nemours.org.

Nemours.

Institutional Animal Care and Use Committee 1600 Rockland Road Wilmington, DE 19803 p (302) 651-6826 f (302)-651-6881 IACUC@nemours.org

MEMORANDUM

DATE:	May 2, 2013
TO:	Kamin Johnson, PhD
FROM:	Paul T. Fawcett, Ph.D., Chair
SUBJECT:	NBR-2012-003 – Male perinatal reproductive malformations

The Institutional Animal Care and Use Committee (IACUC) have reviewed the submitted amendment on the above referenced project and the following decision has been made:

Action:

Amendment approved.

The IACUC requests that you administratively provide a sample of references regarding the numerous publications discussed in the amendment where 500 mg/kg/day of dibutyl phthalate is used without health problems to the animals.

If you have questions regarding this memorandum, please contact Paul T. Fawcett, Ph.D. at x 6776 or email: pfawcett@nemours.org.

Appendix B

SUPPLEMENTARY MICROARRAY DATA

					Gene	Fold Change	FDR- Corrected P
Study	Exposure	Method	Probe ID	Gene Name	Symbol	Control)	Value
GD20	DBP100	LIMMA	-	-	-	-	-
GD20	DBP100	SAM	II MN 1373587	Eukaryotic Translation	Etf1	0.85	<0.05
GD20	DDI 100	SAM	ILMN 1276571	Sideraflavin 1	Etri 1	0.33	<0.05
GD20	DBP100	SAM	ILMIN_13/03/1		SIXII	0.70	< 0.05
GD20	DBP100	SAM	ILMN_1359956	Fyn Binding Protein	Fyb	0.76	< 0.05
GD20	DBP500	LIMMA	ILMN_1650701	Sub-Family A (Abc1), Member 1	Abca1	1.41	0.0311
GD20	DBP500	LIMMA	ILMN_1355841	Abhydrolase Domain Containing 8	Abhd8	0.75	0.0196
GD20	DBP500	LIMMA	ILMN_1367932	Actin, Gamma 2, Smooth Muscle, Enteric	Actg2	0.73	0.0432
GD20	DBP500	LIMMA	ILMN 1352450	Adam Metallopeptidase With Thrombospondin Type 1 Motif. 2	Adamts2	0.72	0.0268
GD20	DBP500	LIMMA	ILMN 2039089	Alcohol Dehydrogenase 1	Adh1	0.79	0.0323
GD20	DBP500	LIMMA	 ILMN_1373231	Alcohol Dehydrogenase 6A (Class V)	Adh6A	1.50	0.0093
GD20	DBP500	LIMMA	ILMN_1361575	Adrenomedullin 2	Adm2	1.25	0.0450
GD20	DBP500	LIMMA	ILMN_1359219	Allograft Inflammatory Factor 1	Aif1	0.71	0.0220
GD20	DBP500	LIMMA	ILMN_1366699	Ankyrin Repeat Domain 10	Ankrd10	1.27	0.0427
GD20	DBP500	LIMMA	ILMN_1360946	Annexin A8	Anxa8	1.27	0.0273
GD20	DBP500	LIMMA	ILMN_1353636	Adaptor-Related Protein Complex 2, Alpha 2 Subunit	Ap2A2	0.74	0.0279
GD20	DBP500	LIMMA	ILMN_1351069	Apelin	Apln	0.65	0.0031
GD20	DBP500	LIMMA	ILMN_1368636	Asparagine Synthetase (Glutamine- Hydrolyzing)	Asns	2.02	0.0004

				Activating Transcription Factor 4			
				(Tax-Responsive			
GD20	DBP500	LIMMA	ILMN 1375100	B67)	Atf4	1.33	0.0287
				Activating			
GD20	DBP500	LIMMA	ILMN_1359736	Transcription Factor 5	Atf5	1.62	0.0311
GD20	DBP500	LIMMA	ILMN_1368656	Beta-2 Microglobulin	B2M	0.80	0.0224
				Brain Abundant, Membrane Attached			
GD20	DBP500	LIMMA	ILMN 1365368	Signal Protein 1	Basp1	0.58	0.0052
				Ben Domain	1		
GD20	DBP500	LIMMA	ILMN_1372980	Containing 5	Bend5	1.41	0.0031
GD20	DBP500	LIMMA	ILMN_1355289	Butyrophilin-Like 7	Btnl7	0.74	0.0424
				Complement			
				Subcomponent A			
GD20	DBP500	LIMMA	ILMN 1352382	Chain	C1Qa	0.74	0.0105
				Complement			
				Component 1, Q			
GD20	DBP500	LIMMA	ILMN 1352142	Subcomponent, B Chain	ClOb	0.76	0.0135
0020	DDI 500	Linnin	1000110002112	C1Q And Tumor		0.70	0.0155
				Necrosis Factor			
GD20	DBP500	LIMMA	ILMN_1363044	Related Protein 2	C1Qtnf2	0.53	0.0123
				Calcium/Calmodulin-			
GD20	DBP500	LIMMA	ILMN 1367246	Kinase Ii Beta	Camk2B	0.82	0.0324
GD20	DBP500	LIMMA	ILMN 1376248	Calpain 6	Capn6	0.73	0.0431
0020	DBICOU	211/11/11		Cysteinyl-Trna	Cupito	0.70	010101
GD20	DBP500	LIMMA	ILMN_1372842	Synthetase	Cars	1.45	0.0039
GD20	DBP500	LIMMA	ILMN_1365636	Cholecystokinin	Cck	0.40	0.0002
GD 3 0	DDD5 00			Chemokine (C-C	a 1	0.00	0.0011
GD20	DBP500	LIMMA	ILMN_1356721	Motif) Receptor I	Cerl	0.80	0.0311
GD20	DBP500	LIMMA	ILMN 1371484	Cadherin (Epithelial)	Cdh1	1.27	0.0477
				Cyclin-Dependent			
				Kinase-Like 1 (Cdc2-			
GD20	DBP500	LIMMA	ILMN_1367106	Related Kinase)	Cdkl1	0.72	0.0454
GD20	DBP500	LIMMA	ILMN 2040450	Kinase Inhibitor 1C	Cdkn1C	0.75	0.0220
0020	221000	2		Chondroitin	2 4	0.70	0.0220
GD20	DBP500	LIMMA	ILMN_1362341	Polymerizing Factor 2	Chpf2	0.78	0.0340
GD20	DBP500	LIMMA	ILMN_1651094	Claudin 1	Cldn1	1.31	0.0379
GD20	DBP500	LIMMA	ILMN_1376751	Claudin 4	Cldn4	1.63	0.0048
				C-Type Lectin			
GD20	DBP500	ΙΙΜΜΔ	II MN 1373158	Domain Family 2, Member I	Clec2I	0.67	0.0030
0020	DD1 300	LIMINIA	15/5150			0.07	0.0057

GD20	DBP500	LIMMA	ILMN_1371901	Cdc-Like Kinase 4	Clk4	1.32	0.0311
GD20	DBP500	LIMMA	ILMN_1355310	Collagen, Type XII, Alpha 1	Col12A1	0.67	0.0039
GD20	DBP500	LIMMA	ILMN_1364468	Coronin, Actin Binding Protein 1A	Coro1A	0.76	0.0201
GD20	DBP500	LIMMA	ILMN_1364825	Carboxypeptidase A6	Cpa6	1.34	0.0156
GD20	DBP500	LIMMA	ILMN_1362981	Carboxypeptidase D	Cpd	0.82	0.0414
GD20	DBP500	LIMMA	ILMN_1357483	Camp Responsive Element Binding Protein 3-Like 1	Creb3L1	0.73	0.0288
GD20	DBP500	LIMMA	ILMN_1349375	Secretory Protein Lccl Domain Containing 2	Crispld2	0.66	0.0109
GD20	DBP500	LIMMA	ILMN 1359951	Cathepsin C	Ctsc	1.34	0.0169
GD20	DBP500	LIMMA	ILMN_1351603	Chemokine (C-X-C Motif) Ligand 12	Cxcl12	0.61	0.0082
GD20	DBP500	LIMMA	ILMN_1376635	Cytochrome P450, Family 1, Subfamily B, Polypeptide 1	Cyp1B1	0.68	0.0093
GD20	DBP500	LIMMA	ILMN_1367505	Desmin	Des	0.64	0.0031
GD20	DBP500	LIMMA	ILMN_1368597	Dehydrogenase/Reduc tase (Sdr Family) Member 7C	Dhrs7C	0.58	0.0037
GD20	DBP500	LIMMA	ILMN_1376321	Dickkopf 3 Homolog	Dkk3	1.45	0.0073
				Cyclin D Binding Myb-Like			
GD20	DBP500	LIMMA	ILMN_1375855	Transcription Factor 1	Dmtf1	1.33	0.0406
GD20	DBP500	LIMMA	ILMN_1373724	Dipeptidase 1 (Renal)	Dpep1	0.69	0.0082
GD20	DBP500	LIMMA	ILMN_1367874	Dual Oxidase 1	Duox1	1.29	0.0405
GD20	DBP500	LIMMA	ILMN_1369425	Phosphatase 22	Dusp22	1.25	0.0311
GD20	DBP500	LIMMA	ILMN_1650631	Lysophosphatidic Acid Receptor 1	Edg2	0.74	0.0215
GD20	DBP500	LIMMA	ILMN_1375038	Ephrin B1	Efnb1	0.77	0.0176
GD20	DBP500	LIMMA	ILMN_1372721	Eukaryotic Translation Initiation Factor 4B	Eif4B	1.43	0.0097
GD20	DBP500	LIMMA	ILMN 1353628	Elongation Of Very Long Chain Fatty Acids (Fen1/Elo2, Sur4/Elo3, Yeast)- Like 3	Elov13	1.48	0.0156
				Elovl Fatty Acid			
GD20	DBP500	LIMMA	ILMN_1353380	Elongase 4	Elovl4	1.46	0.0424
GD20	DBP500	LIMMA	ILMN_1348800	Interfacer 1	Emilin1	0.71	0.0190
GD20	DBP500	LIMMA	ILMN_1356443	Ectonucleoside Triphosphate Diphosphohydrolase 2	Entpd2	0.75	0.0414

				Endothelial Cell-			
GD20	DBP500	LIMMA	ILMN_1360134	Specific Molecule 1	Esm1	0.71	0.0020
				Fatty Acid Desaturase			
GD20	DBP500	LIMMA	ILMN_1355235	1	Fads1	0.71	0.0277
				Family With Sequence			
GD 3 0	DDD			Similarity 114,	Fam114A		0.0156
GD20	DBP500	LIMMA	ILMN_1370964	Member Al	1	0.75	0.0176
				Family With Sequence			
GD20	DBP500	I IMMA	II MN 1372451	Δ	Fam46A	0.72	0.0482
CD20	DDD500		ILIMIT_1372431			0.72	0.0404
GD20	DBP500	LIMMA	ILMN_1359541	Fibrillin I El:506 Dinding Drotain	Fbn1	0.74	0.0494
GD20	DBP500	I IMMA	II MN 1376629	5	Ekbn5	0.73	0.0278
0D20	DBI 500	LIMINIA	1LIVII_1570025	Fibronectin Leucine	Ткорз	0.75	0.0276
				Rich Transmembrane			
GD20	DBP500	LIMMA	ILMN 1350369	Protein 3	Flrt3	0.70	0.0232
			-	Flavin Containing			
GD20	DBP500	LIMMA	ILMN_1366651	Monooxygenase 1	Fmo1	0.67	0.0451
GD20	DBP500	LIMMA	ILMN 1370930	Forkhead Box L2	Foxl2	0.70	0.0297
GD20	DBP500	I IMMA	II MN 1353747	Follistatin	Fst	0.74	0.0135
0020	DBI 500		12011 1333747	Fucosyltransferase 1	1 50	0.74	0.0155
				(Galactoside 2-Alpha-			
				L-Fucosyltransferase,			
GD20	DBP500	LIMMA	ILMN_1349350	H Blood Group)	Fut1	1.55	0.0073
				Glutamate-Cysteine			
				Ligase, Catalytic	~ .		
GD20	DBP500	LIMMA	ILMN_1359516	Subunit	Gele	0.80	0.0444
CD20	DDD500		IL MNI 1274965	Growth Differentiation	Cdfl	0.71	0.0219
GD20	DBP300	LIMINA	ILMIN_13/4803	Growth Differentiation	Gall	0.71	0.0218
GD20	DBP500	LIMMA	ILMN 2039904	Factor 10	Gdf10	0.55	0.0020
0020	DBICOU	Linvitviti		Gamma-	Guillo	0.00	0.0020
GD20	DBP500	LIMMA	ILMN 1351216	Glutamyltransferase 6	Ggt6	1.20	0.0444
			-	Glucosamine (Udp-N-			
				Acetyl)-2-			
				Epimerase/N-			
GD 3 0	DDD		WARL 1250510	Acetylmannosamine			0.0000
GD20	DBP500	LIMMA	ILMN_1370510	Kinase	Gne	0.78	0.0323
				Glutamate Receptor,			
GD20	DBP500	I IMMA	II MN 1356417	(Alpha 2)	Gria?	0.78	0.0168
0020	551500	1.11111111111	1550417	Glutathione S-	01102	0.70	0.0100
GD20	DBP500	LIMMA	ILMN 1355860	Transferase Kappa 1	Gstk1	0.82	0.0462
				Gtp-Binding Protein 8			
GD20	DBP500	LIMMA	ILMN_1358146	(Putative)	Gtpbp8	0.84	0.0483
				Hyaluronan Synthase			
GD20	DBP500	LIMMA	ILMN_1370907	2	Has2	0.65	0.0333
05.00	DDD	IDAC		Haus Augmin-Like		0.51	0.00.77
GD20	DBP500	LIMMA	ILMN_1352509	Complex, Subunit 4	Haus4	0.74	0.0052

	I			Hepatitis A Virus			
GD20	DBP500	LIMMA	ILMN_1359061	Cellular Receptor 2	Haver2	1.22	0.0380
				Hedgehog Interacting			
GD20	DBP500	LIMMA	ILMN_1651179	Protein	Hhip	0.59	0.0031
GD20	DBP500	ιινμα	II MN 1376352	Protein 1	Hin1	0.72	0.0497
GD20	DBP500		ILMN 1360789	Homeobox B2	Hoxb2	0.72	0.0451
GD20	DDI 500	LIMINIA	112WIN_1300783	Htra Serine Peptidase	110X02	0.79	0.0431
GD20	DBP500	LIMMA	ILMN_1349449	1	Htral	0.65	0.0020
				Inhibitor Of Dna			
GD20	DBP500	LIMMA	ILMN_1349207	Binding 2	Id2	0.72	0.0135
				Insulin-Like Growth			
GD20	DBP500	LIMMA	ILMN 1360048	2	Igfbp2	0.75	0.0135
				Interleukin 13	- 0 - F		
GD20	DBP500	LIMMA	ILMN_1376826	Receptor, Alpha 2	Il13Ra2	0.74	0.0489
CD20	DDD500		U.) DI 12(22/2	Insulin Induced Gene	T · 1	0.72	0.0000
GD20	DBP200	LIMMA	ILMN_1362353	l Potassium Voltage	Insigl	0.73	0.0068
				Gated Channel. Shal-			
				Related Subfamily,			
GD20	DBP500	LIMMA	ILMN_1350901	Member 3	Kend3	0.76	0.0146
				Potassium Channel,			
GD20	DBP500	I IMMA	II MN 1356313	Sublamily K, Member	Kenk1	1 25	0.0178
0020	DDIVOU	Linvin		Kruppel-Like Factor		1.20	0.0170
GD20	DBP500	LIMMA	ILMN_1349150	13	Klf13	0.73	0.0277
GD20	DBP500	LIMMA	ILMN_1376868	Kruppel-Like Factor 2	Klf2	0.74	0.0406
GD20	DBP500	LIMMA	ILMN_1356588	Keratin 7	Krt7	1.61	0.0418
GD20	DBP500	LIMMA	ILMN 1373748	Laminin, Alpha 2	Lama2	0.74	0.0200
				Leucyl-Trna			
GD20	DBP500	LIMMA	ILMN_1356375	Synthetase	Lars	1.50	0.0031
GD20			II MN 1260814	Lactate Debydrogenase P	I dhh	1 20	0.0316
GD20			ILMIN_1309814	Visco420	Luno	1.29	0.0310
GD20	DBP300	LIMMA	1LMIN_1352800	Lectin Mannose-	скар	1.48	0.0077
GD20	DBP500	LIMMA	ILMN 1361804	Binding, 1	Lman1	0.81	0.0427
GD20	DBP500	LIMMA	ILMN 1371638	Lim Domain Only 4	Lmo4	0.81	0.0427
				Calcium Channel			
				Flower Domain	Loc29659		
GD20	DBP500	LIMMA	ILMN_1372487	Containing 1	9	0.82	0.0450
				Similar To Gtpase	Loc36207		
GD20	DBP500	LIMMA	ILMN 1353753	Testicular Gap1	4	0.72	0.0218
				Epithelial Splicing	Loc50040		
GD20	DBP500	LIMMA	ILMN_1371635	Regulatory Protein 1	9	1.29	0.0135
CD20	DDDC00			Similar To Cdna	Loc50097	1.07	0.0401
GD20	DR5200	LIMMA	1LMIN_1365562	Sequence Bc0244/9	4	1.27	0.0481

1				Similar To			
				Lymphocyte Antigen			
CD20	DDD500		IL MAN 1265407	6 Complex, Locus E	Loc50128	0.76	0.0115
GD20	DBP300	LIMIMA	1LIVIIN_1303487	Liganu Similar To 40S	2	0.76	0.0113
				Ribosomal Protein	Loc50259		
GD20	DBP500	LIMMA	ILMN 1353297	S26	9	1.26	0.0353
				Similar To Golgi	Loc68286		
GD20	DBP500	LIMMA	ILMN_1352204	Phosphoprotein 2	9	0.76	0.0277
				Hypothetical Protein	Loc69176		
GD20	DBP500	LIMMA	ILMN_1354120	Loc691762	2	0.69	0.0468
GD20	DBP500	LIMMA	ILMN_1376846	Lysyl Oxidase-Like 1	Lox11	0.76	0.0068
GD20	DBP500	LIMMA	ILMN_1351352	Lysyl Oxidase-Like 2	Loxl2	0.78	0.0146
GD20	DBP500	LIMMA	ILMN_1360586	Latrophilin 1	Lphn1	0.73	0.0477
				Latent Transforming			
				Growth Factor Beta			
GD20	DBP500	LIMMA	ILMN_1361640	Binding Protein 2	Ltbp2	0.55	0.0004
GD20	DDD500		II MNI 1267499	Lymphocyte Antigen	LycD	1 4 4	0.0291
0D20	DBF300	LIMINIA	1LWIN_1307488	Leucine Zinner	Lyon	1.44	0.0381
				Transcription Factor-			
GD20	DBP500	LIMMA	ILMN 1355269	Like 1	Lztfl1	1.32	0.0270
			_	Mitogen-Activated			
				Protein Kinase 8			
GD20	DBP500	LIMMA	ILMN_1359487	Interacting Protein 3	Mapk8Ip3	1.22	0.0424
				Myristoylated			
GD20	DBP500	тімма	II MN 1357013	Kinase C Substrate	Maroks	0.67	0.0450
0D20	DDI 500	LIMINIA	112WIIN_1337013	Methionyl-Trna	Wateks	0.07	0.0430
GD20	DBP500	LIMMA	ILMN 1367069	Synthetase	Mars	1.43	0.0094
				Mediator Complex			
GD20	DBP500	LIMMA	ILMN_1359059	Subunit 27	Med27	0.82	0.0427
				Microfibrillar-			
GD20	DBP500	LIMMA	ILMN_1370378	Associated Protein 2	Mfap2	0.75	0.0278
GD20	DBP500	I IMMA	II MN 1365208	Microfibrillar	Mfan5	0.63	0.0177
0D20	DDI 500	LIMINIA	1LIVII_1505298	Milk Fat Globule-Egf	Witap5	0.05	0.0177
GD20	DBP500	LIMMA	ILMN 1363839	Factor 8 Protein	Mfge8	0.81	0.0423
				Major Facilitator			
				Superfamily Domain-			
GD20	DBP500	LIMMA	ILMN_1360239	Containing Protein 2	Mfsd2	1.28	0.0349
GD20	DBP500	LIMMA	ILMN_1374266	Protein Mgl-1	Mgl1	0.78	0.0465
GD20	DBP500	LIMMA	ILMN_1351917	Matrix Gla Protein	Mgp	0.65	0.0218
				Microsomal			
CDCC	DDDCCC	IDOC	H) OL 1250051	Glutathione S-		1.07	0.01/7
GD20	DBF200	LIMMA	ILMN_1370971	I ransterase 1 Mid1 Interacting	Mgstl	1.37	0.0147
GD20	DBP500	LIMMA	ILMN 1352005	Protein 1	Mid1In1	0.78	0.0305
CD20			IL MNI 1252175	Mh	MI-11	0.70	0.0265
0D20	DBL200	LIMINIA	1LIVIIN_13331/3	IVIKI	IVIKII	0.80	0.0303

				(Megakaryoblastic			
				-Like 1			
				Makorin Ring Finger	1		+
GD20	DBP500	LIMMA	ILMN_1362843	Protein 2	Mkrn2	1.29	0.0424
				Matrix			
CDAO	555500			Metallopeptidase 11			0.00
GD20	DBP500	LIMMA	ILMN_1354279	(Stromelysin 3)	Mmp11	1.56	0.0260
				A-Domains Subfamily			
GD20	DBP500	LIMMA	ILMN 1358694	A. Member 4A	Ms4A4A	0.76	0.0444
GD20	DBP500	LIMMA	ILMN 1372614	Neurocalcin Delta	Ncald	1.37	0.0227
GD20	DBP500	LIMMA	ILMN 1358752	Necdin	Ndn	0.81	0.0469
0020	DBICOU	L'IIIIII -	1200102	N-Myc Downstream	11011	0.01	0.0102
GD20	DBP500	LIMMA	ILMN_2040297	Regulated 1	Ndrg1	1.48	0.0210
				Neural Precursor Cell			
				Expressed,			
GD20			U MNI 1376442	Developmentally	NaddQ	1.20	0.0450
0D20	DDL200	LIMINIA	1LIVIIN_13/0442	Down-Regulated 9	Incuu?	1.20	0.0450
GD20	DBP500	LIMMA	ILMN 1371630	Phd Fingers Family 1	Neud4	0.76	0.0268
GD20	DBP500	LIMMA	ILMN 1376576	Nuclear Factor I/A	Nfia	0.77	0.0497
_				Nuclear Factor I/X			
				(Ccaat-Binding			
GD20	DBP500	LIMMA	ILMN_1350522	Transcription Factor)	Nfix	0.75	0.0146
				Nuclear Protein,			
GD20	DRP500	LIMMA	ILMN 1354048	Regulator 1	Nupr1	2 67	0.0058
0020	DDI 500	LIMINI		Ornithine	Trupii	2.07	0.0050
				Decarboxylase,			
GD20	DBP500	LIMMA	ILMN_1369735	Structural 1	Odc1	0.75	0.0305
CD20	DDDC00		N. D. 125(000	Odz, Odd Oz/Ten-M	014	0.74	0.0404
GD20	DBP500	LIMMA	ILMN_1356890	Homolog 4	Odz4	0.74	0.0424
GD20	DBP500	LIMMA	ILMN_1358934	Olfactomedin 1	Olfm1	0.75	0.0317
GD20	DBP500	LIMMA	ILMN_1355412	Olfactomedin-Like 2B	Olfml2B	0.69	0.0210
GD20	DBP500	LIMMA	ILMN_1367643	Olfactomedin-Like 3	Olfml3	0.81	0.0469
GD20	DBP500	LIMMA	ILMN_1374464	Orosomucoid 1	Orm1	1.63	0.0405
				Odd-Skipped Related			
GD20	DBP500	LIMMA	ILMN_1353643	1	Osr1	0.63	0.0094
GD20	DBP500	LIMMA	ILMN_1366065	Protocadherin 19	Pcdh19	0.80	0.0349
0000	555700		HIDI 12(7005	Cadherin-Related	D 11.01	0.77	0.0450
GD20	DBF200	LIMMA	ILMN_1367005	Family Member 1	Pcdh21	0.77	0.0450
				Cytidylyltransferase 2			
GD20	DBP500	LIMMA	ILMN 1365622	Ethanolamine	Pcyt2	0.79	0.0497
				Programmed Cell			
GD20	DBP500	LIMMA	ILMN_1354952	Death 7	Pdcd7	1.21	0.0277
GD20	DBP500	LIMMA	ILMN 1353897	Phosphodiesterase 7A	Pde7A	1.36	0.0297
				Platelet-Derived			
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				Growth Factor			
CD20	DDD500		IL MAN 1255000	Receptor, Alpha	Dilafa	1 (7	0.0424
GD20	DBP500		ILMIN_1355008	Polypeptide	Pugira	1.07	0.0424
GD20	DBP500	LIMMA	ILMN_1352410	Preproenkephalin Placental Growth	Penk	0.62	0.0068
GD20	DBP500	LIMMA	ILMN 1374315	Factor	Pof	0.78	0 0297
0.0.20	DDIVOU			Procollagen-Lysine, 2-	- 8-	0.70	0.0257
				Oxoglutarate 5-			
GD20	DBP500	LIMMA	ILMN_1364313	Dioxygenase 3	Plod3	0.79	0.0218
GDAA				Peripheral Myelin	D 00		0.01.5.6
GD20	DBP500	LIMMA	ILMN_13/38/6	Protein 22	Pmp22	0.73	0.0156
GD20	DBP500	ιινιλα	II MN 1355335	Protein O- Fucosyltransferase 2	Pofut?	0.80	0.0176
0D20	DBI 500	LIIVIIVIA	112WIIN_1333333	Protein Kinase Camp-	101012	0.80	0.0170
				Dependent,			
				Regulatory, Type Ii,			
GD20	DBP500	LIMMA	ILMN_1353803	Beta	Prkar2B	1.30	0.0323
GD20	DBP500	LIMMA	ILMN_1366296	Peripherin	Prph1	0.69	0.0039
				Two-Component			
				Response Regulator-			
GD20	DBP500	LIMMA	ILMN_1361375	Like Aprr7	Prr7	0.62	0.0068
GD20	DBP500	I IMMA	II MN 1358252	Phosphoserine	Psph	1.62	0.0052
0D20	DBI 500	LIIVIIVIA	1121v11v_1556252	Prostaglandin I2	1 spii	1.02	0.0032
				(Prostacyclin)			
GD20	DBP500	LIMMA	ILMN_1361790	Synthase	Ptgis	0.68	0.0127
				Protein Tyrosine			
GD 00		1004	H) O I 1050445	Phosphatase-Like A	D. 1.11	0.00	0.0407
GD20	DBP500	LIMMA	ILMN_1350417	Domain Containing I	Ptplad I	0.80	0.0497
GD20	DBP500	LIMMA	ILMN_1363515	Pumilio Homolog I	Puml	0.80	0.0497
GD20	DBP500	LIMMA	ILMN_1349337	Pumilio Homolog 2	Pum2	1.24	0.0268
GD20	DBP500	LIMMA	ILMN 1359481	Retinoic Acid Recentor Beta	Rarh	1 30	0.0260
0020	DBI500			Retinoic Acid	Ituro	1.50	0.0200
				Receptor Responder			
				(Tazarotene Induced)			
GD20	DBP500	LIMMA	ILMN_1370339	2	Rarres2	0.75	0.0297
CD20				Rna Binding Motif	D1	1.20	0.0242
GD20	DBP500	LIMMA	ILMIN_1366226	Protein 4 / Similar To Piken	R0m4/ Rad12056	1.20	0.0342
GD20	DBP500	LIMMA	ILMN 1349662	Cdna 1500015O10	45	0.67	0.0272
-				Androgen-Dependent			
				Tfpi-Regulating	Rgd13056		
GD20	DBP500	LIMMA	ILMN_1368297	Protein	79	1.54	0.0311
				Similar To	D = 112004		
GD20	DBP500	LIMMA	II MN 2040277	1/00123020K1K Protein	Kg013084	1 28	0.0433
			$\frac{12040277}{110000000000000000000000000000000000$	Similar Ta	Ded15(02	1.20	0.0433
GD20	DR5200	LIMMA	ILMIN 1369242	Similar 10	Kga15603	1.85	0.0078

				Hypothetical Protein C130079G13	24		
				Similar To Hypothetical Upf0184			
GDAA	DDD500		H . D . 12(5552	Protein C9Orf16	Rgd15611	0.02	0.0475
GD20	DBP500	LIMMA	ILMN_1365552	Homolog	13 Ded15(41	0.83	0.0475
GD20	DBP500	LIMMA	ILMN 1357903	Protein Loc499656	Rg015641	1 24	0.0382
0020	DD1500		12000	Similar To 60S	/1	1.21	0.0302
				Ribosomal Protein	Rgd15649		
GD20	DBP500	LIMMA	ILMN_1353357	L29 (P23)	80	1.33	0.0311
				Similar To 60S			
CD20	DDD500		U.M.N. 125(590	Ribosomal Protein	Rgd15655	1 20	0.0020
GD20	DBP300	LIMIMA	1LMIN_1350589	L/A Similar To Novel	20 Rad15660	1.38	0.0039
GD20	DBP500	LIMMA	ILMN 1374368	Protein	99	0.77	0.0168
0020	DDIVOV	Environ		Ribosomal Protein	,,,	0.77	0.0100
GD20	DBP500	LIMMA	ILMN_1366973	L21	Rpl21	1.22	0.0250
				Ras-Related			
GD 90	DDD500		H) D I 10 ((001	Associated With	D 1		0.0050
GD20	DBP500	LIMMA	ILMN_1366091	Diabetes	Rrad	1.56	0.0073
GD20	DBP500	I IMMA	II MN 1368544	N2	Rt1-N2	1 22	0.0464
0020	DDI 500		1210111_1300344	Stearoyl-Coa	Rt1-112	1,22	0.0404
				Desaturase (Delta-9-			
GD20	DBP500	LIMMA	ILMN_1374191	Desaturase)	Scd	1.94	0.0020
				Short Chain			
				Dehydrogenase/Reduc			
GD20	DBP500	LIMMA	II MN 1355135	tase Family 16C, Member 5	Sdr16C5	1.41	0.0039
0D20	DDI 500	LININA	112WIIN_1333133	Short Chain	Surrocs	1.41	0.0039
				Dehydrogenase/Reduc			
				tase Family 16C,			
GD20	DBP500	LIMMA	ILMN_1372753	Member 6	Sdr16C6	1.47	0.0227
GD20	DBP500	LIMMA	ILMN_1370842	Selenoprotein M	Selm	0.74	0.0189
				Solute Carrier Family			
GD20	DBP500	LIMMA	ILMN_1360427	38, Member 4	Slc38A4	0.83	0.0260
				Solute Carrier Family			
				Dibasic And Neutral			
				Amino Acid			
GD20	DBP500	LIMMA	ILMN_1372377	Transport), Member 2	Slc3A2	1.35	0.0218
				Solute Carrier Family			
				4, Sodium Bicarbonate			
CD20	DDD500		IL MNL 1267206	Cotransporter,	Slo4A0	1 2 1	0.0228
0D20	0061900	LIMINIA	1LIVIIN_130/200	Solute Carrier Family	5104A9	1.31	0.0228
				7 (Cationic Amino			
				Acid Transporter, Y+			
GD20	DBP500	LIMMA	ILMN 1351408	System), Member 1	Slc7A1	1.40	0.0146

1	I	1	1	Solute Corrier Family	Ì		1
				7 (Amino Acid			
				Transporter Light			
				Chain, L System),			
GD20	DBP500	LIMMA	ILMN_1365729	Member 5	Slc7A5	1.45	0.0178
GD20	DBP500	LIMMA	ILMN 1357807	Slit Homolog 3	Slit3	0.74	0.0127
			_	Swi/Snf Related,			
				Matrix Associated,			
				Actin Dependent			
				Regulator Of			
GD20	DBB500		II MN 1258824	A Member 1	Smaraa1	1.27	0.0406
UD20	DBF300	LIMIMA	1LWIN_1558824	Sparc/Osteonectin	Siliarcal	1.27	0.0400
				Cwcv And Kazal-Like			
				Domains Proteoglycan			
GD20	DBP500	LIMMA	ILMN_1373684	(Testican) 1	Spock1	0.72	0.0212
				Spondin 1,			
CDAO	DDD500	1000	H) D L 1650224	Extracellular Matrix	G 1	0.70	0.0407
GD20	DBP500	LIMMA	ILMN_1650334	Protein	Spon1	0.78	0.0497
GD20	DBP500	I IMMA	II MN 1650693	Protein 1B	Sprr1B	1.50	0.0218
GD20	DBI 500		1050075	Siogren Syndrome	Spirib	1.50	0.0210
				Antigen			
GD20	DBP500	LIMMA	ILMN_1360596	B (Autoantigen La)	Ssb	1.33	0.0428
				Stromal Interaction			
GD20	DBP500	LIMMA	ILMN_1371376	Molecule 1	Stim1	0.73	0.0212
GD20	DBP500	LIMMA	ILMN_1376842	Transgelin	Tagln	0.64	0.0020
GD20	DBP500	LIMMA	ILMN_1353956	Tap Binding Protein	Tapbp	0.79	0.0242
GD 3 0	DDD 500	IDOG	H . D . 1050100	Threonyl-Trna	-	1.01	0.01.45
GD20	DBP500	LIMMA	ILMN_1358103	Synthetase	Tars	1.31	0.0147
GD20	DBP500	LIMMA	ILMN_1650153	Thrombospondin 2	Thbs2	0.61	0.0242
GD20	DBP500	LIMMA	ILMN_1356610	Tho Complex 1	Thoc1	1.31	0.0268
				T-Cell Lymphoma			
GD20	DDD500		II MNI 1264008	Invasion And Motostogia 2	Tiom?	1.25	0.0216
0D20	DBF300	LIMIMA	1LWIN_1504098	Transmembrane Bax		1.23	0.0310
				Inhibitor Motif			
GD20	DBP500	LIMMA	ILMN_1375110	Containing 1	Tmbim1	1.22	0.0424
				Transmembrane	Tmem161		
GD20	DBP500	LIMMA	ILMN_1368630	Protein 161B	В	1.35	0.0424
CDAO	DDD500	1000	H) D L 12(2025	Traf2 And Nck	T 1	1.25	0.0070
GD20	DBF200	LIMMA	ILMN_1363025	Interacting Kinase	Inik	1.35	0.0068
GD20	DBP500	LIMMA	ILMN 1349592	Topoisomerase (Dia)	Ton3A	0 79	0.0497
0020	001000	1.1111111111	121111 1377372	Tubulin	100571	0.17	0.0777
				Polymerization-			
				Promoting Protein			
GD20	DBP500	LIMMA	ILMN_1356424	Family Member 3	Тррр3	0.72	0.0462
GD20	DBP500	LIMMA	ILMN 1353347	Tripartite Motif	Trim29	1.34	0.0218

				Containing 29			
GD20	DBP500	LIMMA	ILMN 1354206	Tubulin, Alpha 1A	Tuba1A	0.81	0.0218
				Ubiquitin-Conjugating			
GD20	DBP500	LIMMA	ILMN_1374643	Enzyme E2S	Ube2S	0.81	0.0438
GD20	DBP500	LIMMA	ILMN_1361603	Ezrin	Vil2	1.26	0.0232
GD20	DDD500		II MN 1254624	Wd Repeat And Fyve	Wdful	0.74	0.0120
0D20	DBF300	LIMINA	1LMIN_1554054	Wingless-Type Mmty	wuiyi	0.74	0.0139
				Integration Site			
GD20	DBP500	LIMMA	ILMN_1362710	Family Member 2	Wnt2	0.75	0.0311
				Wingless-Related			
GD20	DDD500		II MN 1256425	Mmtv Integration Site	Wnt4	0.70	0.0211
0D20	DBF300	LIMINA	1LMIN_1550455	4 Tvrosvl-Trna	W 1114	0.70	0.0311
GD20	DBP500	LIMMA	ILMN 1374460	Synthetase	Yars	1.40	0.0217
				Zinc Finger, Cchc			
GD20	DBP500	LIMMA	ILMN_1364338	Domain Containing 12	Zcchc12	0.75	0.0311
GD20	DBP500	LIMMA	ILMN_1357208	Zinc Finger Protein 36	Zfp36	1.41	0.0104
				Gametogenetin	TA 46 A		
GD20	DBP500	LIMMA	ILMN_1376892	Binding Protein 2	Zfp403	1.23	0.0277
GD20	DBP500	SAM	II MN 1355841	Abhydrolase Domain Containing 8	Abhd8	0.77	<0.05
0D20	DDI 500	SAM	120111_1333041	Alcohol	Aundo	0.77	<0.05
				Dehydrogenase 6A			
GD20	DBP500	SAM	ILMN_1373231	(Class V)	Adh6A	1.46	< 0.05
				Aldehyde			
				Denydrogenase Family 1 Subfamily			
GD20	DBP500	SAM	ILMN 1359926	A2	Aldh1A2	0.87	< 0.05
GD20	DBP500	SAM	ILMN 1351069	Anelin	Anln	0.66	<0.05
0020	DDI000	<u>Di livi</u>		Adp-Ribosylation-	1 ipin	0.00	0.02
				Like Factor 6			
GD20	DBP500	SAM	ILMN_1348986	Interacting Protein 5	Arl6Ip5	0.84	< 0.05
				Asparagine Synthetase			
GD20	DBP500	SAM	ILMN 1368636	(Glutamine- Hydrolyzing)	Asns	1.95	<0.05
GD20	DBP500	SAM	ILMN 1368656	Beta 2 Microglobulin	B2M	0.81	<0.05
0D20	DDI 500	SAM	1200000	Brain Abundant.	DZIVI	0.01	<0.05
				Membrane Attached			
GD20	DBP500	SAM	ILMN_1365368	Signal Protein 1	Basp1	0.61	< 0.05
				Complement			
				Component I, Q			
GD20	DBP500	SAM	ILMN 1352382	Chain	C1Oa	0.77	< 0.05
				C1Q And Tumor			
				Necrosis Factor			
GD20	DBP500	SAM	ILMN_1365038	Related Protein 1	C1Qtnf1	0.55	< 0.05
GD20	DBD500	SAM	II MN 1267246	Calcium/Calmodulin-	Camb 2P	0.81	<0.05
0D20	000100	SAM	1LIVIIN_130/240	Dependent Floteni	Callik2D	0.01	<u>\0.03</u>

				Kinase Ii Beta			
				Cysteinyl-Trna			
GD20	DBP500	SAM	ILMN_1372842	Synthetase	Cars	1.44	< 0.05
GD20	DBP500	SAM	ILMN_1365636	Cholecystokinin	Cck	0.43	< 0.05
GD20	DBP500	SAM	ILMN_1356721	Chemokine (C-C Motif) Receptor 1	Ccr1	0.80	< 0.05
GD20	DBP500	SAM	ILMN_1349057	Cell Division Cycle 25A	Cdc25A	0.86	< 0.05
GD20	DBP500	SAM	ILMN_1376751	Claudin 4	Cldn4	1.57	< 0.05
GD20	DBP500	SAM	ILMN_1373158	C-Type Lectin Domain Family 2, Member L	Clec2L	0.67	<0.05
GD20	DBP500	SAM	ILMN_1372636	Collagen, Type Ix, Alpha 3	Col9A3	0.85	< 0.05
GD20	DBP500	SAM	ILMN_1364825	Carboxypeptidase A6	Cpa6	1.34	< 0.05
GD20	DBP500	SAM	ILMN_1362981	Carboxypeptidase D	Cpd	0.82	< 0.05
GD20	DBP500	SAM	ILMN_1359951	Cathepsin C	Ctsc	1.37	< 0.05
GD20	DBP500	SAM	ILMN 1376635	Cytochrome P450, Family 1, Subfamily B, Polypeptide 1	Cvp1B1	0.69	<0.05
GD20	DBP500	SAM	ILMN 1367505	Desmin	Des	0.66	<0.05
0020	DDIVVO	<u>or nor</u>		Dehydrogenase/Reduc tase (Sdr Family)		0.00	0.00
GD20	DBP500	SAM	ILMN_1368597	Member 7C	Dhrs7C	0.54	< 0.05
GD20	DBP500	SAM	ILMN_1376321	Dickkopf 3 Homolog	Dkk3	1.39	< 0.05
GD20	DBP500	SAM	ILMN_1371630	D4, Zinc And Double Phd Fingers Family 1	Dpfl	0.77	< 0.05
GD20	DBP500	SAM	ILMN_1375038	Ephrin B1	Efnb1	0.77	< 0.05
GD20	DBP500	SAM	ILMN_1372721	Eukaryotic Translation Initiation Factor 4B	Eif4B	1.44	< 0.05
GD20	DBP500	SAM	ILMN_1360134	Endothelial Cell- Specific Molecule 1	Esm1	0.70	< 0.05
GD20	DBP500	SAM	ILMN_1361603	Ezrin	Ezr	1.27	< 0.05
GD20	DBP500	SAM	ILMN_1350538	Family With Sequence Similarity 114, Member A1	Fam114A 1	1.04	< 0.05
CD20	DDD500	CAM	UNDI 127((20	Fk506 Binding Protein	F1 h = 6	0.74	<0.05
GD20	DBb200	SAM	ILMIN_13/6629	5 Fibronectin Leucine	Екоро	0.74	<0.05
				Rich Transmembrane			
GD20	DBP500	SAM	ILMN_1350369	Protein 3	Flrt3	0.70	< 0.05
GD20	DBP500	SAM	ILMN_1370930	Forkhead Box L2	Foxl2	0.69	< 0.05
GD20	DBP500	SAM	ILMN_1353747	Follistatin	Fst	0.75	< 0.05
GD20	DBP500	SAM	ILMN 1349350	Fucosyltransferase 1 (Galactoside 2-Alpha- L-Fucosyltransferase, H Blood Group)	Fut1	1.50	<0.05

1				Growth Differentiation	ĺ		
GD20	DBP500	SAM	ILMN_1360218	Factor 1	Gdf1	0.72	< 0.05
				Growth Differentiation			
GD20	DBP500	SAM	ILMN_2039904	Factor 10	Gdf10	0.57	< 0.05
				Glucosamine (Udp-N-			
				Acetyl)-2-			
				Epimerase/N-			
CD20	DDD500	SAM	II MNI 1270510	Acetylmannosamine	Cma	0.77	<0.05
0D20	DBF300	SAM	1LIVIN_13/0310	Glyaerol 3 Dhosphate	Olle	0.77	<0.03
GD20	DBP500	SAM	II MN 1353571	Dehydrogenase 1	Gnd1	1 18	<0.05
GD20	DDI 500	57 1141		Glutamate Receptor	Opui	1.10	-0.05
				Ionotropic, Ampa2			
GD20	DBP500	SAM	ILMN 1356417	(Alpha 2)	Gria2	0.81	< 0.05
			_	Glutathione S-			
GD20	DBP500	SAM	ILMN_1355860	Transferase Kappa 1	Gstk1	0.82	< 0.05
				Gtp-Binding Protein 8			
GD20	DBP500	SAM	ILMN_1358146	(Putative)	Gtpbp8	0.85	< 0.05
				Haus Augmin-Like			
GD20	DBP500	SAM	ILMN_1352509	Complex, Subunit 4	Haus4	0.75	< 0.05
CD20	DDD500	GAM	H MOL 1651170	Hedgehog Interacting	TTL 1.	0.00	<0.05
GD20	DBP200	SAM	ILMN_1651179	Protein	Hnip	0.60	< 0.05
GD20	DPP500	SAM	II MN 1340440	I Hira Serine Pepildase	Utro 1	0.66	<0.05
UD20	DBF300	SAM	1LIVIIN_1349449	Inhibitor Of Dna	IIIIai	0.00	<0.03
GD20	DBP500	SAM	ILMN 1349207	Binding 2	Id2	0.73	<0.05
				Insulin-Like Growth			
				Factor Binding Protein			
GD20	DBP500	SAM	ILMN_1360048	2	Igfbp2	0.75	< 0.05
				Insulin Induced Gene			
GD20	DBP500	SAM	ILMN_1362353	1	Insig1	0.75	< 0.05
				Potassium Voltage-			
				Gated Channel, Shal-			
GD20	DBP500	SAM	ILMN 1350901	Member 3	Kend3	0 74	<0.05
0020	DDI 500	57 1111		Kruppel-Like Factor	itelias	0.71	.0.05
GD20	DBP500	SAM	ILMN 1354316	11	Klf11	1.17	< 0.05
GD20	DBP500	SAM	ILMN 1373748	Laminin Alpha 2	Lama2	0.75	<0.05
0020	DDICCO	<u>Di liti</u>		Leucyl-Trna	200002	0.70	0.00
GD20	DBP500	SAM	ILMN 1356375	Synthetase	Lars	1.48	< 0.05
				Lactate			
GD20	DBP500	SAM	ILMN_1369814	Dehydrogenase B	Ldhb	1.33	< 0.05
				Lipoic Acid			
GD20	DBP500	SAM	ILMN_1376103	Synthetase	Lias	1.04	< 0.05
GD20	DBP500	SAM	ILMN_1371638	Lim Domain Only 4	Lmo4	0.81	< 0.05
				Similar To Gtpase			
OD 20	DDDC00	0.014		Activating Protein	Loc36207	1 4 4	-0.05
GD20	DRA200	SAM	ILMN_1353753	Testicular Gap1	4	1.44	< 0.05
CD20		C A M	IL MNI 1252000	Similar 10 Limkain	Llon	0.76	<0.05
0D20	DDF300	SAM	1LIVIIN 1332800	DI	і ілкар	0.70	~0.03

				Golgi Membrane	Loc68069		
GD20	DBP500	SAM	ILMN_1352204	Protein 1	2	0.77	< 0.05
GD20	DBP500	SAM	ILMN_1376846	Lysyl Oxidase-Like 1	Lox11	0.80	< 0.05
GD20	DBP500	SAM	ILMN_1351352	Lysyl Oxidase-Like 2	Loxl2	0.75	< 0.05
				Lysophosphatidic	_		
GD20	DBP500	SAM	ILMN_1650631	Acid Receptor 1	Lparl	0.56	< 0.05
				Growth Factor Beta			
GD20	DBP500	SAM	ILMN 1361640	Binding Protein 2	Ltbp2	0.86	< 0.05
				Lysophospholipase-			
GD20	DBP500	SAM	ILMN_1649832	Like 1	Lyplal1	1.45	< 0.05
		<i></i>		Methionyl-Trna			
GD20	DBP500	SAM	ILMN_1367069	Synthetase	Mars	1.34	< 0.05
				Microsomal Glutathione S			
GD20	DBP500	SAM	ILMN 1370971	Transferase 1	Mgst1	0 79	<0.05
0020	DBICOO	011101		Mkl	1119501	0.17	0.00
				(Megakaryoblastic			
				Leukemia)/Myocardin			
GD20	DBP500	SAM	ILMN_1353175	-Like 1	Mkl1	1.57	< 0.05
				Matrix			
GD20	DPP500	SAM	II MN 1354270	(Stromelysin 2)	Mmp11	0.75	<0.05
UD20	DBI 500	SAM	1LIVIIN_1334279	Membrane-Spanning	winipii	0.75	<0.03
				4-Domains, Subfamily			
GD20	DBP500	SAM	ILMN_1358694	A, Member 4A	Ms4A4A	0.80	< 0.05
GD20	DBP500	SAM	ILMN 1358752	Necdin	Ndn	0.96	< 0.05
				N-Myc Downstream			
GD20	DBP500	SAM	ILMN_2040297	Regulated 1	Ndrg1	2.72	< 0.05
				Nuclear Protein,			
CD20	DDD500	SAM	II MNI 1254049	Transcriptional	Nume1	0.74	<0.05
GD20	DBP300	SAM	1LIVIN_1554048	Ornithine	Nupri	0.74	<0.03
				Decarboxylase.			
GD20	DBP500	SAM	ILMN_1369735	Structural 1	Odc1	0.70	< 0.05
GD20	DBP500	SAM	ILMN 1355412	Olfactomedin-Like 2B	Olfml2B	0.85	< 0.05
			-	Origin Recognition			
GD20	DBP500	SAM	ILMN_1373022	Complex, Subunit 6	Orc6L	0.81	< 0.05
GD20	DBP500	SAM	ILMN_1366065	Protocadherin 19	Pcdh19	0.65	< 0.05
GD20	DBP500	SAM	ILMN_1352410	Preproenkephalin	Penk	0.77	< 0.05
				Placental Growth			
GD20	DBP500	SAM	ILMN_1374315	Factor	Pgf	0.81	< 0.05
GD20	DBB500	SAM	II MN 1255225	Protein O- Eucosyltransferrase 2	Dofut?	1 10	<0.05
	DBP300	SAM		Pucosyntansierase 2		1.19	<u>\0.03</u>
GD20	DBP500	SAM	ILMN_1650690	Pragma Of Rnd2	Pragmin	0.69	< 0.05
GD20	DBP500	SAM	ILMN_1366296	Peripherin	Prph	0.66	< 0.05
CD20			HINDL 12(1275	Two-Component	D7	1.57	-0.05
GD20	DRA200	SAM	ILMN_1361375	Kesponse Regulator-	Prr/	1.57	< 0.05

				Like Aprr7			
				Phosphoserine			
GD20	DBP500	SAM	ILMN_1358252	Phosphatase	Psph	0.69	< 0.05
				Prostaglandin I2			
CD20	DDDC00	CAN	H M L 12(1700	(Prostacyclin)	D(0.76	-0.05
GD20	DBP500	SAM	ILMN_1361790	Synthase	Ptgis	0.76	< 0.05
				Retinoic Acid			
				(Tagaratana Induaad)			
GD20		SAM	II MNI 1270220	(Tazarotene Induced)	Darrag?	1 26	<0.05
0D20	DBF300	SAM	ILIVIN_13/0339	2 Short Chain	Kallesz	1.50	<0.03
				Dehydrogenase/Reduc			
				tase Family 16C			
GD20	DBP500	SAM	ILMN 1355135	Member 5	Rdhe2	0.87	<0.05
0020	DBICOU	01101		Mitochondrial	Ttulie2	0.07	-0.02
				Assembly Of			
				Ribosomal Large	Rgd13069		
GD20	DBP500	SAM	ILMN 1372302	Subunit 1	36	0.88	< 0.05
				Myosin, Light Chain			
				12A, Regulatory, Non-	Rgd13095		
GD20	DBP500	SAM	ILMN_1350721	Sarcomeric	37	0.82	< 0.05
				Px Domain Containing	Rgd13113		
GD20	DBP500	SAM	ILMN_1363886	1	07	1.15	< 0.05
					Rgd15602		
GD20	DBP500	SAM	ILMN_1350478	Rgd1560270	70	1.84	< 0.05
				Similar To			
				Hypothetical Protein	Rgd15603		
GD20	DBP500	SAM	ILMN_1369242	C130079G13	24	0.83	< 0.05
				Similar To			
				Hypothetical Upf0184	D 115(11		
CD20	DDD500	GAM	H MOL 12(5552	Protein C9Orf16	Rgd15611	1.02	<0.05
GD20	DBP200	SAM	ILMIN_1365552	Homolog	13	1.02	<0.05
GD20		SAM	II MN 1267821	Similar 10 Kibosomai Protein I 7A	Rg015640	1 1 5	<0.05
0D20	DBF300	SAM	1LIVIIN_1307831	Similar To	29	1.13	<0.03
				Hypothetical Protein	Rad15641		
GD20	DBP500	SAM	ILMN 1360662	Fli39743	34	1 14	<0.05
0020	221000	<u>Di Ini</u>		Similar To 60S	5.		0.00
				Ribosomal Protein	Rgd15647		
GD20	DBP500	SAM	ILMN 1369963	L29 (P23)	64	0.78	< 0.05
			-	Similar To Novel	Rgd15660		
GD20	DBP500	SAM	ILMN_1374368	Protein	99	1.50	< 0.05
				Ras-Related			
				Associated With			
GD20	DBP500	SAM	ILMN_1366091	Diabetes	Rrad	1.84	< 0.05
				Stearoyl-Coenzyme A			
GD20	DBP500	SAM	ILMN_1374191	Desaturase 1	Scd1	1.37	< 0.05
				Solute Carrier Family			
0.5.5	DDD	a		3 (Activators Of	G1 0 / 5		0.05
GD20	DBP500	SAM	ILMN_1372377	Dibasic And Neutral	SIC3A2	1.50	< 0.05

I				Amino Acid			
				Transport), Member 2			
				Solute Carrier Family			
				7 (Amino Acid			
				Transporter Light			
GD20		SAM	II MN 1265720	Chain, L System), Momber 5	S107A5	0.72	<0.05
0D20	DBF300	SAW	1LIVIIN_1505729	Sparc/Osteonectin	SIC/AS	0.72	<0.03
				Cwcy And Kazal-Like			
				Domains Proteoglycan			
GD20	DBP500	SAM	ILMN_1373684	(Testican) 1	Spock1	1.51	< 0.05
				Small Proline-Rich			
GD20	DBP500	SAM	ILMN_1650693	Protein 1B	Sprr1B	0.64	< 0.05
GD20	DBP500	SAM	ILMN_1376842	Transgelin	Tagln	0.97	< 0.05
				T Cell Lymphoma			
CD20	DDD500	GAM	H M 12(4000	Invasion And	T:	1.25	<0.05
GD20	DBb200	SAM	ILMIN_1364098	Metastasis 2	Tiam2	1.25	<0.05
GD20	DBP500	SAM	ILMN 1349592	Topolsonierase (Dila) Jii Alnha	Ton3A	1.00	<0.05
0020	DBICOU	57 HVI		Tox High Mobility	Торон	1.00	
				Group Box Family			
GD20	DBP500	SAM	ILMN_1367193	Member 3	Tox3	0.80	< 0.05
				Tripartite Motif			
GD20	DBP500	SAM	ILMN_1353347	Containing 29	Trim29	1.34	< 0.05
GD20	DBP500	SAM	ILMN_1361459	Tubulin, Alpha 3A	Tuba3A	0.80	< 0.05
GD20	DBP500	SAM	ILMN_2038783	Thioredoxin 1	Txn1	0.91	< 0.05
CD20	DDD500	GAN	H) DI 1254624	Wd Repeat And Fyve	W/10 1	0.74	-0.05
GD20	DBP200	SAM	ILMN_1354634	Domain Containing I	Wdfyl	0.74	< 0.05
GD20	DBP500	SAM	ILMN 1349806	Syndrome Candidate 2	Whse?	0.88	<0.05
0.020	DBI500	57 1111	121011 (_151)000	Wingless-Related	11502	0.00	.0.05
				Mmtv Integration Site			
GD20	DBP500	SAM	ILMN_1356435	4	Wnt4	0.71	< 0.05
				Tyrosyl-Trna			
GD20	DBP500	SAM	ILMN_1374460	Synthetase	Yars	1.42	< 0.05
GD20	DBP500	SAM	ILMN_1357208	Zinc Finger Protein 36	Zfp36	1.41	< 0.05
PND5	DBP100	LIMMA	-	-	-	-	-
				A Kinase (Prka)			
PND5	DBP100	SAM	ILMN_1355272	Anchor Protein 8	Akap8	0.84	< 0.05
				Cbl Proto-Oncogene,			
PND5	DBP100	SAM	ILMN 1351226	Ligase B	Chlb	0 79	<0.05
PND5	DBP100	SAM	ILMN 1650840	Cyclin I 2	Cenl2	0.73	<0.05
11105	100	SAW	1050040	Heterogeneous		0.75	~0.05
				Nuclear			
PND5	DBP100	SAM	ILMN_1369798	Ribonucleoprotein F	Hnrpf	0.89	< 0.05
				Heterogeneous			
PND5	DBP100	SAM	ILMN_1370138	Nuclear	Hnrph1	0.83	< 0.05

				Ribonucleoprotein H1			
PND5	DBP100	SAM	ILMN_1354288	Kinesin Family Member 5B	Kif5B	0.82	<0.05
PND5	DBP100	SAM	ILMN 1357555	Similar To Riken Cdna 6430548M08	Rgd13048 84	0.81	< 0.05
			_	Phd Finger Protein 20-			
PND5	DBP100	SAM	ILMN_1350792	Like 1	Phf20L1	0.83	< 0.05
PND5	DBP100	SAM	ILMN 1369444	Similar To Orf4	2	0.70	< 0.05
				Similar To Retrovirus-			
	DDD100	GAM		Related Pol	Rgd15661	0.00	<0.05
PND5	DBP100	SAM	ILMN_136/2//	Polyprotein Kritt Anlarin Panaet	09	0.69	<0.05
PND5	DBP100	SAM	ILMN 1359410	Containing	Krit1	0.76	< 0.05
					Rgd15660		
PND5	DBP100	SAM	ILMN_1369406	Similar To Lrrg00116	46	0.65	< 0.05
DND5	DDD100	SAM	II MN 1255604	Similar To A a1262	Loc36349	0.66	<0.05
FNDS	DBF100	SAM	1LWIN_1555094	Sillinai 10 Ac1202	2 Loc49804	0.00	<0.03
PND5	DBP100	SAM	ILMN_1371063	Similar To Orf4	8	0.69	< 0.05
				Purine Rich Element			
PND5	DBP100	SAM	ILMN_1364794	Binding Protein B	Purb	0.86	< 0.05
PND5	DBP100	SAM	II MN 1368776	Loc498674	Loc49867	0.79	<0.05
11105	DDI 100	SAW	12/01/_1500770	Similar To Orf2	т	0.79	<0.05
				Consensus Sequence Encoding Endonuclease And Reverse Transcriptase	Loc49955		
PND5	DBP100	SAM	ILMN_1363227	Minus Rnaseh	4 L = = 50020	0.69	< 0.05
PND5	DBP100	SAM	ILMN_1361017	Similar To Lrrgt00082	Loc50039 8	0.80	< 0.05
PND5	DBP100	SAM	ILMN 1365562	Similar To Cdna Sequence Bc024479	Loc50097 4	0 79	<0.05
11105	DBI100	57111	1210111_1505502	Sequence De024479	Rgd15629	0.75	-0.05
PND5	DBP100	SAM	ILMN_1366649	Similar To Lrrgt00057	99	0.66	< 0.05
DND5		SAM	II MN 1271120	Similar To I rra00125	Loc50163	0.48	<0.05
TND5	DBF100	SAW	1121v11v_1371120	Similar To Acyl-	/	0.48	<0.03
				Coenzyme A Binding	Loc68259		
PND5	DBP100	SAM	ILMN_1351553	Domain Containing 5	3	1.01	< 0.05
DND5	DDD100	GAM	IL MAN 127(515	Origin Recognition	0	0.70	<0.05
PND5	DBP100	SAM	ILMIN_13/0515	Prn39 Pre-Mrna	Ofc2L	0.79	<0.05
				Processing Factor 39			
PND5	DBP100	SAM	ILMN_1355423	Homolog	Prpf39	0.77	< 0.05
DND5		CAM	H MN 1262029	Polypyrimidine Tract	Dthn?	0.66	<0.05
		SAW		Dinuing Flotein 2	Prop2	0.00	<0.05
PND5	DRA100	SAM	ILMN_2039717	Kev1, Polymerase	Revil	0.87	< 0.05
PND5	DBP100	SAM	ILMN_1357105	Similar To Formin-	Rgd15602	0.86	< 0.05

				Like 2 Isoform B	48		
PND5	DBP100	SAM	ILMN_1354105	Similar To Riken Cdna 2810403A07	Rgd15657 75	0.74	< 0.05
PND5	DBP100	SAM	ILMN 1356527	Rho Family Gtpase 2	Rnd2	0.81	< 0.05
PND5	DBP100	SAM	ILMN_1376454	Tar Dna Binding Protein	Tardbp	0.83	< 0.05
PND5	DBP100	SAM	ILMN 1370492	Tetraspanin 2	Tspan2	0.82	< 0.05
PND5	DBP100	SAM	ILMN 1364779	Zinc Finger Ccch- Type Containing 7A	Zc3H7A	0.81	< 0.05
PND5	DBP100	SAM	ILMN 1367665	Zinc Finger, Fyve Domain Containing 21	Zfyve21	0.83	< 0.05
PND5	DBP100	SAM		Zinc Finger With Ufm1-Specific Peptidase Domain	Zufsp	0.79	< 0.05
PND5	DBP500	LIMMA	ILMN_1369444	Predicted: Rattus Norvegicus Similar To Orf4 (Loc361942)	Loc36194 2	0.60	0.0037
PND5	DBP500	LIMMA	ILMN 1355694	Predicted: Rattus Norvegicus Similar To Ac1262 (Loc363492)	Loc36349 2	0.59	0.0037
DNID5				Predicted: Rattus Norvegicus Similar To Lrrg00116	Loc36254	0.59	0.0054
PND5	DBP500	LIMMA	ILMN 1371063	Predicted: Rattus Norvegicus Similar To Orf4 (Loc498048)	Loc49804	0.58	0.0054
PND5	DBP500	LIMMA	ILMN 1350792	Predicted: Rattus Norvegicus Similar To Phd Finger Protein 20- Like 1 Isoform 1 (Loc314964)	Loc31496 4	0.74	0.0069
PND5	DBP500	LIMMA	ILMN 1373694	Predicted: Rattus Norvegicus Similar To Retrovirus-Related Pol Polyprotein (Loc362315)	Loc36231 5	0.54	0.0069
PND5	DBP500	LIMMA	ILMN_1354030	Predicted: Rattus Norvegicus Triple Functional Domain (Ptprf Interacting) (Trio)	Trio	0.36	0.0069
PND5	DBP500	LIMMA	ILMN_1363939	Rattus Norvegicus Cyclin L1 (Ccnl1)	Cenl1	0.71	0.0103
PND5	DBP500	LIMMA	ILMN_1650840	Predicted: Rattus Norvegicus Cyclin L2 (Predicted) (Ccnl2)	Ccnl2	0.66	0.0103
PND5	DBP500	LIMMA	ILMN 1349971	Predicted: Rattus Norvegicus Desmoplakin,	Dsp	0.60	0.0103

				Transcript Variant 2			
				(Dsp)			
				Predicted: Rattus			
				Norvegicus Similar To			
				Lrrg00116	Loc50086		
PND5	DBP500	LIMMA	ILMN 1375194	(Loc500867)	7	0.61	0.0103
			-	Predicted: Rattus			
				Norvegicus Similar To			
				Lrrgt00057	Loc50108		
PND5	DBP500	LIMMA	ILMN_1366649	(Loc501087)	7	0.58	0.0103
				Predicted: Rattus			
				Norvegicus			
				Hypothetical Gene			
				Supported By			
				Nm_019349	Loc49774		
PND5	DBP500	LIMMA	ILMN_1352738	(Loc497743)	3	0.72	0.0103
				Predicted: Rattus			
				Norvegicus Similar To			
				Lrrgt00008	Loc50038		
PND5	DBP500	LIMMA	ILMN_1355226	(Loc500380)	0	0.55	0.0103
				Predicted: Rattus			
				Norvegicus			
				Loc500721	Loc50072		
PND5	DBP500	LIMMA	ILMN_1366540	(Loc500721)	1	0.42	0.0103
				Rattus Norvegicus			
	DDD500		U. M.N. 1270402	Tetraspanin 2	T	0.74	0.0102
PND5	DBP500	LIMMA	ILMIN_13/0492	(Ispan2)	I span2	0.74	0.0103
				Norwagiana A			
				Disintegrin And			
				Metalloprotease			
				Domain 33 (Predicted)			
PND5	DBP500	I IMMA	ILMN 1351087	(Adam33)	Adam33	0.57	0.0108
11105	DBI 500		120111_1351007	Predicted: Rattus	7 Idulii 5 5	0.57	0.0100
				Norvegicus Similar To	Loc49864		
PND5	DBP500	LIMMA	ILMN 1350958	Ac1-163 (Loc498644)	4	0.71	0.0109
11.20	DDICOU			Predicted: Rattus		0171	0.0109
				Norvegicus Similar To			
				Modulator Of			
				Estrogen Induced			
				Transcription,			
				Transcript Variant 1			
				(Rgd1307526), Misc	Rgd13075		
PND5	DBP500	LIMMA	ILMN_1359196	Rna.	26	0.60	0.0109
				Predicted: Rattus			
				Norvegicus Zinc			
				Finger Ccch Type			
				Containing 7 A			
				(Predicted), Transcript			
PND5	DBP500	LIMMA	ILMN_1364779	Variant 2 (Zc3H7A)	Zc3H7A	0.68	0.0109

1				Rattus Norvegicus			I
				Cytochrome C			
				Oxidase Subunit Xvii			
				Assembly Protein			
				Homolog (S			
PND5	DBP500	LIMMA	ILMN 1353069	Cerevisiae) (Cox17)	Cox17	1.35	0.0117
				Predicted: Rattus			
				Norvegicus Ahnak 1			
				(Loc499315), Misc	Loc49931		
PND5	DBP500	LIMMA	ILMN 1359062	Rna.	5	0.62	0.0117
			-	Predicted: Rattus			
				Norvegicus Similar To			
				Lrrgt00176	Loc49953		
PND5	DBP500	LIMMA	ILMN 1362603	(Loc499531)	1	0.52	0.0117
				Predicted: Rattus			
				Norvegicus Pumilio 1			
				(Drosophila)			
PND5	DBP500	LIMMA	ILMN 1363515	(Predicted) (Pum1)	Pum1	0.72	0.0117
			-	Predicted: Rattus			
				Norvegicus Similar To			
				Sr Rich Protein	Rgd13073		
PND5	DBP500	LIMMA	ILMN 1374578	(Rgd1307395)	95	0.61	0.0132
			_	Predicted: Rattus			
				Norvegicus Cellular			
				Retinoic Acid Binding			
				Protein 1 (Mapped)			
PND5	DBP500	LIMMA	ILMN 1349215	(Crabp1)	Crabp1	1.36	0.0151
			_	Predicted: Rattus			
				Norvegicus			
				Proline/Serine-Rich			
PND5	DBP500	LIMMA	ILMN_1368627	Coiled-Coil 2 (Psrc2)	Psrc2	0.67	0.0157
			-	Predicted: Rattus			
				Norvegicus S-			
				Adenosylhomocystein			
				e Hydrolase-Like 1			
PND5	DBP500	LIMMA	ILMN_1366513	(Predicted) (Ahcyl1)	Ahcyl1	0.74	0.0175
				Rattus Norvegicus			
				Aryl Hydrocarbon			
PND5	DBP500	LIMMA	ILMN_1376339	Receptor (Ahr)	Ahr	0.61	0.0175
				Rattus Norvegicus			
PND5	DBP500	LIMMA	ILMN_1356426	Allantoicase (Allc)	Allc	1.59	0.0175
				Rattus Norvegicus			
PND5	DBP500	LIMMA	ILMN_1373630	Aquaporin 11 (Aqp11)	Aqp11	1.29	0.0175
				Predicted: Rattus			
				Norvegicus Caspase			
				14 (Predicted)			
PND5	DBP500	LIMMA	ILMN_1362320	(Casp14)	Casp14	0.63	0.0175
				Predicted: Rattus			
				Norvegicus Cdc23			
				(Cell Division Cycle			
PND5	DBP500	LIMMA	ILMN_1353529	23, Yeast, Homolog)	Cdc23	0.78	0.0175

				(Cdc23)			
				Predicted: Rattus			
				Norvegicus Dead			
				(Asp-Glu-Ala-Asp)			
				Box Polypeptide 17			
PND5	DBP500	LIMMA	ILMN_1355095	(Ddx17)	Ddx17	0.67	0.0175
				Predicted: Rattus			
				Norvegicus Kinesin			
				Family Member 5B			
PND5	DBP500	LIMMA	ILMN_1354288	(Kif5B)	Kif5B	0.75	0.0175
				Predicted: Rattus			
				Norvegicus Similar To	1 2(100		
	DDDC00		H M 12(1(25	Lrrgt00194	Loc36188	0.55	0.0175
PND5	DBP200	LIMMA	ILMN_1361625	(Loc361885)	5	0.55	0.0175
				Predicted: Rattus			
				Norvegicus Similar 10			
				Sequence Encoding			
				Endonuclease And			
				Reverse Transcriptage			
				Minus Rnaseh	Loc49955		
PND5	DBP500	LIMMA	ILMN 1363227	$(L_{0}c499554)$	4	0.61	0.0175
11100	DBI 500	Linnin	12001(_1505227	Predicted: Rattus		0.01	0.0175
				Norvegicus Similar To	Loc50096		
PND5	DBP500	LIMMA	ILMN 1371124	Da1-12 (Loc500960)	0	0.61	0.0175
				Predicted: Rattus	-		
				Norvegicus Similar To			
				Lrrg00135	Loc50163		
PND5	DBP500	LIMMA	ILMN 1371120	(Loc501637)	7	0.38	0.0175
			-	Predicted: Rattus			
				Norvegicus Similar To			
				Riken Cdna			
				6330406I15			
				(Predicted)	Rgd13073		
PND5	DBP500	LIMMA	ILMN_1367232	(Rgd1307396)	96	0.81	0.0175
				Rattus Norvegicus			
				Timp			
	DDD			Metallopeptidase	T : 2	0.50	0.01.55
PND5	DBP500	LIMMA	ILMN_1348821	Inhibitor 3 (Timp3)	Timp3	0.76	0.0175
				Kattus Norvegicus			
				Zinc Finger Protein			
DND5	DBB200		II MN 1260012	(7 fn 361.2)	7fn261 2	0.54	0.0175
TND5	DBr 300	LIMINIA	12/01/01/2	Dredicted: Pattus	Z1p30L2	0.34	0.0175
				Norvegious Putative			
				Iso12(R) Protein			
PND5	DBP500	LIMMA	ILMN 1354070	(Isg12(B))	Isg12(B)	1 41	0.0176
11100	551,500	1.1111111111	12000 120000	Rattus Norvegicus	15512(15)	1.71	0.0170
				C10 And Tumor			
PND5	DBP500	LIMMA	ILMN 1366657	Necrosis Factor	C1Qtnf6	0.75	0.0179

				Related Protein 6	ĺ		
				(C1Qtnf6)			
				Predicted: Rattus			
				Norvegicus Kinectin 1			
PND5	DBP500	LIMMA	ILMN 1366075	(Predicted) (Ktn1)	Ktn1	0.75	0.0182
				Predicted: Rattus			
				Norvegicus Deah			
				(Asp-Glu-Ala-			
				Asp/His) Box			
				Polypeptide 57			
PND5	DBP500	LIMMA	ILMN 1373580	(Dhx57)	Dhx57	0.80	0.0191
				Predicted: Rattus			
				Norvegicus Similar To			
				Krey Interaction			
				Trapped Protein 1			
				(Krey Interaction			
				Trapped 1) (Cerebral			
				Cavernous			
				Malformations 1			
				Protein Homolog)	Loc36231		
PND5	DBP500	LIMMA	ILMN 1359410	(Loc_{362317})	7	0.75	0.0191
11100	DBI500	Linnin		Predicted: Rattus	,	0.75	0.0171
				Norvegicus Similar To			
				Atp-Binding Cassette			
				Sub Family G			
				(White) Member 3			
				(Write), Weinber 5 (Predicted)	Rad15647		
PND5	DBP500	LIMMA	II MN 1360371	(Pad1564700)	Ngu15047	0.72	0.0101
TNDJ	DBI 500	LININA	1200371	Rattus Norvegicus	0)	0.72	0.0171
				Ribosomal I 1 Domain			
PND5	DBP500	ιιмма	II MN 1376915	Containing 1 (Rsl1D1)	Rel1D1	1.28	0.0191
TNDJ	DBI 500	LININA	1LIVIIN_1370913	Predicted: Rattus	KSIIDI	1.20	0.0191
				Norvegious Ia Motif			
				Containing Gtasse			
				Activating Protain 1			
DND5	DBB200		II MN 1272750	(Predicted) (Iggan1)	Iggan1	0.75	0.0103
11103	DD1 300	LIMINIA	11.1VIIN_13/3/39	Predicted: Pattus	iqgapi	0.75	0.0175
				Norvegious Similar To			
				I rroffilla	Loc36101		
PND5	DBP500	LIMMA	II MN 1362018	$(I_{0}, 361, 912)$	2	0.60	0.0103
TNDS	DBF500	LIIVIIVIA	1LIVIN_1302918	(L0C301912) Predicted: Pattus	2	0.00	0.0195
				Norvegious Similar To			
				Signal Decognition			
				Dortiolo 72 V do	L 00/0925		
DNID5	DBB200		II MN 1255550	Fallicie, /2 Kua Subunit (Leg/09251)	1	0.67	0.0102
TNDS	001300	LIMINIA	11.1111 1333330	Dradiated: Dattas	1	0.07	0.0195
				Norwagians Similar Ta			
				Norvegicus Similar 10 Dibogomol Drotoir	L aa 40022		
DND	DDD500		II MAL 1240(11	KIDOSOMAI Protein	L0C49932	0.71	0.0102
PND5	DBP300	LIMMA	1LIVIIN_1349011	L2/A (L00499321)	1 1 = = 50154	0./1	0.0193
DND	DDD500		II MAL 125(549	Nervegious Similar T	0	0.29	0.0102
rindo	DBL200	LIMINA	1LIVIIN_1330348	Norvegicus Similar 10	0	0.38	0.0193

				Lrrg00135			l
				(Loc501548)			
				Predicted: Rattus			
				Norvegicus Rna			
				Binding Motif Protein			
				24 (Predicted)			
PND5	DBP500	LIMMA	ILMN_1350785	(Rbm24)	Rbm24	0.77	0.0193
				Predicted: Rattus			
				Norvegicus Similar To			
				Zinc Finger, Fyve			
				Domain Containing 16	$D = \frac{115(47)}{15}$		
DND5			II MAN 1272142	(Predicted) (Pad1564784)	Rg015647	0.72	0.0102
PND5	DBP300	LIMMA	ILMIN_13/2143	(Rg01504/84)	84	0.75	0.0193
				Nervegieve Similar Te			
				Indivegicus Similar 10	L 00/10056		
PND5	DBP500	LIMMA	II MN 1650107	(Loc/00564)	1	0.54	0.0194
TNDJ	DBI 500	LININA	112WIN_1030107	Rattus Norvegicus	4	0.54	0.0194
PND5	DBP500	LIMMA	ILMN 1356055	Attractin (Atrn)	Atrn	0.80	0.0196
11100	DB1500	Linnin	1200000	Predicted: Rattus	71111	0.00	0.0170
				Norvegicus Similar To			
				Isopentenvl			
				Diphosphate Delta-			
				Isomerase Type 2	Loc49878		
PND5	DBP500	LIMMA	ILMN 1368435	(Loc498787)	7	2.11	0.0196
			—	Rattus Norvegicus			
				Origin Recognition			
				Complex, Subunit 2-			
PND5	DBP500	LIMMA	ILMN_1376515	Like (Yeast) (Orc2L)	Orc2L	0.79	0.0196
				Predicted: Rattus			
				Norvegicus Similar To			
				Lrrgt00176	Loc49958		
PND5	DBP500	LIMMA	ILMN_1362770	(Loc499582)	2	0.63	0.0198
				Predicted: Rattus			
				Norvegicus Similar To			
				Riken Cdna	D 115655		
	DDD500		H MAL 1254105	2810403A07	Rgd15657	0.69	0.0100
PND5	DR5200	LIMMA	1LMIN_1354105	(Kg01505775)	/5	0.68	0.0198
				Guanine Nucleotide			
				Binding Protein			
PND5	DBP500	ιιмма	II MN 1361160	Alpha 11 (Gna11)	Gna11	0.75	0.0210
1105	DDI 500		12/01/01/100	Predicted: Rattus		0.75	0.0210
				Norvegicus Similar To			
				60S Ribosomal			
				Protein L23A			
				(Predicted)	Rgd15658		
PND5	DBP500	LIMMA	ILMN 1363683	(Rgd1565806)	06	1.29	0.0210
				Predicted: Rattus		-	-
				Norvegicus Similar To	Loc30403		
PND5	DBP500	LIMMA	ILMN_1360884	Adp-Ribosylation	7	0.76	0.0210

				Factor-Like 2-Like 1			
				(L0C304037) Pattus Norvagious			
				Mdm4 P53 Binding			
				Protein Homolog			
PND5	DBP500	LIMMA	ILMN 1376455	(Mouse) (Mdm4)	Mdm4	0.71	0.0210
				Predicted: Rattus			
				Norvegicus Prp39 Pre-			
				Mrna Processing			
				Factor 39 Homolog			
DND5	DDD500		II MNL 1255422	(Yeast) (Predicted)	$D_{m} f^{2} 0$	0.72	0.0210
PND5	DBP500	LIMMA	ILMIN_1555425	(PIPI39) Predicted: Pattus	РГРІЗУ	0.73	0.0210
				Norvegicus			
				Hypothetical			
				Loc315216 (Predicted)	Rgd13119		
PND5	DBP500	LIMMA	ILMN_1373365	(Rgd1311907)	07	0.78	0.0210
				Predicted: Rattus			
				Norvegicus Similar To			
				Dual Specificity			
				(T. Dan 11) (Dradiated)	Dad15600		
PND5	DBP500	I IMMA	II MN 1353786	(1-Dsp11) (Fredicied) (Rgd1560049)	A9	0.66	0.0210
11105	DBI 500	LIMINIA	1210111_1333700	Predicted Rattus	-12	0.00	0.0210
				Norvegicus Wd			
				Repeat Domain 47			
PND5	DBP500	LIMMA	ILMN_1356955	(Wdr47)	Wdr47	0.78	0.0210
				Predicted: Rattus			
				Norvegicus			
				Glyceraldehyde 3-			
				Phosphate			
PND5	DBP500	LIMMA	ILMN 1649859	(Gandh)	Gandh	1 36	0.0221
11100	DBI500	Linnin	1019039	Predicted: Rattus	Gupun	1.50	0.0221
				Norvegicus Similar To			
				Putative Rna Binding	Loc50150		
PND5	DBP500	LIMMA	ILMN_1362324	Protein 1 (Loc501503)	3	0.60	0.0221
				Rattus Norvegicus			
DNDS	DDD500		U MAL 127(005	Abl-Interactor I	A 1. : 1	0.79	0.0226
PND5	DBP300	LIMMA	ILMIN_13/0905	(ADII) Predicted: Pattus	ADII	0.78	0.0226
				Norvegicus Dual			
				Specificity			
				Phosphatase 19			
PND5	DBP500	LIMMA	ILMN_1369598	(Predicted) (Dusp19)	Dusp19	1.23	0.0226
				Predicted: Rattus			
				Norvegicus Similar To	D. 115606		
DND5	DDD500		II MNI 1251202	vanin-3 (Predicted)	Kgd15606	1 / 1	0.0226
PND5	0064900	LIMINA	1LIVIIN_1331302	(Rgu1300009)	09	1.41	0.0220
PND5	DBP500	ΙΙΜΜΔ	II MN 1353725	Norvegicus Atavia	Atm	0.76	0.0227
11105	DD1300		1000120	1 101 VOSICUS MUAIA	4 1 111	0.70	0.0447

				Telangiectasia			
				Mutated Homolog			
				(Human) (Mapped)			
				(Atm)			
				Rattus Norvegicus			
				Gonadotropin-			
	DDD			Releasing Hormone 1	G 11	0.50	
PND5	DBP500	LIMMA	ILMN_1373686	(Gnrh1)	Gnrhl	0.73	0.0227
				Predicted: Rattus			
				Norvegicus Similar To	T 00500		
DUD 5	DDD500		H . D . 12(7010	Hoxa-9 (Predicted)	Loc29709	0.73	0.0007
PND5	DBP200	LIMMA	ILMN_136/919	(Loc297099)	9	0.73	0.0227
				Predicted: Rattus			
				Norvegicus Similar To			
	DDD			Lrrgt00176	Loc49862	0.55	0.0005
PND5	DBP500	LIMMA	ILMN_1350803	(Loc498623)	3	0.55	0.0227
				Predicted: Rattus			
				Norvegicus Similar To			
				Hypothetical Protein	D 110007		
DUD 5	DDD500		H) O I 1272140	Flj13910 (Predicted)	Rgd13097	0.77	0.0007
PND5	DBP500	LIMMA	ILMN_1353149	(Rgd1309766)	66	0.77	0.0227
				Predicted: Rattus			
				Norvegicus			
				Trichorhinophalangeal			
DUD 5	DDD500		H . O . 1240020	Syndrome I		0.57	0.0007
PND5	DBP500	LIMMA	ILMN_1349929	(Predicted) (Trps1)	Trps1	0.57	0.0227
				Rattus Norvegicus			
				Trna Splicing			
				Endonuclease 34			
	DDDC00		H M L 12(5704	Homolog (S.	T 24	1.24	0.0227
PND5	DBP500	LIMMA	ILMN_1365/04	Cerevisiae) (1sen34)	I sen34	1.34	0.0227
				Predicted: Rattus			
				Norvegicus			
				Karyopherin			
DUD 5	DDD500		H) O L 1272 402	(Importin) Beta I	77 1 1	0.74	0.0000
PND5	DBP500	LIMMA	ILMN_13/3492	(Kpnbl)	Kpnbl	0.76	0.0233
				Kattus Norvegicus			
	DDD500		H M L 12(7025	Lecithin Cholesterol	т (0.70	0.0222
PND5	DBP200	LIMMA	ILMN_136/035	Acyltransferase (Lcat)	Leat	0.78	0.0233
				Predicted: Rattus			
				Norvegicus Similar To	L 409.66		
	DDD500		IL MAL 1250000	LirgiUU1/b	L0C49866	0.50	0.0222
PND5	DBR200	LIMMA	1LIMIN_1359908	(L0C498009)	9	0.39	0.0233
				Predicted: Kattus			
				INORVEGICUS SIMILAR 10	L 2250001		
DND5			II MNI 1271641	L_{1}	L0C30091	0.57	0.0222
PNDS	DBP300	LIMINA	1LIVIIN_13/1041	(LOCOUVID) Dradiatad: Dattera	0	0.37	0.0233
				Norwagiaus Similar Ta	1 0069257		
DND	DDD500		IL MAL 12(5502	Spindlin (Lag(22571)	1	0.74	0.0222
PND5	DR5200	LIMMA	1LMIN_1365592	Spindlin (Loc6825/1)	1	0./4	0.0233

				Predicted: Rattus			
				Norvegicus Similar To			
				Acyl-Coenzyme A			
				Binding Domain			
				Containing 5	Loc68259		
PND5	DBP500	LIMMA	ILMN_1351553	(Loc682593)	3	0.77	0.0233
				Rattus Norvegicus			
				Meningioma			
				Expressed Antigen 5			
				(Hyaluronidase)			
PND5	DBP500	LIMMA	ILMN_1370257	(Mgea5)	Mgea5	0.79	0.0233
				Predicted: Rattus			
				Norvegicus			
				Microsomal			
				Glutathione S-			
				Transferase 2			
PND5	DBP500	LIMMA	ILMN_1370709	(Predicted) (Mgst2)	Mgst2	1.56	0.0233
				Rattus Norvegicus			
				Similar To	D 110105		
	DDD500		H MAL 1240756	Hypothetical Protein	Rgd13105	1.20	0.0222
PND5	DBP200	LIMMA	ILMIN_1349/56	(Rgd13105/1)	/1	1.26	0.0233
				Predicted: Rattus			
				Norvegicus Similar 10			
				Use alog (Dradiated)	Dad15650		
DND5	DDD500		II MAL 1272072	(Dad1565047)	AZ	1 40	0.0222
FNDS	DBF300	LIIVIIVIA	1LIVIN_15/59/5	(Rgu1303047) Dradiatad: Dattus	4/	1.40	0.0233
				Norvegious Similar To			
				Flog26 Protoin			
				(Predicted)	Loc29208		
PND5	DBP500	LIMMA	II MN 1373089	(I oc 292082)	2	0.67	0.0239
11105	DBI 500		121011(_137500)	Predicted: Rattus	2	0.07	0.0237
				Norvegicus			
				Mitchondrial			
				Ribosomal Protein S7			
PND5	DBP500	LIMMA	ILMN 1367484	(Mrps7)	Mrps7	1.30	0.0239
				Predicted: Rattus	· · ·		
				Norvegicus Similar To			
				Orf2 Consensus			
				Sequence Encoding			
				Endonuclease And			
				Reverse Transcriptase			
				Minus Rnaseh	Loc50156		
PND5	DBP500	LIMMA	ILMN_1363743	(Loc501562)	2	0.76	0.0248
				Rattus Norvegicus			
				Cap-Gly Domain			
				Containing Linker			
PND5	DBP500	LIMMA	ILMN_1356649	Protein 1 (Clip1)	Clip1	0.76	0.0250
				Rattus Norvegicus			
				Ribonuclease, Rnase			
PND5	DBP500	LIMMA	ILMN 1376375	A Family, 12 (Non-	Rnase12	1.61	0.0250

				Active) (Rnase12)			
				Rattus Norvegicus			
				Similar To Riken			
				Cdna D630029K19	Rgd13071		
PND5	DBP500	LIMMA	ILMN 1369614	(Rgd1307100)	00	0.79	0.0251
			_	Rattus Norvegicus			
				Carnosine Dipeptidase			
				1 (Metallopeptidase			
PND5	DBP500	LIMMA	ILMN_1363987	M20 Family) (Cndp1)	Cndp1	1.28	0.0252
				Myristoylated			
				Alanine-Rich Protein			
PND5	DBP500	LIMMA	ILMN_1357013	Kinase C Substrate	Marcks	0.45	0.0252
				Rattus Norvegicus			
				Upregulated During			
				Skeletal Muscle			
PND5	DBP500	LIMMA	ILMN_1352524	Growth 5 (Usmg5)	Usmg5	1.31	0.0252
				Rattus Norvegicus			
				Caveolin, Caveolae			
				Protein 1 (Cav1),			
PND5	DBP500	LIMMA	ILMN_1376388	Transcript Variant 1	Cav1	0.76	0.0274
				Rattus Norvegicus			
				High Mobility Group			
				Nucleosomal Binding			
PND5	DBP500	LIMMA	ILMN_1362726	Domain 3 (Hmgn3)	Hmgn3	0.66	0.0274
				Rattus Norvegicus			
				Cap, Adenylate			
				Cyclase-Associated			
				Protein 1 (Yeast)			
PND5	DBP500	LIMMA	ILMN_1651181	(Cap1)	Capl	0.80	0.0274
				Predicted: Rattus			
				Norvegicus Protein			
				Phosphatase 2			
				(Formerly 2A),			
				Regulatory Subunit			
	DDD500		H) 01 1051004	B", Alpha, Transcript	D 0004	0.70	0.0077
PND5	DBP500	LIMMA	ILMN_1351234	Variant 2 (Ppp2R3A)	Ppp2R3A	0.70	0.0277
				Predicted: Kattus			
				Norvegicus Similar To			
				KIKEN Cana			
				Dradiated)	Dad12002		
DND5	DBP500		II MN 1259091	(Fredicted) (Rad1308200)	Ngu13082	0.67	0.0277
TND5	DBr 300	LININIA	12/010_1330901	Rattus Norvegious	20	0.07	0.0277
				A denosine Deaminase			
PND5	DRP500	LIMMA	ILMN 1358817	(Ada)	Ada	2.01	0.0281
11105	001500	1/11/11/1/1/1/1	1550017	Predicted: Rattus	1100	2.01	0.0201
				Norvegicus Similar To			
				Deubiquitinating			
				Enzyme Ubh1	Loc49813		
PND5	DBP500	LIMMA	ILMN 1368861	(Loc498138)	8	1.23	0.0281
				- /	1	-	-

				Predicted: Rattus			
				Mtan4 Protein	Loc50105		
PND5	DBP500	LIMMA	ILMN 1356002	(Loc501057)	7	0.76	0.0281
			-	Predicted: Rattus			
				Norvegicus Similar To			
				Hypothetical Protein			
				D11Ertd99E			
				(Predicted)	Rgd15643		
PND5	DBP500	LIMMA	ILMN_1354146	(Rgd1564337)	37	1.32	0.0281
				Rattus Norvegicus			
DND5	DDD500		II MNI 1271460	(Ring Finger Protein 2	Dnf	0.91	0.0291
PNDS	DBP300	LIMINA	ILMIN_13/1400	(KIII2) Pattus Norvegious	KIII2	0.81	0.0281
PND5	DBP500	I IMMA	II MN 1376612	Tsukushin (Tsku)	Tsku	1 27	0.0281
11105	DBI 500	LIMINIA	112WIN_1370012	Predicted: Rattus	1 SKu	1.27	0.0201
				Norvegicus			
				Loc498469	Loc49846		
PND5	DBP500	LIMMA	ILMN 2038882	(Loc498469)	9	0.79	0.0282
			-	Rattus Norvegicus			
				Transcription Factor			
PND5	DBP500	LIMMA	ILMN_1361164	Myocardin (Myocd)	Myocd	0.76	0.0282
				Predicted: Rattus			
				Norvegicus Similar To			
				Riken Cdna			
				5/30509K1/Gene (Pradiated)	Pad15610		
PND5	DBP500	ιιмма	ILMN 1375102	(Predicted) (Rad1561042)	A2	0.75	0.0288
11105	DBI 500	LIMINA	1LIVII_1575102	Predicted: Rattus	72	0.75	0.0200
				Norvegicus Cyclin T2			
PND5	DBP500	LIMMA	ILMN 1359160	(Predicted) (Ccnt2)	Ccnt2	0.79	0.0298
			-	Rattus Norvegicus			
				Collagen, Type Xxvii,			
PND5	DBP500	LIMMA	ILMN_1375001	Alpha 1 (Col27A1)	Col27A1	0.80	0.0298
				Rattus Norvegicus D-			
				Serine Modulator-1			
PND5	DBP500	LIMMA	ILMN_1650976	(Dsm-1)	Dsm-1	1.23	0.0298
				Rattus Norvegicus			
PND5	DBP500	LIMMA	II MN 1370814	Protein Like (Ekbnl)	Fkbpl	1.43	0.0298
TND5	DBF300	LIMINA	1LMIN_1370814	Rattus Norvegicus	Гкорг	1.45	0.0298
				Homocysteine-			
				Inducible.			
				Endoplasmic			
				Reticulum Stress-			
				Inducible, Ubiquitin-			
				Like Domain Member			
PND5	DBP500	LIMMA	ILMN_1370868	1 (Herpud1)	Herpud1	1.31	0.0298
				Predicted: Rattus	1 26112		
			HINDI 12(4400	Norvegicus Similar To	Loc36115	0.72	0.0200
PND5	DRA200	LIMMA	1LMIN_1364489	Lrrgt00082	/	0./3	0.0298

				(Loc361157)			
				Predicted: Rattus			
				Norvegicus Similar To			
				Ring Finger Protein	Loc36465		
PND5	DBP500	LIMMA	ILMN 1650595	170 (Loc 364654)	4	0.75	0.0298
TIDU	DDICOU			Predicted: Rattus		0.70	0.0220
				Norvegicus Similar To			
				Glyceraldehyde-3-			
				Phosphate			
				Dehydrogenase	Loc50050		
PND5	DBP500	LIMMA	ILMN 1351960	(Loc500506)	6	0.76	0.0298
				Predicted: Rattus	-		
				Norvegicus Similar To			
				Histone-Lysine N-			
				Methyltransferase, H3			
				Lysine-4 Specific			
				(Histone H3-K4			
				Methyltransferase)			
				(H3-K4-Hmtase) (Set			
				Domain-Containing			
				Protein 7)	Loc50317		
PND5	DBP500	LIMMA	ILMN_1363605	(Loc503176)	6	0.70	0.0298
				Predicted: Rattus			
				Norvegicus Low			
				Density Lipoprotein			
				Receptor-Related			
				Protein 6 (Predicted)			
PND5	DBP500	LIMMA	ILMN_1349678	(Lrp6)	Lrp6	0.71	0.0298
				Predicted: Rattus			
				Norvegicus Mitogen-			
				Activated Protein			
	DDDC00		H M 12/0405	Kinase Kinase Kinase	N 417.2	0.00	0.0200
PND5	DBP200	LIMMA	ILMN_1368495	Kinase 3 (Map4K3)	Мар4К3	0.80	0.0298
				Rattus Norvegicus			
DND5				Opioid Receptor,	On m 1	1 01	0.0208
PNDS	DBP300	LIMINA	1LIVIIN_1303020	Dradiatad: Dattur	Opisi	1.21	0.0298
				Norvegious Playin D2			
PND5	DRP500	ТІММА	II MN 1354034	(Plynh?)	Plynh?	0 78	0.0208
11103	DD1 300	LIMINIA	12//11/13/4034	Rattus Norvegious	1 1/1102	0.70	0.0270
				Similar To Riken			
				Cdna 2700038C09	Rgd13106		
PND5	DBP500	LIMMA	ILMN 1369181	(Rgd1310660)	60	1 31	0.0298
	221000	2	1009101	Rattus Norvegicus		1.01	0.0270
				Secreted And			
				Transmembrane 1			
PND5	DBP500	LIMMA	ILMN 1371209	(Sectm1)	Sectm1	1.66	0.0298
			-	Rattus Norvegicus			
				Splicing Factor,			
				Arginine/Serine-Rich			
PND5	DBP500	LIMMA	ILMN 1372737	11 (Sfrs11)	Sfrs11	0.71	0.0298

				Rattus Norvegicus			
				Sorbin And Sn3			
PND5	DBP500	LIMMA	ILMN 1372136	(Sorbs3)	Sorbs3	1 20	0.0298
111,000	DBICOU	Linnin	121011 (_15 / 2150	Predicted: Rattus	501055	1.20	0.0270
				Norvegicus			
				Transforming Growth			
				Factor Beta Regulated			
				Gene 4 (Predicted)			
PND5	DBP500	LIMMA	ILMN_1375291	(Tbrg4)	Tbrg4	0.76	0.0298
				Rattus Norvegicus			
				Immediate Early			
PND5	DBP500	LIMMA	ILMN_1530409	Response 5 (Ier5)	Ier5	1.30	0.0309
				Rattus Norvegicus			
				Polymerase (Rna) II			
				(Dna Directed)			
DND5			II MN 1256866	(Polr2C)	Polr2G	1.28	0.0300
TND5	DBF500	LIMINA	1LIVIN_1550800	(F0II2O) Rattus Norvegicus	101120	1.20	0.0309
PND5	DBP500	LIMMA	ILMN 1362836	Mk1 Protein (Mk1)	Mk1	1 30	0.0314
11000	DBICOU	Linnin		Rattus Norvegicus	10IRI	1.50	0.0511
				Thyrotrophic			
				Embryonic Factor			
PND5	DBP500	LIMMA	ILMN_1372235	(Tef)	Tef	0.79	0.0321
				Predicted: Rattus			
				Norvegicus Similar To			
				Hypothetical Protein			
				Kiaa0539 (Predicted)	Loc30410		
PND5	DBP500	LIMMA	ILMN_1356329	(Loc304104)	4	0.74	0.0324
				Predicted: Rattus			
				Norvegicus Udp-			
				Galastagultransforaça			
				Polypentide 7			
PND5	DBP500	LIMMA	ILMN 1358161	(Predicted) (B3Galt7)	B3Galt7	1.26	0.0333
11105	DDI 500	Linnin		Rattus Norvegicus	D5Guit7	1.20	0.0555
				Relaxin/Insulin-Like			
				Family Peptide			
PND5	DBP500	LIMMA	ILMN_1348992	Receptor 1 (Rxfp1)	Rxfp1	0.70	0.0334
				Predicted: Rattus			
				Norvegicus Kallikrein			
PND5	DBP500	LIMMA	ILMN_1367128	12 (Predicted) (Klk12)	Klk12	1.40	0.0334
				Rattus Norvegicus			
				Gdp Dissociation	G I'I	0.01	0.0005
PND5	DBP500	LIMMA	ILMN_1360643	Inhibitor I (Gdi I)	Gdil	0.81	0.0335
				Predicted: Kattus			
				Norvegicus Polymerese (Pno) I::			
				(Dna Directed)			
				Polynentide H			
PND5	DBP500	LIMMA	ILMN 1359985	(Predicted) (Polr3H)	Polr3H	1.40	0.0335

				Predicted: Rattus			
				Norvegicus Similar To			
				Riken Cdna			
				2010110M21			
				(Predicted)	Loc29099		
PND5	DBP500	LIMMA	ILMN 1368345	(Loc290999)	9	1.32	0.0338
				Predicted: Rattus			
				Norvegicus Similar To			
				Lrrgt00176	Loc50034		
PND5	DBP500	LIMMA	ILMN 1365109	(Loc500343)	3	0.62	0.0338
			-	Predicted: Rattus			
				Norvegicus Similar To			
				Serine/Threonine/Tyro			
				sine-Interacting			
				Protein (Protein			
				Tyrosine Phosphatase-			
				Like Protein)			
				(Phosphoserine/Three			
				nine/Tyrosine			
				Interaction Protein)	Loc68924		
PND5	DBP500	LIMMA	ILMN 1349539	(Loc689246)	6	0.75	0.0345
11100	DBI500	Linnin		Rattus Norvegicus	0	0.75	0.0515
PND5	DBP500	LIMMA	II MN 1354418	Moesin (Msn)	Msn	0.76	0.0345
11105	DBI 500		12011(_1334410	Rattus Norvegicus	141511	0.70	0.0545
				Rna Binding Motif			
PND5	DBP500	LIMMA	II MN 1364535	Protein 39 (Rhm39)	Rhm39	0.77	0.0346
11105	DBI 500		12011(_150+555	Rattus Norvegicus	Romsy	0.77	0.0540
				A cyl-Coenzyme A			
				Binding Domain			
PND5	DBP500	ιιмма	II MN 1376438	Containing 6 (Achd6)	A chd6	1 22	0.0347
TND5	DBI 500	LININIA	1121011 1 _1370438	Rattus Norvegicus	Acouo	1.22	0.0347
				Solute Carrier Family			
				7 (Cationia Amino			
				A cid Transporter V+			
				System) Member 1			
DND5	DBB200		II MN 1251408	(Slo7A1)	Slo7A1	1 22	0.0347
11105	001300		1551400	Predicted: Rattus		1.23	0.0347
				Norvegicus Similar To			
				Hypothetical Protein			
				Mgc14151 (Predicted)	Rad15506		
PND5	DBP500	τινινα	II MN 1355746	$(\text{R}_{\text{ad}}1559617)$	17	1 25	0.0350
TNDJ	DBI 500	LIMINIA	1LWIN_1333740	(Rgu1559017) Predicted: Pattus	17	1.23	0.0350
				Norvegious Similar To			
				Otthump00000044720			
				(Predicted)	Rad15612		
PND5	DBP500	I IMMA	II MN 1374241	(Rgd1561353)	53	0.76	0.0350
11105	001300		12/11/10_13/4241	Predicted: Rattus	55	0.70	0.0350
				Norvegicus Similar To			
				Genes Associated			
				With Retinoid_Ifn_	Rgd15653		
PND5	DBP500	LIMMA	ILMN 1358223	Induced Mortality 19	58	1 26	0.0350
11100	DD1 300	1.1.1.1.1.1.1.1	1000220	maacea monunty 1)	20	1.20	0.0550

				(Predicted)			
				(Rgd1565358)			
				Rattus Norvegicus			
				Cell Division Cycle 25			
				Homolog B (S.			
PND5	DBP500	LIMMA	ILMN_1363751	Pombe) (Cdc25B)	Cdc25B	1.29	0.0351
				Rattus Norvegicus			
				Similar To			
				Hypothetical Protein			
				Flj10154	Rgd13100		
PND5	DBP500	LIMMA	ILMN_1367208	(Rgd1310061)	61	0.76	0.0351
				Predicted: Rattus			
				Norvegicus Sorting			
	DDD500		H M 1250010	Nexin 14 (Predicted)	0 14	0.67	0.02(0
PND5	DBP200	LIMMA	ILMN_1358019	(Snx14)	Snx14	0.6/	0.0369
				Rattus Norvegicus			
				Lukaryouc Translation			
				Rinding Protein 2			
PND5	DBP500	ιινμα	II MN 1363150	(Fif4Ebn2)	Fif4Ebp2	0.77	0.0370
TND5	DBI 500	LININA	111WII 1303130	Predicted: Rattus	LII4L0p2	0.77	0.0370
				Norvegicus Similar To	Loc29070		
PND5	DBP500	LIMMA	ILMN 1350576	Palladin (Loc290704)	4	0.52	0.0370
11120	DBICOU	Linnin		Predicted: Rattus	•	0.02	0.0370
				Norvegicus Similar To			
				Hypothetical Protein			
				Kiaa1240	Loc31394		
PND5	DBP500	LIMMA	ILMN_1349311	(Loc313940)	0	0.75	0.0370
				Predicted: Rattus			
				Norvegicus Similar To			
				Lrrgt00057	Loc49963		
PND5	DBP500	LIMMA	ILMN_1350345	(Loc499638)	8	0.46	0.0370
				Rattus Norvegicus			
				Mitogen Activated			
				Protein Kinase Kinase		0.00	0.0250
PND5	DBP500	LIMMA	ILMN_1361975	I (Map2K1)	Map2K1	0.82	0.0370
				Predicted: Rattus			
				Transprintian			
				Complex Subunit 7			
PND5	DBP500	ιινμα	II MN 1353588	(Predicted) (Cnot7)	Cnot7	0.78	0.0374
TNDJ	DBI 500	LIMINIA	111WIN_1555588	Rattus Norvegicus	Clift	0.78	0.0374
				Hypoxia Induced			
PND5	DBP500	LIMMA	ILMN 1650956	Gene 1 (Hig1)	Hig1	1.37	0.0374
				Predicted: Rattus		,	
				Norvegicus Similar To			
				Lrrgt00082	Loc50039		
PND5	DBP500	LIMMA	ILMN_1361017	(Loc500398)	8	0.75	0.0374
				Predicted: Rattus			
				Norvegicus Similar To	Rgd15607		
PND5	DBP500	LIMMA	ILMN 1650346	Lim And Senescent	32	0.63	0.0374

I				Cell Antigen-Like			
				Domains 1 (Predicted)			
				(Rgd1560732)			
				Rattus Norvegicus			
				Splicing Factor,			
				Arginine/Serine-Rich			
PND5	DBP500	LIMMA	ILMN_1372737	11 (Sfrs11)	Sfrs11	0.54	0.0374
				Predicted: Rattus			
				Norvegicus Golgi			
				Associated, Gamma			
				Adaptin Ear			
				Containing, Arf			
				Binding Protein 3			
				(Predicted), Transcript			
PND5	DBP500	LIMMA	ILMN_1352867	Variant 2 (Gga3)	Gga3	0.78	0.0385
				Rattus Norvegicus			
DUD 5	DDDC00		H) O I 1271 417	Gastrin Releasing	G	1.22	0.0205
PND5	DBP500	LIMMA	ILMN_13/1417	Peptide (Grp)	Grp	1.32	0.0385
				Predicted: Rattus			
				INORVEGICUS SIMILAR TO	L a 240907		
DND5			II MAN 1259504	Lrrgt00194	L0C4989/	0.65	0.0295
FNDS	DBF300	LIIVIIVIA	1LMIN_1556594	(L0C4989/9) Dradiatad: Dattus	9	0.05	0.0383
				Norvegious Similar To			
				Putative Pro Binding	L 00/10085		
PND5	DBP500	LIMMA	II MN 1352254	Protein 1 (Loc499854)	L0C49983	0.61	0.0385
1105	DBI 500		1552254	Rattus Norvegicus		0.01	0.0505
				Ccr4-Not			
				Transcription			
				Complex. Subunit 6			
PND5	DBP500	LIMMA	ILMN 1357809	(Cnot6)	Cnot6	0.78	0.0386
			—	Rattus Norvegicus			
				Kelch-Like 24			
PND5	DBP500	LIMMA	ILMN_1651132	(Drosophila) (Klhl24)	Klhl24	0.67	0.0386
				Predicted: Rattus			
				Norvegicus Similar To			
				Putative Rna Binding	Loc50042		
PND5	DBP500	LIMMA	ILMN_1361248	Protein 1 (Loc500428)	8	0.74	0.0386
				Predicted: Rattus			
				Norvegicus			
				Polymerase I And			
				Transcript Release			
		IDOG		Factor (Predicted)	D. 0	0.50	0.0005
PND5	DBP500	LIMMA	ILMN_1350794	(Ptrf)	Ptrf	0.69	0.0386
				Predicted: Rattus			
				Norvegicus Similar To			
				Novel Protein Of			
				$(D_{11}f_{12})$ $(D_{11}f_{12})$ $(D_{11}f_{12})$			
				(Dul423) Family Member (Predicted)	Rad15624		
PND5	DBP500	I IMMA	II MN 1371362	$(R_{gd}1563438)$	38	1 24	0.0386
11105	DD1 300		121111 13/1302	(1501202720)	50	1.47	0.0500

				Predicted [.] Rattus			
				Norvegicus Similar To			
				Karvopherin			
				(Importin) Alpha 6			
				(Predicted)	Loc68444		
PND5	DBP500	LIMMA	ILMN_1650917	(Loc684447)	7	0.80	0.0387
				Predicted: Rattus			
				Norvegicus Similar To			
				Kiaa0372 Gene			
				Product (Predicted)	Rgd13060		
PND5	DBP500	LIMMA	ILMN_1356505	(Rgd1306062)	62	0.83	0.0388
				Predicted: Rattus			
				Norvegicus Similar To			
				60S Ribosomal			
				Protein L13			
				(Predicted)	Rgd15609		
PND5	DBP500	LIMMA	ILMN_1365309	(Rgd1560936)	36	1.37	0.0388
				Predicted: Rattus			
				Norvegicus Ubiquitin-			
				Like, Containing Phd			
				And Ring Finger			
				Domains 2 (Predicted)			
PND5	DBP500	LIMMA	ILMN_1530420	(Uhrf2)	Uhrf2	0.71	0.0388
				Predicted: Rattus			
				Norvegicus Growth			
				Factor Receptor			
				Bound Protein 2-			
				Associated Protein 1	~ 1 4		
PND5	DBP500	LIMMA	ILMN_1349894	(Predicted) (Gab1)	Gabl	0.80	0.0390
				Predicted: Rattus			
				Norvegicus Similar To			
				Riken Cdna	I 40007		
	DDDC00		H M 1 1 (50000	2410116105	Loc4980/	0.46	0.0200
PND5	DBP200	LIMMA	ILMN_1650298	(Loc4980/6)	6	0.46	0.0390
				Predicted: Kattus			
				INORVEGICUS SIMILAR TO	L 0050000		
DND5			II MAL 1272251	Lrrgt001/6	Loc50028	0.47	0.0200
PND5	DBP300	LIMMA	ILMIN_13/3251	(LOC300285)	5	0.4 /	0.0390
				Norvegious Similar To			
				Microfilement And			
				Actin Filament Cross			
				Linker Protein Isoform	L 0036258		
PND5	DBP500	LIMMA	ILMN 1354877	A (Loc 362587)	7	0.79	0.0393
				Rattus Norvegicus	-		
				Mitochondrial			
				Ribosomal Protein			
				L44 (Mrpl44), Nuclear			
				Gene Encoding			
PND5	DBP500	LIMMA	ILMN_1364781	Mitochondrial Protein	Mrpl44	1.25	0.0393

				Predicted: Rattus			
				Norvegicus Similar To			
				Hypothetical Protein			
				Flj20729 (Predicted)	Rgd13087		
PND5	DBP500	LIMMA	ILMN_1366921	(Rgd1308723)	23	1.31	0.0396
				Predicted: Rattus			
				Norvegicus Atpase,			
				Class I, Type 8B,			
	DDD500		H MAL 12(0542	Member I (Predicted)	A 4 - 0D 1	0.00	0.0207
PND5	DBP500	LIMMA	ILMIN_1360542	(Atp8B1)	Атрявт	0.69	0.0396
DND5	DBB200		II MN 1358267	Cathensin D (Ctsd)	Cted	1 2 1	0.0307
TND5	DBF500	LIIVIIVIA	1LIVIN_1556207	Predicted: Rattus	Cisu	1.51	0.0397
				Norvegicus Similar To			
				I rrg00135	Loc49956		
PND5	DBP500	LIMMA	ILMN 1649797	(Loc499560)	0	0.71	0.0397
11120	DDICOU			Predicted: Rattus	Ū.	0.171	0.0237
				Norvegicus Similar To			
				60S Ribosomal			
				Protein L7A			
				(Predicted)	Rgd15611		
PND5	DBP500	LIMMA	ILMN_1359928	(Rgd1561198)	98	1.30	0.0397
				Rattus Norvegicus			
				Transcription Factor			
PND5	DBP500	LIMMA	ILMN_1376542	12 (Tcf12)	Tcf12	0.78	0.0397
				Rattus Norvegicus			
DUD 5	DDDCOO			Alpha-2U Globulin	Loc25924	0.74	0.0207
PND5	DBP500	LIMMA	ILMN_1363413	Pgc13 (Loc259244)	4	2.74	0.0397
				Rattus Norvegicus			
				Triphosphate			
				Diphosphohydrolase 5			
PND5	DBP500	LIMMA	ILMN 1373210	(Entpd5)	Entpd5	0.70	0.0406
				Rattus Norvegicus			
				Polypyrimidine Tract			
				Binding Protein 2			
PND5	DBP500	LIMMA	ILMN_1363928	(Ptbp2)	Ptbp2	0.65	0.0414
				Predicted: Rattus			
				Norvegicus			
				Heterogeneous			
				Nuclear			
				Ribonucleoprotein D-			
			HINDL 12/01/4	Like (Predicted)	TT	0.77	0.0415
PND5	DR5200	LIMMA	1LMN_1360164	(Hnrpdl)	Hnrpdl	0.77	0.0415
				Predicted: Kattus			
				608 Ribosomal			
				Protein I 7A			
				(Predicted)	Rød15636		
PND5	DBP500	LIMMA	ILMN 1355120	(Rgd1563679)	79	1.29	0.0416

				Predicted: Rattus			
				Norvegicus Similar To			
				Cg8009-Pa (Predicted)	Loc29191		
PND5	DBP500	LIMMA	ILMN_1358761	(Loc291914)	4	0.82	0.0430
				Predicted: Rattus			
				Norvegicus Similar To	x 000.45		
	DDD500		H M 1256051	Ribosomal Protein	Loc29247	0.00	0.0426
PND5	DBP500	LIMMA	ILMN_1356051	L2/A (Loc2924/4)	4	0.80	0.0436
				A dn Bibogulargining			
PND5	DBP500	I IMMA	II MN 1358621	Hydrolase (Adprh)	Adorh	1 20	0.0442
TND5	DBI 500	LIMINA	112WIN_1338021	Predicted: Rattus	Aupin	1.20	0.0442
				Norvegicus			
				Loc501530	Loc50153		
PND5	DBP500	LIMMA	ILMN 1372175	(Loc 501530)	0	0.62	0.0442
11000	DBICOU	Linnin		Predicted: Rattus		0.02	0.0112
				Norvegicus Upf3			
				Regulator Of			
				Nonsense Transcripts			
				Homolog B (Yeast)			
PND5	DBP500	LIMMA	ILMN_1349703	(Predicted) (Upf3B)	Upf3B	0.81	0.0442
				Rattus Norvegicus			
				Antisense Paternally			
				Expressed Gene 3			
PND5	DBP500	LIMMA	ILMN_1368576	(Apeg3)	Apeg3	0.48	0.0447
				Predicted: Rattus			
				Norvegicus E2F			
DND5	DDD500		II MAN 1251212	Franscription Factor 5	E2E5	0.80	0.0447
PNDS	DBP300	LIMINA	1LMIN_1551215	(E2F3) Predicted: Pattus	E2F3	0.80	0.0447
				Norvegicus Similar To			
				Dna Segment Chr 16			
				Erato Doi 472			
				Expressed (Predicted)	Rgd15638		
PND5	DBP500	LIMMA	ILMN 1370551	(Rgd1563888)	88	0.80	0.0452
			_	Rattus Norvegicus			
				Nuclear Protein E3-3			
				(Rgd708545),	Rgd70854		
PND5	DBP500	LIMMA	ILMN_1370444	Transcript Variant 1	5	1.21	0.0452
				Rattus Norvegicus			
				Utp14, U3 Small			
				Nucleolar			
				Ribonucleoprotein,			
DND5	DDD500		IL MAL 1271024	Homolog A (Yeast) $(Utra 14A)$	I I too 1 4 A	0.77	0.0452
PNDS	DBP300	LIMINA	ILIMIN_15/1924	(Utp14A) Prodictod: Pottus	Utp14A	0.77	0.0432
				Norvegicus Zinc			
				Finger Protein 592			
PND5	DBP500	LIMMA	ILMN 1354654	(Predicted) (Zfp592)	Zfn592	1 23	0.0452
1100	DBICOU	Linnin		Rattus Norvegicus	Elpoyz	1.20	0.0102
PND5	DBP500	LIMMA	ILMN 1369530	Catalase (Cat)	Cat	1.59	0.0452

				Predicted: Rattus			
				Norvegicus Perq			
				Amino Acid Rich,			
				With Gyf Domain 1			
PND5	DBP500	LIMMA	ILMN 1354514	(Predicted) (Perg1)	Perg1	0.69	0.0452
				Rattus Norvegicus		,	
				Mannosidase Beta A			
PND5	DBP500	LIMMA	II MN 1355149	I vsosomal (Manha)	Manha	1 19	0.0457
11105	DBI 500	Liiviivii X	1500147	Predicted: Rattus	Withou	1.17	0.0437
				Norvegious Ellis Van			
				Croyald Syndrome 2			
				(Limbin) (Dradiated)			
DND	DDD500		HINDI 12/1107	(Limbin) (Predicted)	Б. 2	1.00	0.0459
PND5	DBP200	LIMMA	ILMIN_1361107	(Evc2)	EVC2	1.26	0.0458
				Rattus Norvegicus			
				Neuronal			
				Regeneration Related			
PND5	DBP500	LIMMA	ILMN_1357234	Protein (Nrep)	Nrep	0.75	0.0459
				Rattus Norvegicus			
				Vascular Endothelial			
				Growth Factor A			
PND5	DBP500	LIMMA	ILMN_1371686	(Vegfa)	Vegfa	0.79	0.0459
				Predicted: Rattus			
				Norvegicus Similar To			
				Glyceraldehyde-3-			
				Phosphate			
				Dehvdrogenase			
				(Phosphorylating) (Ec			
				12112 (Predicted)	Rød15634		
PND5	DBP500	LIMMA	ILMN 1369945	(Rgd1563464)	64	1 29	0.0463
11120	DBI000	Linnin	121011 (_100)) 10	Predicted: Rattus	01	1.27	0.0105
				Norvegicus Ab2-143			
				$(I \circ c 498829)$ Misc	Loc49882		
PND5	DBP500	ιιмма	II MN 1359572	Rna	Q	0.70	0.0464
TNDJ	DDI 500		1LIVII_1557572	Predicted: Pattus	,	0.70	0.0404
				Norwagious Similar To			
				Norvegicus Similar 10			
				Protein 1 (Nuclear			
				Protein 7 (Nuclear			
				(Zen 112) (Den linted)	D 115(40		
	DDD500		H) DI 12(2520	(Zap113) (Predicted)	Rgd15649	0.00	0.0464
PND5	DR5200	LIMMA	1LMIN_1363528	(Kga1564946)	40	0.80	0.0464
				Kattus Norvegicus			
				Cas-Br-M (Murine)			
				Ecotropic Retroviral			
l				Transforming			
PND5	DBP500	LIMMA	ILMN_1351226	Sequence B (Cblb)	Cblb	0.78	0.0464
				Predicted: Rattus			
				Norvegicus Formin			
				Binding Protein 4			
PND5	DBP500	LIMMA	ILMN_1371331	(Fnbp4)	Fnbp4	0.83	0.0464
				Predicted: Rattus	Loc30947		
PND5	DBP500	LIMMA	ILMN 1361015	Norvegicus Similar To	5	0.78	0.0464

				Transmembrane			
				Protein Tm9Sf3			
				(Loc309475)			
				Predicted: Rattus			
				Norvegicus Similar To			
				Riken Cdna			
DI ID 5	DDD500		H . D.L. 12(0002	1700025B16	Loc50336	1.04	0.0464
PND5	DBP500	LIMMA	ILMN_1369902	(Loc503365)	5	1.24	0.0464
				Predicted: Rattus			
DND5			II MAN 1274140	Norvegicus Dorothymagin (Dtmg)	Dtma	0.72	0.0464
PNDS	DBP300	LIMINA	1LMIN_13/4140	Paratinymosin (Puins)	Pulls	0.75	0.0404
				Norvegicus Similar To			
				Riken Cdna			
				2210421G13	Loc31510		
PND5	DBP500	LIMMA	ILMN 1363539	(Loc315106)	6	0 79	0.0469
11,00	2.21.200		120010	Predicted: Rattus	~	0.12	0.0107
				Norvegicus			
				Loc499620	Loc49962		
PND5	DBP500	LIMMA	ILMN 1370641	(Loc499620)	0	0.68	0.0469
			_	Predicted: Rattus			
				Norvegicus			
				Peroxisome			
				Proliferative Activated			
				Receptor, Gamma,			
				Coactivator-Related 1			
PND5	DBP500	LIMMA	ILMN_1367124	(Predicted) (Pprc1)	Pprc1	0.77	0.0469
				Predicted: Rattus			
				Norvegicus Similar To			
				Riken Cdna			
				2810485105 (Dradiated)	D = 112110		
DND5	DDD500		II MNI 1274785	(Predicted) (Pad1211077)	Rga15110	0.77	0.0460
FNDS	DBF300	LIMINA	1LMIN_15/4/85	(Rgu15110//) Predicted: Pattus	11	0.77	0.0409
				Norvegicus			
				Glutathione S-			
				Transferase, Alpha 4			
PND5	DBP500	LIMMA	ILMN 1352039	(Gsta4)	Gsta4	1.29	0.0472
			-	Predicted: Rattus			
				Norvegicus Similar To			
				Lrrgt00057	Loc49950		
PND5	DBP500	LIMMA	ILMN_1356833	(Loc499501)	1	1.30	0.0472
				Predicted: Rattus			
				Norvegicus Similar To			
				Cg4573-Pa	Loc68524		
PND5	DBP500	LIMMA	ILMN_1349955	(Loc685245)	5	1.35	0.0472
				Predicted: Rattus			
				Norvegicus Similar To			
				Hypothetical Protein	Dad12100		
DND5	DBB200		II MN 1650069	$(P_{ad}1210002)$	Agu13109	0 82	0.0472
FINDS	DDr300	LIMINIA	1LIVIN_1030008	(Kgu1510992)	72	0.82	0.04/2

				Predicted: Rattus			
				Norvegicus Similar To			
				Kiaa1731 Protein			
				(Predicted)	Rgd13117		
PND5	DBP500	LIMMA	ILMN_1360056	(Rgd1311723)	23	0.68	0.0472
				Predicted: Rattus			
				Norvegicus Similar To			
				60S Ribosomal			
				Protein L29 (P23)			
				(Predicted)	Rgd15624		
PND5	DBP500	LIMMA	ILMN_1361028	(Rgd1562489)	89	1.41	0.0472
				Rattus Norvegicus			
				Phospholysine			
				Phosphohistidine			
				Inorganic			
				Pyrophosphate			
PND5	DBP500	LIMMA	ILMN_1530391	Phosphatase (Lhpp)	Lhpp	1.19	0.0491
				Rattus Norvegicus			
				Tropomyosin 4			
PND5	DBP500	LIMMA	ILMN_1357093	(Tpm4)	Tpm4	0.79	0.0491
				Predicted: Rattus			
				Norvegicus Similar To			
				Cg11388-Pa			
				(Predicted)	Rgd13081		
PND5	DBP500	LIMMA	ILMN_1649894	(Rgd1308154)	54	0.77	0.0500
				Predicted: Rattus			
				Norvegicus Similar To	Loc36194		
PND5	DBP500	SAM	ILMN_1369444	Orf4 (Loc361942)	2	0.70	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To	Loc36349		
PND5	DBP500	SAM	ILMN_1355694	Ac1262 (Loc363492)	2	0.66	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
	DDD	<i>a</i> +) <i>(</i>	WART 107000	Lrrg00116	Loc36254	0.65	0.0 <i>5</i>
PND5	DBP500	SAM	ILMN_1352230	(Loc362543)	3	0.65	<0.05
				Rattus Norvegicus			
				Cytocnrome C			
				Assembly Protein			
				Homolog (S			
DND5	DBB200	SAM	II MN 1252060	Corregisian (Cov17)	Cov17	1.20	<0.05
TND5	DBF500	SAM	1LIVIN_1555009	Dradiated: Dattus	COXI/	1.50	<0.03
				Norvegicus Similar To			
				Krey Interaction			
				Tranned Protein 1			
				(Krey Interaction			
				Trapped 1) (Cerebral			
				Cavernous			
				Malformations 1			
				Protein Homolog)	Loc36231		
PND5	DBP500	SAM	ILMN 1359410	(Loc362317)	7	0.76	< 0.05
-				· · · /			-

				Rattus Norvegicus			
				Origin Recognition			
				Complex, Subunit 2-			
PND5	DBP500	SAM	ILMN_1376515	Like (Yeast) (Orc2L)	Orc2L	0.79	< 0.05
			_	Rattus Norvegicus			
				Lecithin Cholesterol			
PND5	DBP500	SAM	ILMN 1367035	Acyltransferase (Lcat)	Lcat	0.77	< 0.05
				Predicted: Rattus			
				Norvegicus E2F			
				Transcription Factor 5			
PND5	DBP500	SAM	ILMN_1351213	(E2F5)	E2F5	0.78	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To	Loc49804		
PND5	DBP500	SAM	ILMN_1371063	Orf4 (Loc498048)	8	0.69	< 0.05
				Predicted: Rattus			
				Norvegicus Cyclin L2			
PND5	DBP500	SAM	ILMN_1650840	(Predicted) (Ccnl2)	Ccnl2	0.73	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Lrrgt00057	Loc50108		
PND5	DBP500	SAM	ILMN_1366649	(Loc501087)	7	0.66	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Phd Finger Protein 20-			
				Like 1 Isoform 1	Loc31496		
PND5	DBP500	SAM	ILMN_1350792	(Loc314964)	4	0.83	< 0.05
				Predicted: Rattus			
				Norvegicus Deah			
				(Asp-Glu-Ala-			
				Asp/His) Box			
		<i></i>		Polypeptide 57			
PND5	DBP500	SAM	ILMN_1373580	(Dhx57)	Dhx57	0.83	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Riken Cdna	D 116655		
	DDDC00			2810403A07	Rgd15657	0.74	-0.05
PND5	DBP500	SAM	ILMN_1354105	(Kgd1565775)	/5	0.74	< 0.05
				Predicted: Rattus			
				Norvegicus Prp39 Pre-			
				Mirna Processing			
				Factor 39 Homolog			
DND4		CANA	II MNL 1255422	(reast) (realitied)	Dmaf20	0.77	<0.05
PND5	DBP200	SAM	1LIVIN_1355423	(rfp139) Dradiatada Datta	PTP159	0.//	<0.05
				Predicted: Kattus			
				A oul Coonsume A			
				Acyl-Coenzyme A			
				Containing 5	L 0069250		
DND5	DPD500	SAM	II MN 1251552	$(1 \circ 682502)$	2	0.78	<0.05
TNDS	001300	SAW	1LIVIIN_1331333		5	0.70	~0.03
	DDDC00		H NOL 107/077	Kattus Norvegicus	D 10	1.55	-0.05
PND5	DRA200	SAM	$1LMN_{13}/63/5$	Kibonuclease, Knase	Knase12	1.55	<0.05

				A Family, 12 (Non-			
				Active) (Rnase12)			
				Rattus Norvegicus			
				High Mobility Group			
				Nucleosomal Binding			
PND5	DBP500	SAM	ILMN_1362726	Domain 3 (Hmgn3)	Hmgn3	0.69	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Novel Protein Of			
				Unknown Function			
				(Duf423) Family			
				Member (Predicted)	Rgd15634		
PND5	DBP500	SAM	ILMN_1371362	(Rgd1563438)	38	1.24	< 0.05
				Rattus Norvegicus			
				Polypyrimidine Tract			
	DDDC00	GANG	H M L 12(2020	Binding Protein 2	D.I. O	0.00	-0.05
PND5	DBP200	SAM	ILMN_1363928	(Ptbp2)	Ptbp2	0.66	< 0.05
				Rattus Norvegicus			
				Linc Finger with			
				Pantidasa Domain			
PND5	DBP500	SAM	II MN 1350027	(Zufen)	Zufen	0.79	<0.05
TND5	DBI 500	SAN	112WIN_1330927	Predicted: Rattus	Zuisp	0.79	<0.05
				Norvegicus			
				Chromodomain			
				Helicase Dna Binding			
				Protein 6 (Predicted)			
PND5	DBP500	SAM	ILMN 1369694	(Chd6)	Chd6	0.83	< 0.05
			_	Rattus Norvegicus			
				Tetraspanin 2			
PND5	DBP500	SAM	ILMN_1370492	(Tspan2)	Tspan2	0.82	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Sr Rich Protein	Rgd13073		
PND5	DBP500	SAM	ILMN_1374578	(Rgd1307395)	95	0.71	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
DUD	DDD	<i>a</i> . . .		Lrrg00135	Loc50163	0.40	.0.07
PND5	DBP500	SAM	ILMN_1371120	(Loc501637)		0.48	< 0.05
				Predicted: Kattus			
				INOIVEGICUS SIMIlar 10 Dutativo Dra Dindina	L 0050150		
PND5	DBP500	SAM	II MN 1362324	Protein 1 (Loc501502)	3	0.64	<0.05
11103	DD1 300	SAW	12/01/0_1502524	Predicted: Rattus	5	0.04	~0.05
				Norvegicus Similar To			
				Cdna Sequence			
				Bc024479			
				(Loc500974). Misc	Loc50097		
PND5	DBP500	SAM	ILMN 1365562	Rna.	4	0.79	< 0.05
			-	Rattus Norvegicus			
PND5	DBP500	SAM	ILMN_2040519	Ring-Box 1 (Rbx1)	Rbx1	1.20	< 0.05

				Predicted: Rattus			
				Norvegicus			
				Desmoplakin,			
				Transcript Variant 2			
PND5	DBP500	SAM	ILMN 1349971	(Dsp)	Dsp	0.73	< 0.05
			-	Rattus Norvegicus	· ·		
				Fgfr1 Oncogene			
PND5	DBP500	SAM	ILMN 1373016	Partner 2 (Fgfr1Op2)	Fgfr1Op2	0.82	< 0.05
			_	Predicted: Rattus	<u> </u>		
				Norvegicus			
				Loc498674	Loc49867		
PND5	DBP500	SAM	ILMN 1368776	(Loc498674)	4	0.79	< 0.05
				Predicted: Rattus			
				Norvegicus Pumilio 1			
				(Drosophila)			
PND5	DBP500	SAM	ILMN 1363515	(Predicted) (Pum1)	Pum1	0 79	<0.05
	221000			Predicted: Rattus		0.12	0.00
				Norvegicus Similar To			
				Retrovirus-Related Pol			
				Polyprotein	Loc36231		
PND5	DBP500	SAM	ILMN 1373694	$(Loc_{3}62315)$	5	0.69	<0.05
11100	DDI 500	57 111		Predicted: Rattus	5	0.07	-0.05
				Norvegicus Similar To			
				I rrot00008	Loc50038		
PND5	DBP500	SAM	II MN 1355226	$(I_{0}c_{5}00380)$	0	0.69	<0.05
TND5	DDI 500	SAN	111VII_1555220	Predicted: Rattus	0	0.07	<0.05
				Norvegicus Similar To			
				Orf? Consensus			
				Sequence Encoding			
				Endonuclease And			
				Reverse Transcriptase			
				Minus Rnaseh	Loc/19955		
DND5	DBB200	SAM	II MN 1262227	$(I \circ c^{4} 0 0 554)$	L0C49955	0.60	<0.05
TNDJ	DDI 500	SAM	1LWIN_1303227	Dradiatad: Dattus	4	0.09	<0.05
				Norvegious Similar To			
				I rra00125	L 0050154		
PND5	DBP500	SAM	II MN 1356549	(Loc501548)	8	0.48	<0.05
11105	DD1 300	SAW	1210111 1330340	Rattus Norvagious	0	0.40	~0.03
DND5	DBB500	SAM	II MN 1256426	Allantoicase (Alla)	Alle	1 / 2	<0.05
TNDS	DBr 300	SAW	1LIVIIN_1330420	Predicted: Dattus	Alle	1.43	~0.03
				Norvegious A			
				Disintegrin And			
				Metalloprotesso			
				Domain 22 (Dradiated)			
DND5	DBB200	SAM	II MN 1251007	(A dam22)	Adam 22	0.60	<0.05
TNDS	DBr 300	SAW	1LIVIIN_133108/	Dradiatad: Dattag	Auaiii33	0.09	~0.03
				Norvegious Similar To			
				Indivegicus Siiiiliai 10 I rrat00176	L 0050001		
DND5		CAM	II MNI 1271641	$L_{10001/0}$	6	0.65	<0.05
PNDS	DBP300	SAM	1LIVIIN_13/1041	(L00300910)	0	0.03	~0.05
		a		Predicted: Rattus		0	
PND5	DBP500	SAM	ILMN_1354030	Norvegicus Triple	Trio	0.62	< 0.05

Image: constraint of the second structureImage: constraint of the second structure(Ptprf Interacting) (Trio)Image: constraint of the second structurePND5DBP500SAMILMN 1375194Predicted: Rattus Norvegicus Similar To Lrrg00116Loc500866-PND5DBP500SAMILMN 1375194(Loc500867)70.75<0.05PND5DBP500SAMILMN_1366540(Loc500721)Loc50072PND5DBP500SAMILMN_1366540(Loc500721)10.57<0.05PND5DBP500SAMILMN_1366540(Loc500721)10.67<0.05PND5DBP500SAMILMN_1362603(Loc499531)10.67<0.05PND5DBP500SAMILMN_1362603(Loc499531)10.67<0.05Predicted: Rattus NorvegicusNorvegicusNorvegicusImage: constraint of the second seco
Image: constraint of the systemImage: constraint of the systemImage: constraint of the systemImage: constraint of the systemPND5DBP500SAMILMN_1375194(Loc500867)70.75<0.05
Image: second
Norvegicus Similar To Loc50086
PND5 DBP500 SAM ILMN_1375194 Lrrg00116 Loc50086 7 0.75 <0.05 PND5 DBP500 SAM ILMN_1375194 (Loc500867) 7 0.75 <0.05
PND5 DBP500 SAM ILMN 1375194 (Loc500867) 7 0.75 <0.05 PND5 DBP500 SAM ILMN_1375194 Predicted: Rattus Norvegicus Loc500721 Loc50072 I 0.75 <0.05
PND5DBP500SAMILMN_1366540Predicted: Rattus Norvegicus Loc500721Loc50072PND5DBP500SAMILMN_1366540(Loc500721)10.57<0.05
PND5DBP500SAMILMN_1366540Norvegicus Loc500721Loc500720.57<0.05PND5DBP500SAMILMN_1366540(Loc500721)10.57<0.05
PND5 DBP500 SAM ILMN_1366540 Loc500721 (Loc500721) Loc50072 1 0.57 <0.05 PND5 DBP500 SAM ILMN_1366540 Predicted: Rattus Norvegicus Similar To Lrrgt00176 Loc49953 -
PND5 DBP500 SAM ILMN_1366540 (Loc500721) 1 0.57 <0.05 PND5 DBP500 SAM ILMN_1366540 (Loc500721) 1 0.57 <0.05
PND5 DBP500 SAM ILMN_1362603 (Loc499531) 1 0.67 <0.05
PND5 DBP500 SAM ILMN_1362603 (Loc499531) 1 0.67 <0.05
PND5 DBP500 SAM ILMN_1362603 (Loc499531) 1 0.67 <0.05 Predicted: Rattus Norvegicus Norvegicus Norv
PND5 DBP500 SAM ILMN_1362603 (Loc499531) 1 0.67 <0.05 Predicted: Rattus Norvegicus Norvegicus 1 0.67 <0.05
Norvegicus
Norvegicus
Dualing/Opting Dish
PND5 DBD500 SAM HAN 1268627 Coiled Coil 2 (Dare 2) Dare 2 0.70 <0.05
PND3 DBP300 SAWI ILIVIN_1308027 Colled-Coll 2 (PSIC2) PSIC2 0.79 <0.03
Norvegicus Kinesin
Family Member 5B
PND5 DBP500 SAM II MN 1354288 (Kif5B) Kif5B 0.82 <0.05
Predicted: Rattus
Norvegicus Kinectin 1
PND5 DBP500 SAM ILMN 1366075 (Predicted) (Ktn1) Ktn1 0.83 <0.05
Predicted: Rattus
Norvegicus Similar To
Lrrgt00057 Loc49956
PND5 DBP500 SAM ILMN 1650107 (Loc499564) 4 0.65 <0.05
Rattus Norvegicus
Transcription Factor
PND5 DBP500 SAM ILMN_1361164 Myocardin (Myocd) Myocd 0.81 <0.05
Rattus Norvegicus
Splicing Factor,
Arginine/Serine-Rich
PND5 DBP500 SAM ILMN_1372737 11 (Sfrs11) Sfrs11 0.76 <0.05
Rattus Norvegicus
Thyrotrophic
Embryonic Factor
PND5 DBP500 SAM ILMN_1372235 (Tet) Tet 0.84 <0.05
Predicted: Rattus
Norvegicus Similar 10
nypointeical Protein Mac14151 (Dredicted) Dad15506
PND5 DBP500 SAM II MN 1355746 (Bad1559617) 17 1 20 <0.05
Rattus Norvagieus
Similar To
Hypothetical Protein
Fli10154 Rgd13100
PND5 DBP500 SAM ILMN 1367208 (Rgd1310061) 61 0.81 <0.05

PND5
11120
PND5
PND5
PND5
PND5
PND5
PND5
PND5
DND
PND5
PND5

				Amino Acid Rich,			
				With Gyf Domain 1			
				(Predicted) (Perq1)			
				Predicted: Rattus			
				Norvegicus			
				Hypothetical Gene			
				Supported By			
	DDD500	<i></i>		Nm_171983	Loc49776	0.00	0.0 7
PND5	DBP500	SAM	ILMN_1372029	(Loc497766)	6	0.82	<0.05
				Predicted: Rattus			
				Norvegicus Cac25			
				(Cell Division Cycle 22 Veest Herneles)			
DND5	DDD500	SAM	II MAN 1252520	25, Yeast, Homolog)	Cda22	0.96	<0.05
PNDS	DBP300	SAM	1LMIN_1555529	(Cuc25) Dradiatad: Dattua	Cdc25	0.80	<0.03
				Nervegieus Similar To			
				Hypothetical Protein			
				King0520 (Predicted)	L 0020410		
PND5	DBP500	SAM	ILMN 1356329	(Loc 304104)	4	0.81	<0.05
11120	DBICOU	011101		Predicted: Rattus	•	0.01	0.00
				Norvegicus Golgi			
				Associated, Gamma			
				Adaptin Ear			
				Containing, Arf			
				Binding Protein 3			
				(Predicted), Transcript			
PND5	DBP500	SAM	ILMN_1352867	Variant 2 (Gga3)	Gga3	0.83	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Microsomal			
				Glutathione S-			
				Transferase 2			
PND5	DBP500	SAM	ILMN_1370709	(Predicted) (Mgst2)	Mgst2	1.37	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Signal Recognition			
	DDD500	<i></i>		Particle,72 Kda	Loc49835		0.0 7
PND5	DBP500	SAM	ILMN_1355550	Subunit (Loc498351)	1	0.78	< 0.05
				Predicted: Rattus			
				Norvegicus Similar 10	L == 409(2		
DND5	DDD500	SAM	II MNI 1250802	LIIg(00170)	L0C49802	0.68	<0.05
TNDS	DBr 300	SAW	1210111 1330803	Dredicted: Pattus	5	0.00	~0.05
				Norvegicus Similar To			
				Histone-Lysine N-			
				Methyltransferase H3			
				Lysine-4 Specific			
				(Histone H3-K4			
				Methyltransferase)			
				(H3-K4-Hmtase) (Set	Loc50317		
PND5	DBP500	SAM	ILMN_1363605	Domain-Containing	6	0.77	< 0.05

				Protein 7)			
				(Loc503176)			
				Predicted: Rattus			
				Norvegicus Similar To			
DND5	DDD500	CAM	UNDI 12(1017	Lrrgt00082	Loc50039	0.90	<0.05
PND5	DBP200	SAM	ILMIN_136101/	(LOC500398) Rettus Norwagious Wd	8	0.80	<0.05
				Repeat And Socs Box-			
				Containing 1 (Wsb1)			
PND5	DBP500	SAM	ILMN 1357658	Transcript Variant 2	Wsb1	0.84	< 0.05
				Rattus Norvegicus			
				Vascular Endothelial			
				Growth Factor C			
PND5	DBP500	SAM	ILMN_1349830	(Vegfc)	Vegfc	0.81	< 0.05
				Predicted: Rattus			
				Norvegicus Cellular			
				Protein 1 (Manned)			
PND5	DBP500	SAM	ILMN 1349215	(Crahn1)	Crabn1	1 19	<0.05
11105	DDI 500	57 1111	12.011(_15.1)215	Predicted: Rattus	Cluopi	1.17	-0.05
				Norvegicus Similar To			
				Lrrgt00194	Loc36188		
PND5	DBP500	SAM	ILMN_1361625	(Loc361885)	5	0.70	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To	T 100.00		
	DDD500	CAN	H M L 1250000	Lrrgt00176	Loc49866	0.71	-0.05
PND5	DBP200	SAM	ILMN_1359908	(L0C498669) Dradiatad: Dattua	9	0.71	< 0.05
				Norvegicus Similar To			
				Fksg26 Protein			
				(Predicted)	Loc29208		
PND5	DBP500	SAM	ILMN_1373089	(Loc292082)	2	0.77	< 0.05
				Rattus Norvegicus			
				Mitogen Activated			
				Protein Kinase Kinase			
PND5	DBP500	SAM	ILMN_1361975	1 (Map2K1)	Map2K1	0.87	< 0.05
				Predicted: Rattus			
				Norvegicus Similar 10 Bilton Cdna			
				1200016B10			
				(Predicted)	Rgd13086		
PND5	DBP500	SAM	ILMN 1372435	(Rgd1308695)	95	0.83	< 0.05
			_	Predicted: Rattus			
				Norvegicus			
				Chondroitin Sulfate			
DUDE	DDD	G 13 f		Proteoglycan 2		0.00	.0.07
PND5	DBP500	SAM	ILMN_1373952	(Cspg2)	Cspg2	0.82	< 0.05
DUDE	DDD	a 13 f		Rattus Norvegicus		0.01	.0.07
PND5	DBP500	SAM	ILMN_1356649	Cap-Gly Domain	Clip1	0.84	< 0.05

Image: state in the s					Containing Linker			
PND5 DBP500 SAM ILMN 1350958 Acl-163 (Loc49864) Acl-163 (Loc49864) Loc49864 A PND5 DBP500 SAM ILMN 1350958 Acl-163 (Loc498644) 4 0.83 <0.05					Protein 1 (Clip1)			
PND5DBP500SAMILMN_1350958Acl-163 (Loc498644)40.683<0.05PND5DBP500SAMILMN_1358817(Ada)Ada1.70<0.05					Predicted: Rattus			
PND5 DBP500 SAM ILMN_1350958 Acl-163 (Loc498644) 4 0.83 <0.05 PND5 DBP500 SAM ILMN_1358817 (Ada) Ada 1.70 <0.05					Norvegicus Similar To	Loc49864		
PND5 DBP500 SAM IL.MN_1358817 Ratus Norvegicus Adenosine Deaminase (Ada) Ada 1.70 <0.05 PND5 DBP500 SAM IL.MN_1358817 (Ada) Ada 1.70 <0.05	PND5	DBP500	SAM	ILMN_1350958	Ac1-163 (Loc498644)	4	0.83	< 0.05
PND5 DBP500 SAM ILMN_1358817 (Ada) Ada 1.70 <0.05 PND5 DBP500 SAM ILMN_1358817 (Ada) Ada 1.70 <0.05					Rattus Norvegicus			
PND5 DBP500 SAM ILMN_1358817 (Ada) Ada 1.70 <0.05 PND5 DBP500 SAM ILMN_1356051 Predicted: Rattus Norvegicus Similar To Ribosomal Protein (Asp-Glu-Ala-Asp) Box Polypeptide 17 Loc29247 4 0.86 <0.05					Adenosine Deaminase			
PND5 DBP500 SAM ILMN 1356051 L27A (Loc292474) Ribosomal Protein Ribosomal Protein Ribosomal Protein Loc29247 4 0.86 <0.05 PND5 DBP500 SAM ILMN 1356051 L27A (Loc292474) 4 0.86 <0.05	PND5	DBP500	SAM	ILMN_1358817	(Ada)	Ada	1.70	< 0.05
PND5 DBP500 SAM ILMN 1356051 L27A (Loc292474) 4 0.86 <0.05 PND5 DBP500 SAM ILMN 1356051 L27A (Loc292474) 4 0.86 <0.05					Predicted: Rattus			
PND5 DBP500 SAM ILMN 1356051 L27A (Loc292474) 4 0.86 <0.05 PND5 DBP500 SAM ILMN 1356051 L27A (Loc292474) 4 0.86 <0.05					Norvegicus Similar To			
PND5 DBP500 SAM ILMN_1356051 L27A (Loc292474) 4 0.86 <0.05 Predicted: Rattus Norvegicus Dead (Asp-Glu-Ala-Asp) Box Polypeptide 17 Norvegicus Cada <t< td=""><td></td><td></td><td><i></i></td><td></td><td>Ribosomal Protein</td><td>Loc29247</td><td>0.07</td><td></td></t<>			<i></i>		Ribosomal Protein	Loc29247	0.07	
PND5 DBP500 SAM ILMN_135509 (Ddx17) Ddx17 0.80 <0.05	PND5	DBP500	SAM	ILMN_1356051	L27A (Loc292474)	4	0.86	< 0.05
PND5 DBP500 SAM ILMN_1355095 (Dakl7) Ddx17 0.80 <0.05 PND5 DBP500 SAM ILMN_1355095 (Ddx17) Ddx17 0.80 <0.05					Predicted: Rattus			
PND5 DBP500 SAM ILMN_1355095 (Ddx17) Ddx17 0.80 <0.05 PND5 DBP500 SAM ILMN_1355095 (Ddx17) Ddx17 0.80 <0.05					Norvegicus Dead			
PND5 DBP500 SAM ILMN_1355095 (Ddx17) Ddx17 0.80 <0.05 PND5 DBP500 SAM ILMN_1355095 (Ddx17) Ddx17 0.80 <0.05					(Asp-Glu-Ala-Asp)			
PND5 DBP500 SAM ILMN_1353095 (DdX17) DdX17 0.80 <0.05 PND5 DBP500 SAM ILMN_1373686 Gonadotropin- Releasing Hormone 1 (Gnrh1) Gnrh1 0.82 <0.05	DND5	DDD500	GAM	U MAL 1255005	Box Polypeptide 1/	DJ 17	0.00	-0.05
PND5DBP500SAMILMN_1373686(Gondadotropin- Releasing Hormone 1 (Girth1)Gnrh10.82<0.05PND5DBP500SAMILMN_1373686(Girth1)Gnrh10.82<0.05	PND5	DBP200	SAM	ILMIN_1355095	(Ddx17)	Ddx1/	0.80	<0.05
PND5DBP500SAMILMN_1373686Gondoutopin- Releasing Hormone 1Gnrh10.82<0.05PND5DBP500SAMILMN_1373686Predicted: Rattus Norvegicus Sorting Nexin 14 (Predicted)Snx140.76<0.05					Canadatronin			
PND5DBP500SAMILMN_1373686(Gnrh1)Gnrh10.82<0.05PND5DBP500SAMILMN_1373686(Gnrh1)Gnrh10.82<0.05					Balaasing Harmona 1			
PND5 DBP500 SAM ILMN_1373086 Offmin 1 0.82 <0.05 PND5 DBP500 SAM ILMN_1358019 Predicted: Rattus Norvegicus Sorting Nexin 14 (Predicted) Snx14 0.76 <0.05	DND5	DDD500	SAM	II MNI 1272686	(Carb1)	Gurh1	0.82	<0.05
PND5DBP500SAMILMN_1358019(Snx14)Snx140.76<0.05PND5DBP500SAMILMN_1358019(Snx14)Snx140.76<0.05	FNDS	DBF300	SAM	ILIMIN_15/5080	(UIIIII) Dradiatad: Dattus	GIIIII	0.82	<0.03
PND5DBP500SAMILMN_1358019Norvegicus Rul (Sux14)Snx140.76<0.05PND5DBP500SAMILMN_1348984Predicted: Rattus Norvegicus Rho Gtpase ActivatingArhgap90.84<0.05					Norvegicus Sorting			
PND5 DBP500 SAM ILMN_1358019 (Snx14) Snx14 0.76 <0.05 PND5 DBP500 SAM ILMN_1358019 (Snx14) Snx14 0.76 <0.05					Notice Soluting			
PND5 DBP500 SAM ILMN_1360017 (JMAT4) 0.70 50.05 PND5 DBP500 SAM ILMN_1348984 Predicted: Rattus Norvegicus Rho 4 <0.05	PND5	DBP500	SAM	II MN 1358019	(Snx14)	Snx14	0.76	<0.05
PND5DBP500SAMILMN_1348984Protein 9 (Arlgap9)Arlgap90.84<0.05PND5DBP500SAMILMN_1348984Protein 9 (Arlgap9)Arlgap90.84<0.05	11105	DDI 500	57 1111	12011(_155001)	Predicted: Rattus	SHAT	0.70	-0.05
PND5DBP500SAMILMN_1348984Protein 9 (Arhgap9)Arhgap90.84<0.05PND5DBP500SAMILMN_1348984Predicted: Rattus Norvegicus Dmx-LikeNorvegicus Dmx-LikePND5DBP500SAMILMN_13607461 (Predicted) (Dmx11)Dmx110.80<0.05					Norvegicus Rho			
PND5DBP500SAMILMN_1348984Protein 9 (Arhgap9)Arhgap90.84<0.05PND5DBP500SAMILMN_1360746Predicted: Rattus Norvegicus Dmx-Like0.80<0.05					Gtpase Activating			
PND5DBP500SAMILMN_1360746Predicted: Rattus Norvegicus Dmx-Like 1 (Predicted) (Dmx11)Dmx110.80<0.05PND5DBP500SAMILMN_13607461 (Predicted) (Dmx11)Dmx110.80<0.05	PND5	DBP500	SAM	ILMN 1348984	Protein 9 (Arhgap9)	Arhgap9	0.84	< 0.05
PND5DBP500SAMILMN_1360746Norvegicus Dmx-Like 1 (Predicted) (Dmx11)Dmx110.80<0.05PND5DBP500SAMILMN_1360746Predicted: Rattus Norvegicus Hypothetical Protein Loc685888, TranscriptLoc68588PND5DBP500SAMILMN_1650963Variant 2 (Loc685888)81.22<0.05				_	Predicted: Rattus	<u> </u>		
PND5DBP500SAMILMN_13607461 (Predicted) (Dmx11)Dmx110.80<0.05Image: PND5Image: PND5Image: PND5Predicted: Ratus Norvegicus Hypothetical Protein Loc685888, TranscriptImage: PND5Image: PND5 <t< td=""><td></td><td></td><td></td><td></td><td>Norvegicus Dmx-Like</td><td></td><td></td><td></td></t<>					Norvegicus Dmx-Like			
PND5DBP500SAMILMN_1650963Predicted: Rattus Norvegicus Hypothetical Protein Loc685888, TranscriptLoc68588 Loc685888PND5DBP500SAMILMN_1650963Variant 2 (Loc685888)81.22<0.05	PND5	DBP500	SAM	ILMN 1360746	1 (Predicted) (Dmxl1)	Dmx11	0.80	< 0.05
PND5DBP500SAMILMN_1650963Norvegicus Hypothetical Protein Loc685888, TranscriptLoc685888 Loc6858881.22<0.05PND5DBP500SAMILMN_1650963Variant 2 (Loc685888)81.22<0.05				_	Predicted: Rattus			
PND5DBP500SAMILMN_1650963Hypothetical Protein Loc685888, TranscriptLoc685888PND5DBP500SAMILMN_1650963Variant 2 (Loc685888)81.22<0.05					Norvegicus			
PND5DBP500SAMILMN_1650963Loc685888, TranscriptLoc6858881.22<0.05PND5DBP500SAMILMN_1650963Variant 2 (Loc685888)81.22<0.05					Hypothetical Protein			
PND5DBP500SAMILMN_1650963Variant 2 (Loc685888)81.22<0.05PR01Predicted: Rattus Norvegicus Similar To Modulator Of Estrogen Induced Transcription, Transcript Variant 1 (Rgd1307526), Misc81.22<0.05					Loc685888, Transcript	Loc68588		
PND5 DBP500 SAM ILMN 1359196 Rna. 26 0.77 <0.05	PND5	DBP500	SAM	ILMN_1650963	Variant 2 (Loc685888)	8	1.22	< 0.05
PND5 DBP500 SAM ILMN 1359196 Rna. 26 0.77 <0.05					Predicted: Rattus			
PND5 DBP500 SAM ILMN 1359196 Rna. 26 0.77 <0.05					Norvegicus Similar To			
PND5DBP500SAMILMN 1359196Rna.Z60.77<0.05					Modulator Of			
PND5DBP500SAMILMN 1359196Rna.Z60.77<0.05					Estrogen Induced			
PND5 DBP500 SAM ILMN 1359196 Rna. Z6 0.77 <0.05					Transcription,			
PND5 DBP500 SAM ILMN 1359196 Rna. Rgd130/526), Misc Rgd130/5 26 0.77 <0.05					Transcript Variant 1	D 112075		
רעאד א א א א א א א א א א א א א א א א א א			CAN	IL MAL 1250106	(Kgd130/526), Misc	Kga13075	0.77	<0.05
Drodieta J. Dattera	PNDS	DBF200	SAM	1LIVIIN_1339196	Killä. Dradiatad: Dattara	20	0.//	<0.05
Predicted: Kattus					Norwagiaus			
INDIVEGICUS Hynothatical Gana					Hypothetical Cana			
Supported By					Supported By			
Nm 001004446 Loc49774					Nm 001004446	Loc49774		
PND5 DBP500 SAM ILMN 1349796 (Loc497742) 2 0.85 <0.05	PND5	DBP500	SAM	ILMN 1349796	(Loc497742)	2	0.85	< 0.05

				Rattus Norvegicus Similar To Riken			
				Cdna D630029K19	Rgd13071		
PND5	DBP500	SAM	ILMN_1369614	(Rgd1307100)	00	0.86	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Cdna Sequence	D . 115615		
DND5	DDD500	SAM	IL MAN 1270146	Bc022692 (Predicted)	Rga15615	0.91	<0.05
FNDS	DBF300	SAM	1LIMIN_13/0140	(Rgu1501555) Predicted: Pattus	55	0.81	<0.03
				Norvegicus Similar To			
				Mtan4 Protein	Loc50105		
PND5	DBP500	SAM	ILMN 1356002	(Loc 501057)	7	0.84	< 0.05
				Predicted: Rattus			
				Norvegicus Cellular			
				Retinoic Acid Binding			
PND5	DBP500	SAM	ILMN_1367834	Protein 2 (Crabp2)	Crabp2	1.31	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
		<i></i>		Ribosomal Protein	Loc49932	a a a	0.05
PND5	DBP500	SAM	ILMN_1349611	L27A (Loc499321)	1	0.82	< 0.05
				Predicted: Rattus			
				Iso12(B) Protein			
PND5	DBP500	SAM	II MN 1354070	$(I_{Sg12}(B))$ roteni $(I_{Sg12}(B))$	$I_{sg12}(B)$	1 23	<0.05
I ND5	DBI 500	SAN	1121011 1 _1334070	Predicted: Rattus	13g12(D)	1.23	<0.05
				Norvegicus Upf3			
				Regulator Of			
				Nonsense Transcripts			
				Homolog B (Yeast)			
PND5	DBP500	SAM	ILMN_1349703	(Predicted) (Upf3B)	Upf3B	0.87	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Suppressor Of			
				Variegation 4-20			
				Homolog 2 (Dresephile)			
				(Drosophila) (Predicted)			
PND5	DBP500	SAM	ILMN 1361143	(Suv420H2)	Suv420H2	0.83	< 0.05
				Rattus Norvegicus			
				Integrin Beta 3			
				Binding Protein			
				(Beta3-Endonexin)			
PND5	DBP500	SAM	ILMN_1373985	(Itgb3Bp)	Itgb3Bp	0.86	< 0.05
				Predicted: Rattus	1		
DND	DDD500	CAM	II MNI 1271124	Norvegicus Similar To	L0C50096	0.77	<0.05
PNDS	0064900	SAM	1LIVIIN_13/1124	Dal-12 (LOCOUU90U) Predicted: Pattus	U	0.//	~0.05
				Norvegicus Similar To			
				Hypothetical Protein	Rgd13079		
PND5	DBP500	SAM	ILMN_1359345	Mgc32132 (Predicted)	15	0.71	< 0.05

				(Rgd1307915)			
				Rattus Norvegicus			
				Retinoid X Receptor			
PND5	DBP500	SAM	ILMN_1376944	Beta (Rxrb)	Rxrb	0.88	< 0.05
				Rattus Norvegicus G			
				Protein-Coupled			
				Receptor Kinase 4			
PND5	DBP500	SAM	ILMN_1362371	(Grk4)	Grk4	0.83	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Hoxa-9 (Predicted)	Loc29709		
PND5	DBP500	SAM	ILMN_1367919	(Loc297099)	9	0.83	< 0.05
				Predicted: Rattus			
				Norvegicus Mitogen-			
				Activated Protein			
DND5	DDD500	GAM	IL MAL 12(9405	Kinase Kinase Kinase	Mar 4V2	0.97	<0.05
PND5	DBP300	SAM	ILMIN_1308495	Rinase 3 (Map4K3)	мар4К3	0.87	<0.05
				Card Not			
				Transprintion			
				Complex Subunit 6			
PND5	DBP500	SAM	II MN 1357809	(Cnot6)	Cnot6	0.85	<0.05
11105	DDI 500	57 111	12011(_155766)	Predicted: Rattus	Choto	0.05	-0.05
				Norvegicus Similar To			
				Hypothetical Protein			
				Dkfzp434H2010			
				(Predicted)	Rgd13110		
PND5	DBP500	SAM	ILMN 1352097	(Rgd1311019)	19	0.81	< 0.05
			_	Rattus Norvegicus			
				Heterogeneous			
				Nuclear			
				Ribonucleoprotein F			
				(Hnrnpf), Transcript			
PND5	DBP500	SAM	ILMN_1369798	Variant 2	Hnrnpf	0.89	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Isopentenyl			
				Diphosphate Delta-	x 400 7 0		
	DDDC00	GAN	H M L 12(0425	Isomerase Type 2	Loc49878	1.64	-0.05
PND5	DBP200	SAM	ILMN_1368435	(Loc498/8/)	/	1.64	<0.05
				Predicted: Rattus			
				Hypothetical Protain			
				Pro1580 (Predicted)	Rad12002		
PND5	DBP500	SAM	II MN 1354787	$(R_{gd}1309263)$	63	1 1 1	<0.05
11105	001500	5/11/1	12/01/12/07	Predicted: Rattus	0.5	1.11	~0.05
				Norvegicus Formin			
				Binding Protein 4			
PND5	DBP500	SAM	ILMN 1371331	(Fnbp4)	Fnbp4	0.88	< 0.05
PND5	DBP500	SAM	II MN 136/3/9	Rattus Norvegious	Car2	1 /10	<0.05
	DD1 300	SAIVI	1LIVIN_1304348	Tanus morvegicus	Carz	1.47	~0.03

				Carbonic Anhydrase Ii			
				(Car2)			
				Predicted: Rattus			
				Norvegicus Similar 10 Bikon Cdna			
				2010201N04	L 0050024		
PND5	DBP500	SAM	II MN 1360749	$(1 \circ (500247))$	7	0.83	<0.05
INDJ	DBI 500	SAN	1LMIN_1300749	Rattus Norvegicus	/	0.05	<0.05
				Golgi Autoantigen			
				Golgin Subfamily A 2			
PND5	DBP500	SAM	ILMN 1368568	(Golga2)	Golga2	0.86	< 0.05
			_	Rattus Norvegicus			
				Tata Box Binding			
				Protein (Tbp)-			
				Associated Factor,			
				Rna Polymerase I, C			
PND5	DBP500	SAM	ILMN_1355555	(TaflC)	Taf1C	0.87	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Riken Cdna			
				5/30509K1/Gene	$D = \frac{115(10)}{10}$		
DND5		SAM	II MNI 1275102	(Predicted) (Predicted)	Rg015610	0.86	<0.05
FNDS	DBF300	SAM	1LMIN_1575102	(Rgu1301042) Predicted: Rattus	42	0.80	<0.03
				Norvegicus Similar To			
				Lrrgt00176	Loc49958		
PND5	DBP500	SAM	ILMN 1362770	(Loc499582)	2	0.78	< 0.05
				Rattus Norvegicus			
				S100 Calcium Binding			
PND5	DBP500	SAM	ILMN_1350690	Protein A8 (S100A8)	S100A8	2.20	< 0.05
				Rattus Norvegicus			
				Aryl Hydrocarbon			
PND5	DBP500	SAM	ILMN_1376339	Receptor (Ahr)	Ahr	0.78	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Kiaa03/2 Gene	D 1120(0		
DND5	DDD500	SAM	II MAN 1256505	(Product (Predicted)	Rgd13060	0.80	<0.05
PNDS	DBP300	SAM	1LMIN_1550505	(Rgu1500002) Predicted: Pattus	02	0.89	<0.03
				Norvegicus Similar To			
				Orf? Consensus			
				Sequence Encoding			
				Endonuclease And			
				Reverse Transcriptase			
				Minus Rnaseh	Loc50082		
PND5	DBP500	SAM	ILMN_1357973	(Loc500829)	9	0.83	< 0.05
				Rattus Norvegicus			
				Phospholipase A2,			
				Group Vii (Platelet-			
	DDD	<i>a</i> . . .		Activating Factor	DI ACT	1.10	.0.07
PND5	DBP500	SAM	ILMN_1366506	Acetylhydrolase,	Pla2G7	1.19	< 0.05

				Plasma) (Pla2G7)			
				Rattus Norvegicus			
				Syndecan Binding			
PND5	DBP500	SAM	ILMN 1372999	Protein (Sdcbp)	Sdcbp	0.87	< 0.05
				Rattus Norvegicus			
				Hemoglobin Beta			
PND5	DBP500	SAM	ILMN_1353696	Chain Complex (Hbb)	Hbb	1.27	< 0.05
				Predicted: Rattus			
				Norvegicus Rb1-			
				Inducible Coiled-Coil			
				1 (Predicted)			
PND5	DBP500	SAM	ILMN_1364648	(Rb1Cc1)	Rb1Cc1	0.85	< 0.05
				Rattus Norvegicus			
				Ring Finger Protein 2			
PND5	DBP500	SAM	ILMN_1371460	(Rnf2)	Rnf2	0.89	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Trichorhinophalangeal			
	DDD500	<i></i>		Syndrome I	T 1		0.05
PND5	DBP500	SAM	ILMN_1349929	(Predicted) (Trps1)	Trps1	0.75	< 0.05
				Predicted: Rattus			
				Norvegicus Similar 10			
				Ribosomal Protein	D 115(20		
DND5	DDD500	CAM	IL MAL 12(20)	L_{21} (Predicted)	Rgd15629	0.77	<0.05
PND5	DBP300	SAM	ILMIN_1308000	(Rg015629/1) Dradiatad: Dattua	/1	0.77	<0.05
				Norwagiana Pro			
				Rinding Motif Protein			
				24 (Predicted)			
PND5	DBP500	SAM	II MN 1350785	(Rhm24)	Rhm24	0.88	<0.05
TNDJ	DBI 500	DAN	111111 1330783	Predicted: Rattus	Rom24	0.00	<0.05
				Norvegicus Similar To			
				Orf2 Consensus			
				Sequence Encoding			
				Endonuclease And			
				Reverse Transcriptase			
				Minus Rnaseh	Loc50156		
PND5	DBP500	SAM	ILMN 1363743	(Loc501562)	2	0.86	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Hypothetical Protein			
				D11Ertd99E			
				(Predicted)	Rgd15643		
PND5	DBP500	SAM	ILMN_1354146	(Rgd1564337)	37	1.16	< 0.05
				Rattus Norvegicus			
				Similar To			
				Chromosome 1 Open	D 112505		
DUD	DDD			Reading Frame 63	Rgd13595	0.00	.0.07
PND5	DBP500	SAM	ILMN_1366485	(Kgd1359529)	29	0.80	< 0.05

1				Rattus Norvegicus			
				Meningioma			
				Expressed Antigen 5			
				(Hyaluronidase)			
PND5	DBP500	SAM	ILMN_1370257	(Mgea5)	Mgea5	0.89	< 0.05
				Predicted: Rattus			
				Norvegicus Zinc			
				Finger, Mynd Domain			
				Containing 17			
PND5	DBP500	SAM	ILMN_1367172	(Predicted) (Zmynd17)	Zmynd17	0.82	< 0.05
				Predicted: Rattus			
				Norvegicus Ral Gef			
				With Ph Domain And			
				Sh3 Binding Motif 2			
PND5	DBP500	SAM	ILMN_1358679	(Ralgps2)	Ralgps2	0.89	< 0.05
				Predicted: Rattus			
				Norvegicus Nadh			
				Dehydrogenase			
				(Ubiquinone) 1 Beta			
				Subcomplex, 9			
PND5	DBP500	SAM	ILMN_1364409	(Predicted) (Ndufb9)	Ndufb9	1.10	< 0.05
				Rattus Norvegicus			
				Tandem C2 Domains,			
PND5	DBP500	SAM	ILMN_1374410	Nuclear (Tc2N)	Tc2N	0.87	< 0.05
				Rattus Norvegicus			
PND5	DBP500	SAM	ILMN_1363939	Cyclin L1 (Ccnl1)	Ccnl1	0.87	< 0.05
				Predicted: Rattus			
				Norvegicus Protein			
				Phosphatase 2			
				(Formerly 2A),			
				Regulatory Subunit			
		~		B", Alpha, Transcript			
PND5	DBP500	SAM	ILMN_1351234	Variant 2 (Ppp2R3A)	Ppp2R3A	0.83	< 0.05
				Predicted: Rattus			
				Norvegicus Ubiquitin-			
				Like, Containing Phd			
				And King Finger			
DND5	DDD500	GAM	H MOL 1520420	Domains 2 (Predicted)	T The C	0.04	-0.05
PND5	DR5200	SAM	1LMIN_1530420	(Unri2)	Unri2	0.84	< 0.05
				Kattus Norvegicus			
DND5	DDD500	SAM	IL MNL 1251266	Drotoogo 48 (Uan 48)	Llan 49	0.97	<0.05
FNDS	DBr300	SAM	1LIVIIN_1331300	Predicted: Pottus	Usp48	0.87	~0.03
				Norvegious Similar To			
				I rra00116	Loc36101		
PND5	DBP500	SAM	II MN 1362018	(Loc361912)	2	0 79	<0.05
11103	DD1 300	SAW	11/1111_1302710	Predicted: Rattus	2	0./7	~0.05
				Norvegicus Similar To			
				Vln Motif Containing			
				Protein 1 (Nuclear	Rod15649		
PND5	DBP500	SAM	ILMN 1363528	Protein Zan3)	46	0.88	<0.05
11100	DD1000	S1 1111	1000020		10	0.00	0.05

				(Zap113) (Predicted)			
				(Kgu1504940)			
				Predicted: Rattus			
				Norvegicus Bcl2-			
				Associated			
				Transcription Factor 1			
PND5	DBP500	SAM	ILMN_1355583	(Bclaf1)	Bclafl	0.87	< 0.05
				Predicted: Rattus			
				Norvegicus			
				I ranscription Factor			
DND5		SAM	II MNL 1274764	(Tefen2P)	Tofon 2D	0.82	<0.05
FNDS	DBF300	SAM	1LIVIIN_15/4/04	(TCTap2D) Predicted: Pattus	Тстар2Б	0.82	<0.03
				Norvegicus			
				Carboxypeptidase D			
PND5	DBP500	SAM	ILMN 1362981	(Cpd)	Cpd	0.75	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Fli-Lrr Associated	Loc36731		
PND5	DBP500	SAM	ILMN_1651039	Protein-1 (Loc367314)	4	0.86	< 0.05
				Predicted: Rattus			
				Norvegicus Atpase,			
				Class I, Type 8B,			
DND5	DDD500	CAM	IL MAL 12(0542	Member I (Predicted)	A 4 = 9 D 1	0.92	<0.05
PNDS	DBP300	SAM	1LMIN_1300342	(Alpob1) Pattus Norvegious	Афові	0.82	<0.03
				Onioid Recentor			
PND5	DBP500	SAM	ILMN 1365626	Sigma 1 (Oprs1)	Oprs1	1 10	<0.05
THE	DBICOU	<u>OI III</u>		Predicted: Rattus	Opibi	1.10	-0.02
				Norvegicus			
				Myeloid/Lymphoid Or			
				Mixed-Lineage			
				Leukemia 5 (Trithorax			
				Homolog, Drosophila)			
PND5	DBP500	SAM	ILMN_1361932	(Mll5)	Mll5	0.84	< 0.05
				Rattus Norvegicus			
				Zinc Finger Protein			
DND5		SAM	IL MNL 1260812	36, C3H Type-Like 2	7fn261 2	0.78	<0.05
FNDS	DDF300	SAW	11.1VIIN_1309812	(LIPSOL2) Rattus Norvegious	ZIPSOL2	0.78	~0.03
				Mdm4 P53 Rinding			
				Protein Homolog			
PND5	DBP500	SAM	ILMN 1376455	(Mouse) (Mdm4)	Mdm4	0.86	< 0.05
			_	Rattus Norvegicus			
				Gastrin Releasing			
PND5	DBP500	SAM	ILMN_1371417	Peptide (Grp)	Grp	1.17	< 0.05
				Predicted: Rattus			
				Norvegicus	T OCOD		
	DDD500	0.034		Hypothetical	Loc36324	0.07	-0.05
PND5	DBF200	SAM	ILMN 1356368	Loc363240	0	0.87	< 0.05

				(Loc363240)			
				(
				Rattus Norvegicus			
				Guanine Nucleotide			
				Binding Protein.			
PND5	DBP500	SAM	ILMN 1361160	Alpha 11 (Gna11)	Gna11	0.88	< 0.05
			—	Predicted: Rattus			
				Norvegicus			
				Loc498469	Loc49846		
PND5	DBP500	SAM	ILMN_2038882	(Loc498469)	9	0.89	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Cg8009-Pa (Predicted)	Loc29191		
PND5	DBP500	SAM	ILMN_1358761	(Loc291914)	4	0.90	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Serologically Defined			
				Colon Cancer Antigen			
				1 Isoform A	Loc50066		
PND5	DBP500	SAM	ILMN_1354572	(Loc500663)	3	0.87	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Glyceraldehyde 3-			
				Phosphate			
DUD 5	DDDCOO	G 4 1 4		Dehydrogenase	G 11	1.17	.0.05
PND5	DBP200	SAM	ILMN_1649859	(Gapdh)	Gapdh	1.16	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Peroxisome Draliforativa Activated			
				Promerative Activated			
				Coactivator Related 1			
PND5	DBP500	SAM	II MN 1367124	(Predicted) (Pprc1)	Pprc1	0.88	<0.05
1105	DDI 500	SAN	112WIN_1307124	Predicted: Rattus	1 pie i	0.00	-0.05
				Norvegicus T-Box18			
PND5	DBP500	SAM	ILMN 1650771	(Predicted) (Tbx18)	Tbx18	0.86	<0.05
11,00	221200	57 1171	1000//1	Rattus Norvegicus	10/110	0.00	
				Ectonucleoside			
				Triphosphate			
				Diphosphohydrolase 5			
PND5	DBP500	SAM	ILMN 1373210	(Entpd5)	Entpd5	0.84	< 0.05
			-	Predicted: Rattus			
				Norvegicus Ataxia			
				Telangiectasia			
				Mutated Homolog			
				(Human) (Mapped)			
PND5	DBP500	SAM	ILMN_1353725	(Atm)	Atm	0.89	< 0.05
				Predicted: Rattus			
				Norvegicus Deah			
				(Asp-Glu-Ala-His)			
PND5	DBP500	SAM	ILMN_1360778	Box Polypeptide 15	Dhx15	0.89	< 0.05

				(Predicted) (Dhx15)			
				Rattus Norvegicus			
				Actin, Gamma 2,			
				Smooth Muscle,			
PND5	DBP500	SAM	ILMN_1367932	Enteric (Actg2)	Actg2	0.79	< 0.05
				Rattus Norvegicus			
				Similar To Riken			
				Cdna 0610007P06	Loc29310		
PND5	DBP500	SAM	ILMN_1352305	(Loc293103)	3	1.13	< 0.05
				Rattus Norvegicus			
		<i>a</i>		Collagen, Type Xxv11,	G 105 4 1	0.01	0.05
PND5	DBP500	SAM	ILMN_1375001	Alpha I (Col2/AI)	Col27A1	0.91	< 0.05
				Rattus Norvegicus			
				Heterochromatin			
DND5	DDD500	SAM	II MNI 1262006	Protein 1, Binding Protein 2 (Un1Dn2)	IIn1Dn2	0.01	<0.05
PNDS	DBP300	SAM	ILIVIN_1302880	Protein 5 (Пртвр5)	прібрэ	0.91	<0.03
				Norwagiana Similar To			
				A dn Pibosylation			
				Factor Like 2 Like 1	L oc30403		
PND5	DBP500	SAM	II MN 1360884	$(I_{0}c_{3}^{2})(4037)$	7	0.90	<0.05
TRDJ	DDI 500	SAN	11210114_1300004	Predicted: Rattus	/	0.70	<0.05
				Norvegicus Ccr4-Not			
				Transcription			
				Complex Subunit 7			
PND5	DBP500	SAM	ILMN 1353588	(Predicted) (Cnot7)	Cnot7	0.89	< 0.05
				Rattus Norvegicus			
				Dimethylarginine			
				Dimethylaminohydrol			
PND5	DBP500	SAM	ILMN 1357122	ase 1 (Ddah1)	Ddah1	0.83	< 0.05
				Rattus Norvegicus			
				Myeloid/Lymphoid Or			
				Mixed-Lineage			
				Leukemia (Trithorax			
				Homolog,			
				Drosophila);			
				Translocated To, 4			
PND5	DBP500	SAM	ILMN_1359100	(Mllt4)	Mllt4	0.91	< 0.05
				Predicted: Rattus			
				Norvegicus	T 40000		
	DDDC00	CAN	H M L 1272025	Loc498208	Loc49820	0.00	-0.05
PND5	DRb200	SAM	1LMN_1372925	(L0C498208)	8	0.80	< 0.05
				Kattus Norvegicus			
				Cdna C/20008C10	Dad12070		
PND5	DBD200	SAM	II MN 1356042	$(R_{ad} 1307047)$	A7	0.86	<0.05
TNDS	DDF 300	SAM	11.1VIIN_1330042	Predicted: Rattus	·+/	0.00	~0.03
				Norvegicus Cleavage			
				And Polyadenvlation			
PND5	DBP500	SAM	ILMN 1351668	Factor Subunit	Pcf11	0.90	<0.05
				· · · · · · · · · · · · · · · · · · ·			

				Homolog (S.			
				Cerevisiae) (Predicted)			
				(PCIII) Predicted: Rattus			
				Norvegicus			
				Hypothetical Gene			
				Supported By			
				Nm 019349	Loc49774		
PND5	DBP500	SAM	ILMN 1352738	(Loc497743)	3	0.90	< 0.05
			_	Predicted: Rattus			
				Norvegicus Hect			
				Domain And Rld 4			
PND5	DBP500	SAM	ILMN_1376365	(Predicted) (Herc4)	Herc4	0.88	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Dual Specificity			
				Protein Phosphatase 3			
DUD 5	DDDCOO	G 4 1 4	H) D 1 1222707	(T-Dsp11) (Predicted)	Rgd15600	0.07	.0.05
PND5	DBP200	SAM	ILMN_1353/86	(Rgd1560049)	49	0.86	<0.05
DND5		SAM	II MNI 1251076	Fibrillin 2 (Ebn2)	Ebn2	0.70	<0.05
PNDS	DBP300	SAM	1LIVIN_1331070	Prodicted: Rettys	F0H2	0.79	<0.03
				Norvegicus Mitogen			
				Activated Protein			
				Kinase Kinase Kinase			
				4 (Predicted)			
PND5	DBP500	SAM	ILMN 1373545	(Map3K4)	Map3K4	1.10	< 0.05
			_	Rattus Norvegicus	1		
				Mast Cell Antigen 32			
PND5	DBP500	SAM	ILMN_1355362	(Mca32)	Mca32	1.20	< 0.05
				Rattus Norvegicus			
				Family With Sequence			
				Similarity 149,			
DUD 5	DDDCOO	G 4 1 4	H . D . 1254004	Member B1	Fam149B	0.01	.0.05
PND5	DBP200	SAM	ILMN_1354804	(Fam149B1)	1	0.91	<0.05
				Predicted: Kattus			
				Hypothetical Protain			
				Kiaal240	Loc31394		
PND5	DBP500	SAM	ILMN 1349311	(Loc 313940)	0	0.89	<0.05
11105	DD1 300	57 1191	101111_1379311	Predicted: Rattus	<u> </u>	0.07	~0.05
				Norvegicus Similar To			
				Riken Cdna			
				6530403A03	Rgd13090		
PND5	DBP500	SAM	ILMN_1362599	(Rgd1309020)	20	0.89	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Tyrosine Kinase-			
				Associated Leucine			
		a		Zipper Protein Lazipii	Rgd15655		
PND5	DBP500	SAM	ILMN_1366571	(Predicted)	84	0.87	< 0.05

				(Rgd1565584)			l
				Predicted: Rattus			
				Norvegicus Fibulin 1			
PND5	DBP500	SAM	ILMN_1370719	(Predicted) (Fbln1)	Fbln1	0.87	< 0.05
				Predicted: Rattus			
				Norvegicus Cullin 1			
PND5	DBP500	SAM	ILMN_1364685	(Predicted) (Cul1)	Cull	0.92	< 0.05
				Rattus Norvegicus			
				Coiled-Coil Domain			
	DDD500	<i></i>		Containing 41	a 1 41	0.00	0.05
PND5	DBP500	SAM	ILMN_1368593	(Ccdc41)	Ccdc41	0.90	< 0.05
				Predicted: Rattus			
				Norvegicus Similar 10			
				Hypothetical Protein	D = 112055		
DND5	DDD500	SAM	II MNI 1257609	(Predicted)	Rga13055	1 1 1	<0.05
PNDS	DBP300	SAM	ILIVIN_1337098	(Rgu1505500)	00	1.11	<0.03
				Ratius Norvegicus			
				Acre) Pox Polymontido			
		SAM	II MN 1267054	Asp) Box Polypeptide 20 (Ddy 20)	Ddy20	0.03	<0.05
TNDS	DBF500	SAM	ILIVIIN_1307934	Dradiated: Pattus	Dux39	0.93	<0.03
				Norvegicus			
				Fibronectin Type Iii			
				Domain Containing			
				3A (Predicted)			
PND5	DBP500	SAM	ILMN 1367087	(Fndc3A)	Fndc3A	0.90	<0.05
11120	221000	<u>Di liti</u>		Predicted: Rattus	11140011	0.50	0.00
				Norvegicus Similar To			
				H2A Histone Family,			
				Member Z	Loc49918		
PND5	DBP500	SAM	ILMN 1352626	(Loc499180)	0	1.14	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Lrrgt00057	Loc49950		
PND5	DBP500	SAM	ILMN_1356833	(Loc499501)	1	1.13	< 0.05
				Rattus Norvegicus			
				Rna Binding Motif			
PND5	DBP500	SAM	ILMN_1364535	Protein 39 (Rbm39)	Rbm39	0.90	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Ubiquitin Protein			
				Ligase E3 Component			
				N-Recognin 2,			
		a		Transcript Variant 3	Loc36318		
PND5	DBP500	SAM	ILMN_1353143	(Loc363188)	8	0.91	< 0.05
DUDE	DDD			Rattus Norvegicus		1.10	.0.07
PND5	DBP500	SAM	ILMN_1358267	Cathepsin D (Ctsd)	Ctsd	1.12	< 0.05
				Predicted: Rattus			
PND5	DBP500	SAM	ILMN_1353460	Norvegicus Ras	Rhot1	0.90	< 0.05

				Homolog Gene			
				Family, Member T1			
				(Predicted) (Rhot1)			
				Predicted: Rattus			
				Norvegicus Aldehyde			
				Dehydrogenase			
				Family 5, Subfamily			
	DDDCOO	G +) (H . O.L. 1272070	AI, Transcript Variant		1.10	.0.05
PND5	DBP200	SAM	ILMN_13/2959	3 (Aldh5A1)	Aldh5Al	1.10	< 0.05
				Rattus Norvegicus			
				Jaamaraaa Family A			
DND5	DDD500	SAM	II MNI 1257600	Momber 4 (Ddie 4)	Ddia4	1 1 2	<0.05
FNDS	DBF300	SAM	ILMIN_1557090	Dradiatad: Dattus	r ula4	1.12	<0.03
				Norwagiana Similar To			
				I rrg00135	Loc/19956		
PND5	DBP500	SAM	II MN 1649797	(Loc499560)	0	0.87	<0.05
TND5	DDI 500	SAN		Predicted: Rattus	0	0.07	<0.05
				Norvegicus Ubiquitin			
				Specific Pentidase 16			
PND5	DBP500	SAM	ILMN 1373990	(Usp16)	Usp16	0.91	< 0.05
				Rattus Norvegicus			
				Fk506 Binding			
PND5	DBP500	SAM	ILMN_1370814	Protein-Like (Fkbpl)	Fkbpl	1.15	< 0.05
			-	Predicted: Rattus			
				Norvegicus			
				Isoleucine-Trna			
				Synthetase 2,			
				Mitochondrial			
PND5	DBP500	SAM	ILMN_1367076	(Predicted) (Iars2)	Iars2	1.10	< 0.05
				Predicted: Rattus			
				Norvegicus Laminin,			
PND5	DBP500	SAM	ILMN_1355835	Gamma 1 (Lamc1)	Lamc1	0.93	< 0.05
				Predicted: Rattus			
				Norvegicus Ahnak 1			
	DDD500	<i></i>		(Loc499315), Misc	Loc49931	0.00	0.0 7
PND5	DBP500	SAM	ILMN_1359062	Rna.	5	0.88	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Topoisomerase I			
				Argining,			
PND5	DBP500	SAM	II MN 1371048	(Predicted) (Topors)	Topors	1 10	<0.05
11105	DD1 300	OAW	15/1940	Rattus Norvegious	100015	1.10	~0.05
				Guanine Nucleotide			
				Binding Protein Beta			
PND5	DBP500	SAM	ILMN 1375069	1 (Gnb1)	Gnb1	0.94	< 0.05
				Predicted: Rattus		· · · · ·	
				Norvegicus Fkbp-			
				Associated Protein			
PND5	DBP500	SAM	ILMN_1369803	(Glmn)	Glmn	0.92	< 0.05

				Predicted: Rattus			
				Norvegicus Similar To			
				Glyceraldehyde-3-			
				Phosphate			
				Dehydrogenase	Loc50050		
PND5	DBP500	SAM	ILMN_1351960	(Loc500506)	6	0.92	< 0.05
				Rattus Norvegicus			
PND5	DBP500	SAM	ILMN_1351361	Netrin 1 (Ntn1)	Ntn1	0.92	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Hypothetical			
				Loc315216 (Predicted)	Rgd13119		
PND5	DBP500	SAM	ILMN_1373365	(Rgd1311907)	07	0.93	< 0.05
				Rattus Norvegicus			
				Nadh Dehydrogenase			
				(Ubiquinone)			
				Flavoprotein 1			
				(Ndufv1), Nuclear			
	DDD500	G + 1 (WARL 10(5000	Gene Encoding			0.0 <i>5</i>
PND5	DBP500	SAM	ILMN_1365082	Mitochondrial Protein	Ndufv1	1.11	< 0.05
				Rattus Norvegicus			
				Nuclear Protein $E3-3$	D . 170954		
DND5	DDD500	GAM	U MAL 1270444	(Kga/08545),	Rga/0854	1.07	<0.05
PND5	DBP200	SAM	ILMIN_13/0444	Transcript Variant I	5	1.07	<0.05
				Nervegious Similar To			
				Zina Eingar, Caba			
				Domain Containing 7			
				Domain Containing 7, Transprint Variant 1	L 2269269		
PND5	DBP500	SAM	II MN 1368615	(Loc683686)	L0008308	0.01	<0.05
TNDS	DBF300	SAW	1LMIN_1308013	(LUC005000) Rattus Norvegicus	0	0.91	<0.05
				Rahl4 Member Ras			
				Oncogene Family			
PND5	DBP500	SAM	ILMN 1348958	(Rab14)	Rab14	0.91	<0.05
11120	DBICOU	01111		Rattus Norvegicus	ItuoIII	0.91	0.00
				Transcription Factor			
PND5	DBP500	SAM	ILMN 1376542	12 (Tcf12)	Tcf12	0.93	< 0.05
				Rattus Norvegicus			
				Ribosomal L1 Domain			
PND5	DBP500	SAM	ILMN 1376915	Containing 1 (Rsl1D1)	Rsl1D1	1.06	< 0.05
			-	Rattus Norvegicus			
				Neuronal			
				Regeneration Related			
PND5	DBP500	SAM	ILMN_1357234	Protein (Nrep)	Nrep	0.92	< 0.05
				Rattus Norvegicus			
				Signal-Regulatory			
PND5	DBP500	SAM	ILMN_1360759	Protein Alpha (Sirpa)	Sirpa	0.94	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Mitochondrial Carrier			_
PND5	DBP500	SAM	ILMN_1364421	Triple Repeat 2	Mcart2	0.92	< 0.05

			[(Predicted) (Mcart2)			
				Predicted: Rattus			
				Norvegicus Similar To			
				Cg4699-Pa Isoform A	Loc36728		
PND5	DBP500	SAM	ILMN 1367936	(Loc_{367289})	9	0.94	<0.05
11120	DDICCO	51101		Predicted: Rattus	-	0.77	0.00
				Norvegicus Retinoic			
				Acid Receptor Beta			
				Transcript Variant 2			
PND5	DBP500	SAM	ILMN 1359481	(Rarb)	Rarb	0 94	<0.05
11120	DDICCO	<u>Di liti</u>		Predicted: Rattus	11010	0.2	0.00
				Norvegicus			
				Loc499775	Loc49977		
PND5	DBP500	SAM	ILMN 1355188	(Loc 499775)	5	0.92	<0.05
11120	DDICCO	51101		Predicted: Rattus	0	0=	0.00
				Norvegicus Similar To			
				Vanin-3 (Predicted)	Rgd15606		
PND5	DBP500	SAM	ILMN 1351302	(Rgd1560609)	09	1.09	<0.05
11120	DDICCO	<u>Di liti</u>		Predicted: Rattus		1.07	0.00
				Norvegicus Leucine			
				Rich Repeat			
				Containing 47			
PND5	DBP500	SAM	ILMN 1360424	(Predicted) (Lrrc47)	Lrrc47	0.95	<0.05
		~~~~~		Rattus Norvegicus			
				Homocysteine-			
				Inducible.			
				Endoplasmic			
				Reticulum Stress-			
				Inducible, Ubiquitin-			
				Like Domain Member			
PND5	DBP500	SAM	ILMN 1370868	1 (Herpud1)	Herpud1	1.06	< 0.05
			_	Rattus Norvegicus	<b>.</b>		
				Eukaryotic Translation			
				Initiation Factor 4A2			
PND5	DBP500	SAM	ILMN 1372755	(Eif4A2)	Eif4A2	0.94	< 0.05
				Predicted: Rattus			
				Norvegicus Nuclear			
				Factor Of Kappa Light			
				Chain Gene Enhancer			
				In B-Cells Inhibitor,			
PND5	DBP500	SAM	ILMN_1356628	Alpha (Nfkbia)	Nfkbia	1.13	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Desmoglein 2			
PND5	DBP500	SAM	ILMN_1358157	(Predicted) (Dsg2)	Dsg2	0.94	< 0.05
				Predicted: Rattus			
				Norvegicus Start			
				Domain Containing 7			
PND5	DBP500	SAM	ILMN_1370199	(Predicted) (Stard7)	Stard7	0.94	< 0.05

Image: Norvegicus Similar To Riken Cdna 2010110M21 (Predicted)         Norvegicus Similar To Riken Cdna 2010110M21 (Predicted)         Image: Norvegicus Similar To Loc29099         Norvegicus Similar To Loc50340         Norvegicus Similar To Cab/P300-Interacting Transactivator, With Glu/Asp-Rich Carboxy-Terminal Eukaryotic Translation Elongation Factor 1         Norvegicus Similar To Ritken Cdna 6330400115         Norvegicus Similar To Ritken Cdna 6330400115         Norvegicus Similar To Ritken Cdna 6330400115         Norvegicus Similar To Ritken Cdna 6330400115         Norvegicus Similar To Ritken Cdna 630400115         Norvegicus Similar To Ritken Cdna 630400115         Norvegicus Carboxy Similar To Ritken Cdna 630400115         Norvegicus Similar To Ritke
PND5       DBP500       SAM       ILMN 1368345       (Loc29099)       9       1.07       <0.05
PND5         DBP500         SAM         ILMN 1368345         (Loc29099)         9         1.07         <0.05           PND5         DBP500         SAM         ILMN 1368345         (Loc29099)         9         1.07         <0.05
PND5         DBP500         SAM         ILMN 1368345         (Predicted)         Loc29099)         9         1.07         <0.05           PND5         DBP500         SAM         ILMN 1368345         Norvegicus Similar To Norvegicus Similar To Ac1147 (Loc50340)         9         0.96         <0.05
PND5         DBP500         SAM         ILMN 1368345         (Loc290999)         9         1.07         <0.05           PND5         DBP500         SAM         ILMN 1368345         (Loc200399)         9         0.96         <0.05
PND5DBP500SAMILMN_1360615Ac1147 (Loc503409)90.96<0.05PND5DBP500SAMILMN_1360615Ac1147 (Loc503409)90.96<0.05
PND5         DBP500         SAM         ILMN_1360615         Ac1147 (Loc503409)         9         0.96         <0.05           PND5         DBP500         SAM         ILMN_1360615         Ac1147 (Loc503409)         9         0.96         <0.05
PND5         DBP500         SAM         ILMN_1360615         Ac1147 (LocS03409)         9         0.96         <0.05           Ratus Norvegicus Cbp/P300-Interacting Transactivator, With Glu/Asp-Rich Carboxy-Terminal
Rattus Norvegicus Cbp/P300-Interacting Transactivator, With Glu/Asp-Rich Carboxy-TerminalRattus Norvegicus Cbg/P300-Interacting Transactivator, With Glu/Asp-Rich Carboxy-TerminalPND5DBP500SAMILMN_1352067Domain, 2 (Cited2)Cited20.94<0.05
PND5DBP500SAMILMN_1352067Cbp/P300-Interacting Transactivator, With Glu/Asp-Rich Carboxy-Terminal Elongation Factor 1Cited20.94<0.05PND5DBP500SAMILMN_2038788Alpha 1 (Eef1A1)Eef1A11.06<0.05
PND5DBP500SAMILMN_1352067Domain, 2 (Cited2)Cited20.94<0.05PND5DBP500SAMILMN_1352067Domain, 2 (Cited2)Cited20.94<0.05
PND5DBP500SAMILMN_1352067Cited2)Cited20.94<0.05PND5DBP500SAMILMN_2038788Alpha 1 (Eef1A1)Eef1A11.06<0.05
PND5DBP500SAMILMN_1352067Domain, 2 (Cited2)Cited20.94<0.05PND5DBP500SAMILMN_2038788Alpha 1 (Eef1A1)Eef1A11.06<0.05
PND5DBP500SAMILMN_1352067Domain, 2 (Cited2)Cited20.94<0.05Rattus Norvegicus Eukaryotic Translation Elongation Factor 1Rattus Norvegicus Elongation Factor 1PND5DBP500SAMILMN_2038788Alpha 1 (Eef1A1)Eef1A11.06<0.05
PND5DBP500SAMILMN_2038788Rattus Norvegicus Eukaryotic Translation Elongation Factor 1Eef1A11.06<0.05PND5DBP500SAMILMN_2038788Alpha 1 (Eef1A1)Eef1A11.06<0.05
PND5DBP500SAMILMN_2038788Alpha 1 (Eef1A1)Eef1A11.06<0.05PND5DBP500SAMILMN_2038788Alpha 1 (Eef1A1)Eef1A11.06<0.05
PND5DBP500SAMILMN_2038788Alpha 1 (Eef1A1)Eef1A11.06<0.05PND5DBP500SAMILMN_2038788Predicted: Rattus Norvegicus Similar To Riken Cdna 6330406115Norvegicus Similar To Riken CdnaPND5DBP500SAMILMN_1367232(Rgd1307396)960.96<0.05
PNDSDBP500SAMILMN_2038788Alpha I (Lef1A1)Eef1A11.06<0.05PNDSPredicted: Rattus Norvegicus Similar To Riken Cdna 6330406115 (Predicted)Norvegicus Similar To Riken Cdna 6330406115 (Predicted)Rgd13073PND5DBP500SAMILMN_1367232(Rgd1307396)960.96<0.05
PND5DBP500SAMILMN_1367232Predicted: Rattus Norvegicus Similar To Riken Cdna 6330406115 (Predicted)Rgd13073 960.96<0.05PND5DBP500SAMILMN_1367232(Rgd1307396)960.96<0.05
Norvegicus Similar To Riken Cdna 6330406115 (Predicted)Rgd13073 96PND5DBP500SAMILMN_1367232(Rgd1307396)960.96<0.05
Riken Cdna 6330406115 (Predicted)Rgd13073PND5DBP500SAMILMN_1367232(Rgd1307396)960.96<0.05
PND5DBP500SAMILMN_1367232(Rgd1307396)960.96<0.05
PND5DBP500SAMILMN_1367232(Predicted)Rgd130739960.96<0.05Rattus NorvegicusTimpRattus NorvegicusTimp </td
PND5DBP500SAMILMN_136/232(Rgd130/396)960.96<0.96<0.05Rattus Norvegicus Timp MetallopeptidaseTimp MetallopeptidaseTimp30.95<0.05
Rattus Norvegicus Timp MetallopeptidaseRattus Norvegicus Timp MetallopeptidaseConstraint ConstraintPND5DBP500SAMILMN_1348821Inhibitor 3 (Timp3)Timp30.95<0.05
Imp MetallopeptidaseMetallopeptidasePND5DBP500SAMILMN_1348821Inhibitor 3 (Timp3)Timp30.95<0.05
PND5DBP500SAMILMN_1348821Inhibitor 3 (Timp3)Timp30.95<0.05PND5DBP500SAMILMN_1356087(Defb4)Defb41.23<0.05
PND5DBP500SAMILMN_1348821Inhibitor 3 (11mp3)11mp30.95<0.05Rattus Norvegicus Defensin Beta 4Defensin Beta 4Defb41.23<0.05
PND5       DBP500       SAM       ILMN_1356087       (Defb4)       Defb4       1.23       <0.05
PND5       DBP500       SAM       ILMN_1356087       (Defb4)       Defb4       1.23       <0.05         Rattus Norvegicus       Zinc Finger, Ran-Binding Domain       Binding Domain          <0.05
PND5       DBP500       SAM       ILMN_1350087       (Defb4)       Defb4       1.23       <0.05         Rattus Norvegicus       Zinc Finger, Ran- Binding Domain       Zinc Finger, Ran- Binding Domain       0.96       <0.05
PND5       DBP500       SAM       ILMN 1359067       Containing 2 (Zranb2)       Zranb2       0.96       <0.05
PND5     DBP500     SAM     ILMN 1359067     Containing 2 (Zranb2)     Zranb2     0.96     <0.05
PND5 DBP500 SAM ILMN 1359067 Containing 2 (Zranb2) Zranb2 0.96 <0.05
$  PND5   DBP500   SAM   ILMIN 1359007   Containing 2 (Zrano2)   Zrano2   0.90   \leq 0.05$
Kattus Norvegicus
Iviisz iviagiiesium Homeostosia Factor
Homelog (S
PND5 DBP500 SAM HMN 1360844 Cerevisiae) (Mrc2) Mrc2 0.96 <0.05
TTVD3         DD1300         SATVI         TLIVITV_1300044         Coleviside) (19152)         19152         0.70         \0.03           Predicted: Dattus         Dredicted: Dattus         0.70         \0.03         \0.03
Norvegieus
Neuralized Like 2
(Drosonhila)
PND5 DBP500 SAM ILMN 1350548 (Predicted) (Neurl2) Neurl2 1.05 <0.05
Predicted Rattus
Norvegious Ia Motif
Containing Gtnase
Activating Protein 1
PND5 DBP500 SAM ILMN 1373759 (Predicted) (Jagan1 0.96 <0.05

				Rattus Norvegicus	I		
				C1Q And Tumor			
				Necrosis Factor			
				Related Protein 6			
PND5	DBP500	SAM	ILMN_1366657	(C1Qtnf6)	C1Qtnf6	0.96	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To	Loc29070		
PND5	DBP500	SAM	ILMN_1350576	Palladin (Loc290704)	4	0.93	< 0.05
				Predicted: Rattus			
				Norvegicus			
PND5	DBP500	SAM	ILMN_1374140	Parathymosin (Ptms)	Ptms	0.96	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Loc499178	Loc49917		
PND5	DBP500	SAM	ILMN_1357213	(Loc499178)	8	0.97	< 0.05
				Predicted: Rattus			
				Norvegicus Dead/H			
				(Asp-Glu-Ala-			
				Asp/His) Box			
				Polypeptide 20, 103Kd			
PND5	DBP500	SAM	ILMN_1368469	(Ddx20)	Ddx20	0.97	< 0.05
				Rattus Norvegicus			
				Ectonucleotide			
				Pyrophosphatase/Phos			
				phodiesterase 2			
PND5	DBP500	SAM	ILMN_1376810	(Enpp2)	Enpp2	0.98	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Transforming Growth			
				Factor Beta Regulated			
				Gene 4 (Predicted)			
PND5	DBP500	SAM	ILMN_1375291	(Tbrg4)	Tbrg4	0.97	< 0.05
				Rattus Norvegicus			
PND5	DBP500	SAM	ILMN_1374374	Dynactin 2 (Dctn2)	Dctn2	0.98	< 0.05
				Predicted: Rattus			
				Norvegicus Udp-			
				Gal:Betaglcnac Beta			
				1,4-			
				Galactosyltransferase,			
				Polypeptide 1			
PND5	DBP500	SAM	ILMN 1372751	(Mapped) (B4Galt1)	B4Galt1	1.04	< 0.05
				Rattus Norvegicus			
				Carbonyl Reductase 1			
PND5	DBP500	SAM	ILMN_1367105	(Cbr1)	Cbr1	1.03	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To	Loc36131		
PND5	DBP500	SAM	ILMN_1650077	Ac2-256 (Loc361315)	5	0.99	< 0.05
				Predicted: Rattus			
				Norvegicus Similar To			
				Myosin Regulatory	Loc50120		
PND5	DBP500	SAM	ILMN_1353763	Light Chain 2-A,	3	0.99	< 0.05

1				Smooth Muscle			
				Isoform (Myosin Rlc-			
				A) (Loc501203)			
				Rattus Norvegicus			
		<i></i>		Casein Kinase 1, Delta			
PND5	DBP500	SAM	ILMN_1371863	(Csnk1D)	Csnk1D	1.02	< 0.05
				Predicted: Rattus			
				Norvegicus Similar 10			
				(Predicted)	Pad15628		
PND5	DBP500	SAM	II MN 1372198	$(R_{ad1562827})$	27	1.06	<0.05
11105	DBI 500	57 1111	12WII 1372170	Predicted: Rattus	21	1.00	-0.05
				Norvegicus Similar To			
				Cg31855-Pa	Loc68410		
PND5	DBP500	SAM	ILMN 1360290	(Loc684106)	6	1.03	< 0.05
			_	Rattus Norvegicus			
				Tropomyosin 4			
PND5	DBP500	SAM	ILMN_1357093	(Tpm4)	Tpm4	0.98	< 0.05
				Rattus Norvegicus			
PND5	DBP500	SAM	ILMN_1361170	Janus Kinase 2 (Jak2)	Jak2	1.00	< 0.05
				Rattus Norvegicus			
				Tumor Necrosis			
				Factor Receptor			
				Superfamily, Member			
DND5	DBB200	SAM	II MN 1274220	(Trafaef11B)	Tufraf 11P	1.06	<0.05
FNDS	DBF300	SAM	1LIMIN_13/4220	(IIIIISIIID) Rattus Norvegicus	THIISITID	1.00	<0.03
				Lysophospholipase 2			
PND5	DBP500	SAM	ILMN 1353790	(Lypla2)	Lypla2	1.01	<0.05
11100	DBI000	<u>OI III</u>		Predicted: Rattus	Lypiaz	1.01	-0.02
				Norvegicus Sorting			
				Nexin 6 (Predicted)			
PND5	DBP500	SAM	ILMN_2038940	(Snx6)	Snx6	1.01	< 0.05
				Predicted: Rattus			
				Norvegicus			
				Polymerase I And			
				Transcript Release			
D) ID 5	DDD500	<b>C 1 1 (</b>	H . O.L. 1250504	Factor (Predicted)	D	1.00	.0.05
PND5	DBP500	SAM	ILMN_1350/94	(Ptrf)	Ptrf	1.00	< 0.05
	Flutonside			Small Nuclear			
DND5	Flutamide		II MNL 1250611	Ribonucleoprotein Dolymontido E	Surnf	0.04	0.0296
TND5	J Flutamide	LIMINIA	120011	тотурерние г	Silipi	0.94	0.0380
PND5	5	SAM	10844869	Atnase H+	Atn4h	1 34	<0.05
	Flutamide	57 1191	10077007	Arginine Vasonressin	11111-10	1.37	~0.05
PND5	5	SAM	10729024	Receptor 1A	Avpr1a	1.27	< 0.05
	Flutamide			C1Galt1-Specific		,	
PND5	5	SAM	10719064	Chaperone 1	C1galt1	1.37	< 0.05
				Calcium Channel,			
	Flutamide			Voltage-Dependent, T			
PND5	5	SAM	10722814	Type, Alpha 11	Cacnali	1.14	< 0.05

				Subunit			
	Flutamide						
PND5	5	SAM	10709751	Claudin 16	Cldn16	1.27	< 0.05
PND5	Flutamide	SAM	10916430	Claudin 19	Cldn19	1 39	<0.05
TND5	Flutamide	SAN	10910450	Ciliary Neurotrophic	Cluiry	1.39	<0.05
PND5	5	SAM	10833617	Factor Receptor	Cntf	1.33	< 0.05
	Flutamide			Component Of Sp100-			
PND5	5	SAM	10704120	Rs	Csprs	1.27	< 0.05
				Family With Sequence			
	Flutamide			Similarity 113,			
PND5	5	SAM	10871561	Member B	Fam113b	1.24	< 0.05
D) ID 5	Flutamide	<b>G 4 1 4</b>	10000706	Glutamate Receptor,	0.16	1.00	-0.05
PND5	5	SAM	10830796	Ionotropic, Kainate 5	Grik5	1.23	< 0.05
	Elutomido			Higi Hypoxia			
DND5	r iutainide	SAM	10706085	Family Member 1P	Higd1b	0.75	<0.05
TND5	5	SAM	10/90985	Gamma 2A	Inguit	0.75	<0.05
	Flutamide			Immunoglobulin			
PND5	5	SAM	10874963	Heavy Chain	IgG-2a	1.27	< 0.05
	Flutamide				-8		
PND5	5	SAM	10880009	Karyopherin Alpha 2	Kpna2	1.29	< 0.05
	Flutamide			Keratin Associated			
PND5	5	SAM	10875009	Protein 9-1	Krtap9-1	1.35	< 0.05
	Flutamide				LOC2576		
PND5	5	SAM	10789460	Hippyragranin	50	1.28	< 0.05
				Similar To Slit And			
	Flutamide	<i></i>	10050001	Ntrk-Like Family,	LOC3024	1.04	0.05
PND5	5	SAM	108/9221	Member 4	73	1.24	< 0.05
				Similar To	1.004002		
DND5	Flutamide	SAM	10024582	Nicotinamide Riboside	LUC4993	1.29	<0.05
FNDS	5	SAM	10934383	Microtubule	30	1.20	<0.03
	Flutamide			Associated Protein			
PND5	5	SAM	10701475	Tau	Mapt	1.65	< 0.05
	Flutamide				p ·		
PND5	5	SAM	10938302	Microrna Mir-24-1	Mir24-1	0.75	< 0.05
	Flutamide			Muted Homolog			
PND5	5	SAM	10726244	(Mouse)	Muted	0.82	< 0.05
				N-Acyl			
	Flutamide			Phosphatidylethanola			
PND5	5	SAM	10897764	mine Phospholipase D	Napepld	1.20	< 0.05
	Flutamide	GAN	10700202	NIr Family, Pyrin	NIIO	1.00	-0.05
PND5	5	SAM	10/00383	Domain Containing 9	NIrp9	1.88	< 0.05
	Elutomida			Nuclear Receptor			
PND5	riutamide 5	SAM	10898940	Member 1	Nr6a1	1 29	<0.05
11105	Flutamide	GANI	10020240	Olfactory Recentor	111001	1.27	~0.05
PND5	5	SAM	10718786	1340	Olr1340	1.30	< 0.05
DND5	Flutomida	SAM	10755027	Olfactory Pasantar	01r1606	1.25	<0.05
TNDS	Futannue	SAIVI	10/3302/	Onactory Receptor	011090	1.23	~0.03

	5			1696			
	Flutamide			Olfactory Receptor			
PND5	5	SAM	10828841	1726	Olr1726	1.41	< 0.05
	Flutamide			Olfactory Receptor			
PND5	5	SAM	10884732	241	Olr241	1.34	< 0.05
	Flutamide			Olfactory Receptor			
PND5	5	SAM	10916167	270	Olr270	1.31	< 0.05
	Flutamide	<i></i>	10510645	Olfactory Receptor	01.551	1.12	0.05
PND5	5	SAM	10718647	551	Olr551	1.13	< 0.05
DND5	Flutamide	CAN	10000021	Outrin 2	0	1.12	<0.05
PND5	) Elutomido	SAM	10908831	Opsin 3	Opn3	1.12	<0.05
DND5	Flutamide	SAM	10867705	Pat112 Like (Venst)	Dot1121	1.27	<0.05
FNDS	5 Elutamida	SAM	10807795	Pr Domain Containing	Fell121	1.27	<0.03
PND5	5	SAM	10719754	10	Prdm10	1.16	<0.05
1105	Flutamide	57 1111	10/19/51	Rab44 Member Ras	Trainito	1.10	-0.05
PND5	5	SAM	10816176	Oncogene Family	Rab44	1.22	< 0.05
11.00	Flutamide	01111	10010170	Similar To Kiaa0467	RGD1308		0.00
PND5	5	SAM	10744947	Protein	616	1.25	< 0.05
	Flutamide			Similar To Zinc Finger	RGD1308		
PND5	5	SAM	10890168	Protein Ozf (Pozf-1)	782	1.60	< 0.05
				Similar To Na+			
	Flutamide			Dependent Glucose	RGD1561		
PND5	5	SAM	10832496	Transporter 1	777	1.34	< 0.05
				Similar To Family			
				With Sequence			
	Flutamide			Similarity 55, Member	RGD1562		
PND5	5	SAM	10700401	С	319	1.61	< 0.05
	Flutamide			Similar To	RGD1564		
PND5	5	SAM	10748382	Hypothetical Protein	053	1.23	< 0.05
				Serine (Or Cysteine)			
	Flutamide			Peptidase Inhibitor,			
PND5	5	SAM	10887657	Clade F, Member 2	Serpinf2	1.31	< 0.05
				Solute Carrier Family			
				37 (Glycerol-3-			
				Phosphate			
	Flutamide	CAN	10720744	Transporter), Member	01 07 0	1.17	-0.05
PND5	5	SAM	10/38/44	2	SIC3/a2	1.1/	< 0.05
				Small Nuclear			
DND5	Flutamide	SAM	10201010	Ribonucleoprotein Dolymontido E	Sprof	0.77	<0.05
FNDS	J Flutamida	SAM	10091010	Somatostatin Pagantor	Silipi	0.//	~0.03
PND5	5	SAM	10924803		Sstr1	1 1 8	<0.05
11103	Flutamide	GAIVI	10724003	Sushi Domain	5301	1.10	~0.05
PND5	5	SAM	10701145	Containing ?	Susd?	1.81	<0.05
	Flutamide	D7 1111	10/01175	Testis-Specific Serine	54542	1.01	-0.05
PND5	5	SAM	10770154	Kinase 3	Tssk3	1.18	< 0.05
	Flutamide			Vomeronasal 1			
PND5	5	SAM	10853132	Receptor, 35	Vom1r35	1.22	< 0.05

				Xk, Kell Blood Group			
				Complex Subunit-			
	Flutamide	C A M	10757052	Related Family,	VI O	0.00	-0.05
PND5	5	SAM	10/5/253	Member 9	Xkr9	2.32	< 0.05
	Flutamide	<b>GAN</b> (	10714054	Hypothetical	LOC4993	1.20	-0.05
PND5	5	SAM	10/14254	Protein Loc499330	30	1.30	< 0.05
DND	Flutamide	GAN	10700701	Offactory Receptor	01-241	1.25	<0.05
PND5	<u> </u>	SAM	10/09/21	241	Olr241	1.25	< 0.05
DND5	Flutamide	CAM	10020020	Offactory Receptor	01-1726	1.25	<0.05
PND5	5	SAM	10830830	1720	Olf1/26	1.35	<0.05
				Core I Synthase,			
				A catylgalactosamina			
				3 Beta			
	Flutamide			Galactosyltransferase			
PND5	5	SAM	10853691	1	C1galt1	1 18	<0.05
11.00	Flutamide	51111	100000001	<u>*</u>	LOC2576		0.00
PND5	5	SAM	10737944	Hippyragranin	50	1.21	< 0.05
	Flutamide			Arginine Vasopressin			
PND5	5	SAM	10895747	Receptor 1A	Avpr1a	1.19	< 0.05
	Flutamide			Olfactory Receptor			
PND5	5	SAM	10847053	551	Olr551	1.24	< 0.05
	Flutamide			Hypothetical Protein	LOC3024		
PND5	5	SAM	10940016	Loc302473	73	1.38	< 0.05
				Small Nuclear			
	Flutamide			Ribonucleoprotein			
PND5	5	SAM	10901920	Polypeptide F	Snrpf	0.74	< 0.05
				Hypoxia Inducible			
	Flutamide			Domain Family,			
PND5	5	SAM	10738628	Member 1B.	Higd1b	0.75	< 0.05
	Flutamide						
PND5	5	SAM	10794685	Muted Homolog	Muted	0.88	< 0.05

# Appendix C

#### COMMON GENES FROM GD20 DBP500 LIMMA AND GD20 DBP500 SAM ANALYSES

Illumina ID	Gene Name	Symbol
ILMN_1355841	Abhydrolase Domain Containing 8	Abhd8
ILMN_1373231	Alcohol Dehydrogenase 6A (Class V)	Adh6A
ILMN_1351069	Apelin	Apln
ILMN_1368636	Asparagine Synthetase (Glutamine-Hydrolyzing)	Asns
ILMN_1368656	Beta-2 Microglobulin	B2M
ILMN_1365368	Brain Abundant, Membrane Attached Signal Protein 1	Basp1
ILMN_1352382	Complement Component 1, Q Subcomponent, A Chain	C1Qa
ILMN_1367246	Calcium/Calmodulin-Dependent Protein Kinase Ii Beta	Camk2B
ILMN_1372842	Cysteinyl-Trna Synthetase	Cars
ILMN_1365636	Cholecystokinin	Cck
ILMN_1356721	Chemokine (C-C Motif) Receptor 1	Cerl
ILMN_1376751	Claudin 4	Cldn4
ILMN_1373158	C-Type Lectin Domain Family 2, Member L	Clec2L
ILMN_1364825	Carboxypeptidase A6	Cpa6
ILMN_1362981	Carboxypeptidase D	Cpd
ILMN_1359951	Cathepsin C	Ctsc
ILMN_1376635	Cytochrome P450, Family 1, Subfamily B, Polypeptide 1	Cyp1B1
ILMN_1367505	Desmin	Des
ILMN_1368597	Dehydrogenase/Reductase (Sdr Family) Member 7C	Dhrs7C
ILMN_1376321	Dickkopf 3 Homolog	Dkk3
ILMN_1375038	Ephrin B1	Efnb1
ILMN_1372721	Eukaryotic Translation Initiation Factor 4B	Eif4B
ILMN_1360134	Endothelial Cell-Specific Molecule 1	Esm1
ILMN_1370964	Family With Sequence Similarity 114, Member A1	Fam114A1
ILMN_1376629	Fk506 Binding Protein 5	Fkbp5
ILMN_1350369	Fibronectin Leucine Rich Transmembrane Protein 3	Flrt3
ILMN_1370930	Forkhead Box L2	Foxl2
ILMN_1353747	Follistatin	Fst
	Fucosyltransferase 1 (Galactoside 2-Alpha-L-	
ILMN_1349350	Fucosyltransferase, H Blood Group)	Fut1
ILMN_1374865	Growth Differentiation Factor 1	Gdf1
ILMN_2039904	Growth Differentiation Factor 10	Gdf10
	Glucosamine (Udp-N-Acetyl)-2-Epimerase/N-	
ILMN_1370510	Acetylmannosamine Kinase	Gne
ILMN_1356417	Glutamate Receptor, Ionotropic, Ampa2 (Alpha 2)	Gria2
ILMN 1355860	Glutathione S-Transferase Kappa 1	Gstk1

ILMN_1358146	Gtp-Binding Protein 8 (Putative)	Gtpbp8
ILMN_1352509	Haus Augmin-Like Complex, Subunit 4	Haus4
ILMN_1651179	Hedgehog Interacting Protein	Hhip
ILMN_1349449	Htra Serine Peptidase 1	Htra1
ILMN_1349207	Inhibitor Of Dna Binding 2	Id2
ILMN_1360048	Insulin-Like Growth Factor Binding Protein 2	Igfbp2
ILMN_1362353	Insulin Induced Gene 1	Insig1
	Potassium Voltage-Gated Channel, Shal-Related Subfamily,	
ILMN_1350901	Member 3	Kcnd3
ILMN_1373748	Laminin, Alpha 2	Lama2
ILMN_1356375	Leucyl-Trna Synthetase	Lars
ILMN_1369814	Lactate Dehydrogenase B	Ldhb
ILMN_1352800	Kiaa0430	Lkap
ILMN_1371638	Lim Domain Only 4	Lmo4
ILMN_1353753	Similar To Gtpase Activating Protein Testicular Gap1	Loc362074
ILMN_1376846	Lysyl Oxidase-Like 1	Lox11
ILMN 1351352	Lysyl Oxidase-Like 2	Loxl2
ILMN 1361640	Latent Transforming Growth Factor Beta Binding Protein 2	Ltbp2
ILMN 1367069	Methionyl-Trna Synthetase	Mars
ILMN 1370971	Microsomal Glutathione S-Transferase 1	Mgst1
ILMN 1353175	Mkl (Megakaryoblastic Leukemia)/Myocardin-Like 1	Mkl1
ILMN 1354279	Matrix Metallopeptidase 11 (Stromelysin 3)	Mmp11
ILMN 1358694	Membrane-Spanning 4-Domains, Subfamily A, Member 4A	Ms4A4A
ILMN 1358752	Necdin	Ndn
ILMN 2040297	N-Mvc Downstream Regulated 1	Ndrg1
ILMN 1354048	Nuclear Protein, Transcriptional Regulator, 1	Nupr1
ILMN 1369735	Ornithine Decarboxylase. Structural 1	Odc1
ILMN 1355412	Olfactomedin-Like 2B	Olfml2B
ILMN 1366065	Protocadherin 19	Pcdh19
ILMN 1352410	Preproenkenhalin	Penk
ILMN 1374315	Placental Growth Factor	Pgf
ILMN 1355335	Protein O-Fucosyltransferase 2	Pofut2
ILMN 1361375	Two-Component Response Regulator-Like Aprr7	Prr7
ILMN 1358252	Phosphoserine Phosphatase	Psph
ILMN 1361790	Prostaglandin I2 (Prostacvclin) Synthase	Ptgis
ILMN 1370339	Retinoic Acid Receptor Responder (Tazarotene Induced) 2	Rarres2
ILMN 1369242	Similar To Hypothetical Protein C130079G13	Rgd1560324
ILMN 1365552	Similar To Hypothetical Upf0184 Protein C9Orf16 Homolog	Rgd1561113
ILMN 1374368	Similar To Novel Protein	Rgd1566099
ILMN 1366091	Ras-Related Associated With Diabetes	Rrad
	Solute Carrier Family 3 (Activators Of Dibasic And Neutral	
ILMN 1372377	Amino Acid Transport). Member 2	Slc3A2
	Solute Carrier Family 7 (Amino Acid Transporter Light Chain.	
ILMN 1365729	L System). Member 5	Slc7A5
	Sparc/Osteonectin, Cwcv And Kazal-Like Domains	
ILMN 1373684	Proteoglycan (Testican) 1	Spock1
ILMN 1650693	Small Proline-Rich Protein 1B	Sprr1B
ILMN 1376842	Transgelin	Tagln
ILMN 1364098	T-Cell Lymphoma Invasion And Metastasis 2	Tiam2

ILMN_1349592	Topoisomerase (Dna) Iii Alpha	Тор3А
ILMN_1353347	Tripartite Motif Containing 29	Trim29
ILMN_1354634	Wd Repeat And Fyve Domain Containing 1	Wdfy1
ILMN_1356435	Wingless-Related Mmtv Integration Site 4	Wnt4
ILMN_1374460	Tyrosyl-Trna Synthetase	Yars
ILMN_1357208	Zinc Finger Protein 36	Zfp36

# Appendix D

#### COMMON GENES FROM PND5 DBP500 LIMMA AND PND5 DBP500 SAM ANALYSES

Illumina ID	Gene Name	Symbol
ILMN_1369444	Predicted: Rattus Norvegicus Similar To Orf4 (Loc361942)	Loc361942
ILMN 1355694	Predicted: Rattus Norvegicus Similar To Ac1262 (Loc363492)	Loc363492
	Predicted: Rattus Norvegicus Similar To Lrrg00116	
ILMN 1352230	(Loc362543)	Loc362543
ILMN 1371063	Predicted: Rattus Norvegicus Similar To Orf4 (Loc498048)	Loc498048
	Predicted: Rattus Norvegicus Similar To Phd Finger Protein	
ILMN 1350792	20-Like 1 Isoform 1 (Loc314964)	Loc314964
	Predicted: Rattus Norvegicus Similar To Retrovirus-Related	
ILMN 1373694	Pol Polyprotein (Loc362315)	Loc362315
	Predicted: Rattus Norvegicus Triple Functional Domain (Ptprf	
ILMN 1354030	Interacting) (Trio)	Trio
ILMN 1363939	Rattus Norvegicus Cyclin L1 (Ccnl1)	Ccnl1
ILMN 1650840	Predicted: Rattus Norvegicus Cyclin L2 (Predicted) (Ccnl2)	Ccnl2
	Predicted: Rattus Norvegicus Desmoplakin, Transcript Variant	
ILMN_1349971	2 (Dsp)	Dsp
	Predicted: Rattus Norvegicus Similar To Lrrg00116	
ILMN_1375194	(Loc500867)	Loc500867
	Predicted: Rattus Norvegicus Similar To Lrrgt00057	
ILMN_1366649	(Loc501087)	Loc501087
	Predicted: Rattus Norvegicus Hypothetical Gene Supported By	
ILMN_1352738	Nm_019349 (Loc497743)	Loc497743
	Predicted: Rattus Norvegicus Similar To Lrrgt00008	
ILMN_1355226	(Loc500380)	Loc500380
ILMN_1366540	Predicted: Rattus Norvegicus Loc500721 (Loc500721)	Loc500721
ILMN_1370492	Rattus Norvegicus Tetraspanin 2 (Tspan2)	Tspan2
	Predicted: Rattus Norvegicus A Disintegrin And	
ILMN_1351087	Metalloprotease Domain 33 (Predicted) (Adam33)	Adam33
	Predicted: Rattus Norvegicus Similar To Ac1-163	
ILMN_1350958	(Loc498644)	Loc498644
	Predicted: Rattus Norvegicus Similar To Modulator Of	
	Estrogen Induced Transcription, Transcript Variant 1	
ILMN_1359196	(Rgd1307526), Misc Rna.	Rgd1307526
	Predicted: Rattus Norvegicus Zinc Finger Ccch Type	
ILMN_1364779	Containing 7 A (Predicted), Transcript Variant 2 (Zc3H7A)	Zc3H7A
	Rattus Norvegicus Cytochrome C Oxidase, Subunit Xvii	
ILMN_1353069	Assembly Protein Homolog (S. Cerevisiae) (Cox17)	Cox17
ILMN 1359062	Predicted: Rattus Norvegicus Ahnak 1 (Loc499315), Misc Rna.	Loc499315

II MN 1262602	Predicted: Rattus Norvegicus Similar To Lrrgt00176	L 00/100531
11.1v11v_1302003	Predicted: Pattus Norvegicus Pumilio 1 (Drosonhila)	100499331
ILMN 1363515	(Predicted) (Pum1)	Pum1
	Predicted Rattus Norvegicus Similar To Sr Rich Protein	
ILMN 1374578	(Rgd1307395)	Rgd1307395
	Predicted: Rattus Norvegicus Cellular Retinoic Acid Binding	
ILMN_1349215	Protein 1 (Mapped) (Crabp1)	Crabp1
	Predicted: Rattus Norvegicus Proline/Serine-Rich Coiled-Coil	
ILMN_1368627	2 (Psrc2)	Psrc2
ILMN_1376339	Rattus Norvegicus Aryl Hydrocarbon Receptor (Ahr)	Ahr
ILMN_1356426	Rattus Norvegicus Allantoicase (Allc)	Allc
	Predicted: Rattus Norvegicus Cdc23 (Cell Division Cycle 23,	
ILMN_1353529	Yeast, Homolog) (Cdc23)	Cdc23
	Predicted: Rattus Norvegicus Dead (Asp-Glu-Ala-Asp) Box	
ILMN_1355095	Polypeptide 17 (Ddx17)	Ddx17
	Predicted: Rattus Norvegicus Kinesin Family Member 5B	
ILMN_1354288	(Kif5B)	Kif5B
	Predicted: Rattus Norvegicus Similar To Lrrgt00194	
ILMN_1361625	(Loc361885)	Loc361885
	Predicted: Rattus Norvegicus Similar To Orf2 Consensus	
	Sequence Encoding Endonuclease And Reverse Transcriptase	T 400 554
ILMN_1363227	Minus Rnaseh (Loc499554)	Loc499554
ILMN_1371124	Predicted: Rattus Norvegicus Similar To Dal-12 (Loc500960)	Loc500960
	Predicted: Rattus Norvegicus Similar To Lrrg00135	
ILMN_1371120	(Loc501637)	Loc501637
H ) D 1 10(7000	Predicted: Rattus Norvegicus Similar To Riken Cdna	D 11205206
ILMN_136/232	6330406115 (Predicted) (Rgd130/396)	Rgd1307396
ILMN_1348821	Rattus Norvegicus Timp Metallopeptidase Inhibitor 3 (Timp3)	Timp3
	Rattus Norvegicus Zinc Finger Protein 36, C3H Type-Like 2	76 201 2
ILMN_1369812	$\frac{(Zip_{3}6L2)}{(Zip_{3}6L2)}$	Zfp36L2
H MOL 1254070	Predicted: Rattus Norvegicus Putative Isg12(B) Protein	$L_{\rm res}$ 12(D)
ILMIN_1354070	(ISg12(B))	Isg12(B)
II MNI 1266657	Rattus Norvegicus CIQ And Tumor Necrosis Factor Related	ClOtaff
ILMIN_1300037	Prodicted: Pottus Nervegious Kinestin 1 (Predicted) (Ktn1)	Vtn1
1LIVIN_1300073	Predicted: Rattus Norvegicus Kinectini I (Fledicted) (Kini)	Kull
II MN 1373580	Rox Polypentide 57 (Dhy 57)	Dhy57
1LIVIIN_1373300	Predicted: Pattus Norvegicus Similar To Krey Interaction	DIIX37
	Trapped Protein 1 (Krey Interaction Trapped 1) (Cerebral	
II MN 1359410	Cavernous Malformations 1 Protein Homolog) (Loc362317)	Loc362317
1210111_1555410	Rattus Norvegicus Ribosomal I 1 Domain Containing 1	
II MN 1376915	(Rs11D1)	Rs11D1
12,0010	Predicted: Rattus Norvegicus Ia Motif Containing Gtpase	
ILMN 1373759	Activating Protein 1 (Predicted) (Jagan1)	lagap1
	Predicted: Rattus Norvegicus Similar To Lrrg00116	10"r -
ILMN 1362918	(Loc361912)	Loc361912
	Predicted: Rattus Norvegicus Similar To Signal Recognition	
ILMN 1355550	Particle,72 Kda Subunit (Loc498351)	Loc498351
ILMN 1349611	Predicted: Rattus Norvegicus Similar To Ribosomal Protein	Loc499321

	L27A (Loc499321)	
	Predicted: Rattus Norvegicus Similar To Lrrg00135	
ILMN_1356548	(Loc501548)	Loc501548
	Predicted: Rattus Norvegicus Rna Binding Motif Protein 24	
ILMN 1350785	(Predicted) (Rbm24)	Rbm24
	Predicted: Rattus Norvegicus Similar To Lrrgt00057	
ILMN 1650107	(Loc499564)	Loc499564
	Predicted Rattus Norvegicus Similar To Isopentenyl	
ILMN 1368435	Diphosphate Delta-Isomerase Type 2 (Loc498787)	Loc498787
	Rattus Norvegicus Origin Recognition Complex Subunit 2-	200130707
ILMN 1376515	Like (Yeast) (Orc2L)	Orc2L
	Predicted: Rattus Norvegicus Similar To L rrgt00176	OIULL
ILMN 1362770	(Loc499582)	Loc499582
<u>ILIVII 1502770</u>	Predicted: Rattus Norvegicus Similar To Riken Cdna	200477502
II MN 1354105	$2810403 \wedge 07$ (Rad1565775)	Rad1565775
11.0111 1334103	Pattus Norvagious Guanina Nucleotida Binding Protein Alpha	Rgu1505775
II MN 1361160	11 (Gnall)	Gnall
1LWIN_1301100	Predicted: Pattus Norwagious Similar To Adn Dihosylation	Ullat I
II MNI 1260994	Factor Like 2 Like 1 (Lee204027)	L 2204027
1LWIN_1300884	Pattus Namusiaus Mdm4 D52 Dinding Protein Homolog	L00304037
II MAN 1276455	(Mouro) (Mdm4)	M due 4
ILMIN_13/0433	(Mouse) (Mulli4)	Ividiii4
II MAN 1255422	Fredicied: Ratius Norvegicus Prp39 Pre-Mina Processing	D
ILMIN_1355425	Practice 39 Homolog (Yeast) (Predicted) (Prp139)	PTp139
H M L 12722/5	Predicted: Kattus Norvegicus Hypothetical Loc315216	D 11211007
ILMIN_13/3365	(Predicted) (Rga1311907)	Kgd1311907
IL MAL 1252796	Predicted: Kattus Norvegicus Similar To Dual Specificity	$D = \frac{11500040}{100000000000000000000000000000000$
ILMIN_1353/80	Protein Phosphatase 5 (1-Dsp11) (Predicted) (Rgd1560049)	Kgd1560049
H MOL 1640950	Predicted: Ratius Norvegicus Gryceraidenyde 3-Phosphale	C 11
ILMIN_1049859	Denydrogenase (Gapan)	Gapun
H M L 12(2224	Predicted: Rattus Norvegicus Similar To Putative Rna Binding	1 501502
ILMN_1362324	Protein 1 (Loc501503)	L0C501503
H M L 1251202	Predicted: Rattus Norvegicus Similar To Vanin-3 (Predicted)	D 115(0(00
ILMN_1351302	(Rgd1560609)	Rgd1560609
	Predicted: Rattus Norvegicus Ataxia Telangiectasia Mutated	
ILMN_1353725	Homolog (Human) (Mapped) (Atm)	Atm
	Rattus Norvegicus Gonadotropin-Releasing Hormone I	G 11
ILMN_1373686	(Gnrh1)	Gnrhl
	Predicted: Rattus Norvegicus Similar To Hoxa-9 (Predicted)	T 005000
ILMN_1367919	(Loc29/099)	Loc297099
	Predicted: Rattus Norvegicus Similar To Lrrgt00176	
ILMN_1350803	(Loc498623)	Loc498623
	Predicted: Rattus Norvegicus Trichorhinophalangeal Syndrome	
ILMN_1349929	1 (Predicted) (Trps1)	Trps1
ILMN_1367035	Rattus Norvegicus Lecithin Cholesterol Acyltransferase (Lcat)	Lcat
	Predicted: Rattus Norvegicus Similar To Lrrgt00176	
ILMN_1359908	(Loc498669)	Loc498669
	Predicted: Rattus Norvegicus Similar To Lrrgt00176	
ILMN_1371641	(Loc500916)	Loc500916
	Predicted: Rattus Norvegicus Similar To Acyl-Coenzyme A	
ILMN_1351553	Binding Domain Containing 5 (Loc682593)	Loc682593

	Rattus Norvegicus Meningioma Expressed Antigen 5	
ILMN 1370257	(Hvaluronidase) (Mgea5)	Mgea5
	Predicted: Rattus Norvegicus Microsomal Glutathione S-	-0
ILMN 1370709	Transferase 2 (Predicted) (Mgst2)	Mgst2
	Predicted: Rattus Norvegicus Similar To Fksg26 Protein	
ILMN 1373089	(Predicted) (Loc292082)	Loc292082
_	Predicted: Rattus Norvegicus Mitchondrial Ribosomal Protein	
ILMN 1367484	S7 (Mrps7)	Mrps7
	Predicted: Rattus Norvegicus Similar To Orf2 Consensus	
	Sequence Encoding Endonuclease And Reverse Transcriptase	
ILMN_1363743	Minus Rnaseh (Loc501562)	Loc501562
	Rattus Norvegicus Cap-Gly Domain Containing Linker Protein	
ILMN_1356649	1 (Clip1)	Clip1
	Rattus Norvegicus Ribonuclease, Rnase A Family, 12 (Non-	
ILMN_1376375	Active) (Rnase12)	Rnase12
	Rattus Norvegicus Similar To Riken Cdna D630029K19	
ILMN_1369614	(Rgd1307100)	Rgd1307100
	Rattus Norvegicus High Mobility Group Nucleosomal Binding	
ILMN_1362726	Domain 3 (Hmgn3)	Hmgn3
	Predicted: Rattus Norvegicus Protein Phosphatase 2 (Formerly	
H MOL 1251224	2A), Regulatory Subunit B", Alpha, Transcript Variant 2	D
ILMIN_1351234	(Ppp2R3A)	Ppp2K3A
ILMIN_1358817	Rattus Norvegicus Adenosine Deaminase (Ada)	Ada
II MN 1356002	(Loc501057)	L 00501057
1LIVIIN_1330002	(LOC501057) Predicted: Pattus Norvegious Similar To Hypothetical Protein	100301037
II MN 1354146	D11Ertd99E (Predicted) (Rgd1564337)	Rgd1564337
ILMN 1371460	Rattus Norvegicus Ring Finger Protein 2 (Rnf2)	Rgd1504557
ILMN 2038882	Predicted: Rattus Norvegicus Loc498469 (Loc498469)	Loc498469
ILMN 1361164	Rattus Norvegicus Transcription Factor Myocardin (Myocd)	Myocd
	Predicted: Rattus Norvegicus Similar To Riken Cdna	iiiyoou
ILMN 1375102	5730509K17 Gene (Predicted) (Rgd1561042)	Rgd1561042
ILMN 1359160	Predicted: Rattus Norvegicus Cvclin T2 (Predicted) (Ccnt2)	Cent2
ILMN 1375001	Rattus Norvegicus Collagen, Type Xxvii, Alpha 1 (Col27A1)	Col27A1
ILMN 1370814	Rattus Norvegicus Fk506 Binding Protein-Like (Fkbpl)	Fkbpl
_	Rattus Norvegicus Homocysteine-Inducible, Endoplasmic	
	Reticulum Stress-Inducible, Ubiquitin-Like Domain Member 1	
ILMN_1370868	(Herpud1)	Herpud1
	Predicted: Rattus Norvegicus Similar To Glyceraldehyde-3-	
ILMN_1351960	Phosphate Dehydrogenase (Loc500506)	Loc500506
	Predicted: Rattus Norvegicus Similar To Histone-Lysine N-	
	Methyltransferase, H3 Lysine-4 Specific (Histone H3-K4	
	Methyltransferase) (H3-K4-Hmtase) (Set Domain-Containing	
ILMN_1363605	Protein 7) (Loc503176)	Loc503176
	Predicted: Rattus Norvegicus Mitogen-Activated Protein	
ILMN_1368495	Kinase Kinase Kinase 3 (Map4K3)	Map4K3
ILMN_1365626	Rattus Norvegicus Opioid Receptor, Sigma I (Oprs1)	Oprs1
IL MNI 1272727	Kattus Norvegicus Splicing Factor, Arginine/Serine-Rich II	Sfra11
ILIVIN_13/2/3/	(SIIS11) Desiliated, Detter Nemerica Transforming Courth Date	SIISI I
T ILIVUN 13/5291	redicted: Kattus Norvegicus Transforming Growth Factor	i i brg4

	Beta Regulated Gene 4 (Predicted) (Tbrg4)	
ILMN_1372235	Rattus Norvegicus Thyrotrophic Embryonic Factor (Tef)	Tef
	Predicted: Rattus Norvegicus Similar To Hypothetical Protein	
ILMN_1356329	Kiaa0539 (Predicted) (Loc304104)	Loc304104
	Predicted: Rattus Norvegicus Similar To Riken Cdna	
ILMN_1368345	2010110M21 (Predicted) (Loc290999)	Loc290999
ILMN_1364535	Rattus Norvegicus Rna Binding Motif Protein 39 (Rbm39)	Rbm39
	Predicted: Rattus Norvegicus Similar To Hypothetical Protein	
ILMN_1355746	Mgc14151 (Predicted) (Rgd1559617)	Rgd1559617
	Rattus Norvegicus Similar To Hypothetical Protein Flj10154	
ILMN_1367208	(Rgd1310061)	Rgd1310061
	Predicted: Rattus Norvegicus Sorting Nexin 14 (Predicted)	
ILMN_1358019	(Snx14)	Snx14
ILMN_1350576	Predicted: Rattus Norvegicus Similar To Palladin (Loc290704)	Loc290704
	Predicted: Rattus Norvegicus Similar To Hypothetical Protein	
ILMN_1349311	Kiaa1240 (Loc313940)	Loc313940
	Rattus Norvegicus Mitogen Activated Protein Kinase Kinase 1	
ILMN_1361975	(Map2K1)	Map2K1
H ) D 1 1050500	Predicted: Rattus Norvegicus Ccr4-Not Transcription	0.17
ILMN_1353588	Complex, Subunit / (Predicted) (Cnot/)	Cnot7
H M L 12(1017	Predicted: Rattus Norvegicus Similar To Lrrgt00082	1 500200
ILMN_1361017		L0C500398
	Predicted: Rattus Norvegicus Golgi Associated, Gamma	
H MAL 12520(7	Adaptin Ear Containing, Art Binding Protein 3 (Predicted),	G 2
ILMIN_1352867	Patter New ariant 2 (Gga3)	Gga3
ILMN_13/141/	Rattus Norvegicus Gastrin Releasing Peptide (Grp)	Grp
IL MAL 1257900	Rattus Norvegicus Ccr4-Not Transcription Complex, Subunit 6	Creat(
ILMIN_1357809	(Cholo)	Cholo
II MNI 1250704	Predicted: Rattus Norvegicus Polymerase I And Transcript	Dtef
ILIVIN_1550794	Predicted: Pattus Norvegieus Similar To Novel Protein Of	rui
	Unknown Function (Duff23) Family Member (Predicted)	
II MN 1371362	(Rad1563438)	Rad1563438
112/01/13/1302	Predicted: Rattus Norvegicus Similar To Kiaa0372 Gene	Rgu1505456
ILMN 1356505	Product (Predicted) (Rgd1306062)	Rgd1306062
	Predicted: Rattus Norvegicus Ubiquitin-Like Containing Phd	itguiboooo2
ILMN 1530420	And Ring Finger Domains 2 (Predicted) (Uhrf2)	Uhrf2
	Predicted Rattus Norvegicus Similar To Microfilament And	0
ILMN 1354877	Actin Filament Cross-Linker Protein Isoform A (Loc362587)	Loc362587
	Predicted: Rattus Norvegicus Atpase, Class I, Type 8B,	
ILMN 1360542	Member 1 (Predicted) (Atp8B1)	Atp8B1
ILMN 1358267	Rattus Norvegicus Cathepsin D (Ctsd)	Ctsd
_	Predicted: Rattus Norvegicus Similar To Lrrg00135	
ILMN_1649797	(Loc499560)	Loc499560
ILMN 1376542	Rattus Norvegicus Transcription Factor 12 (Tcf12)	Tcf12
_	Rattus Norvegicus Ectonucleoside Triphosphate	
ILMN_1373210	Diphosphohydrolase 5 (Entpd5)	Entpd5
	Rattus Norvegicus Polypyrimidine Tract Binding Protein 2	
ILMN_1363928	(Ptbp2)	Ptbp2

	(Predicted) (Loc291914)	
	Predicted: Rattus Norvegicus Similar To Ribosomal Protein	
ILMN_1356051	L27A (Loc292474)	Loc292474
	Predicted: Rattus Norvegicus Upf3 Regulator Of Nonsense	
ILMN_1349703	Transcripts Homolog B (Yeast) (Predicted) (Upf3B)	Upf3B
	Predicted: Rattus Norvegicus E2F Transcription Factor 5	
ILMN_1351213	(E2F5)	E2F5
	Rattus Norvegicus Nuclear Protein E3-3 (Rgd708545),	
ILMN_1370444	Transcript Variant 1	Rgd708545
	Predicted: Rattus Norvegicus Perq Amino Acid Rich, With Gyf	
ILMN_1354514	Domain 1 (Predicted) (Perq1)	Perq1
	Rattus Norvegicus Neuronal Regeneration Related Protein	
ILMN_1357234	(Nrep)	Nrep
	Predicted: Rattus Norvegicus Similar To Ylp Motif Containing	
	Protein 1 (Nuclear Protein Zap3) (Zap113) (Predicted)	
ILMN_1363528	(Rgd1564946)	Rgd1564946
	Predicted: Rattus Norvegicus Formin Binding Protein 4	
ILMN_1371331	(Fnbp4)	Fnbp4
	Predicted: Rattus Norvegicus Similar To Transmembrane	
ILMN_1361015	Protein Tm9Sf3 (Loc309475)	Loc309475
ILMN_1374140	Predicted: Rattus Norvegicus Parathymosin (Ptms)	Ptms
	Predicted: Rattus Norvegicus Peroxisome Proliferative	
	Activated Receptor, Gamma, Coactivator-Related 1 (Predicted)	
ILMN_1367124	(Pprc1)	Pprc1
	Predicted: Rattus Norvegicus Similar To Lrrgt00057	
ILMN_1356833	(Loc499501)	Loc499501
ILMN 1357093	Rattus Norvegicus Tropomyosin 4 (Tpm4)	Tpm4

# Appendix E

#### COMMON GENES FROM PND5 DBP500 LIMMA AND PND5 DBP100 SAM ANALYSES

ILMN_1351226	Cbl Proto-Oncogene, E3 Ubiquitin Protein Ligase B	Cblb
ILMN_1650840	Cyclin L2	Ccnl2
ILMN_1354288	Kinesin Family Member 5B	Kif5B
ILMN_1369444	Similar To Orf4	Loc361942
ILMN_1355694	Similar To Ac1262	Loc363492
ILMN_1371063	Similar To Orf4	Loc498048
	Similar To Orf2 Consensus Sequence Encoding Endonuclease	
ILMN_1363227	And Reverse Transcriptase Minus Rnaseh	Loc499554
ILMN_1361017	Similar To Lrrgt00082	Loc500398
ILMN_1371120	Similar To Lrrg00135	Loc501637
ILMN_1351553	Similar To Acyl-Coenzyme A Binding Domain Containing 5	Loc682593
ILMN_1376515	Origin Recognition Complex, Subunit 2	Orc2L
ILMN_1355423	Prp39 Pre-Mrna Processing Factor 39 Homolog	Prpf39
ILMN_1363928	Polypyrimidine Tract Binding Protein 2	Ptbp2
ILMN_1354105	Similar To Riken Cdna 2810403A07	Rgd1565775
ILMN_1370492	Tetraspanin 2	Tspan2
ILMN_1364779	Zinc Finger Ccch-Type Containing 7A	Zc3H7A
	Rattus Norvegicus Splicing Factor, Arginine/Serine-Rich 11	
ILMN 1372737	(Sfrs11)	Sfrs11

# Appendix F

#### COMMON GENES FROM PND5 DBP500 SAM AND PND5 DBP100 SAM ANALYSES

ILMN_1369444	Predicted: Rattus Norvegicus Similar To Orf4 (Loc361942)	Loc361942
ILMN_1355694	Predicted: Rattus Norvegicus Similar To Ac1262 (Loc363492)	Loc363492
	Rattus Norvegicus Origin Recognition Complex, Subunit 2-	
ILMN_1376515	Like (Yeast) (Orc2L)	Orc2L
ILMN_1371063	Predicted: Rattus Norvegicus Similar To Orf4 (Loc498048)	Loc498048
ILMN_1650840	Predicted: Rattus Norvegicus Cyclin L2 (Predicted) (Ccnl2)	Ccnl2
	Predicted: Rattus Norvegicus Similar To Riken Cdna	
ILMN_1354105	2810403A07 (Rgd1565775)	Rgd1565775
	Predicted: Rattus Norvegicus Prp39 Pre-Mrna Processing	
ILMN_1355423	Factor 39 Homolog (Yeast) (Predicted) (Prpf39)	Prpf39
	Predicted: Rattus Norvegicus Similar To Acyl-Coenzyme A	
ILMN_1351553	Binding Domain Containing 5 (Loc682593)	Loc682593
	Rattus Norvegicus Polypyrimidine Tract Binding Protein 2	
ILMN_1363928	(Ptbp2)	Ptbp2
	Rattus Norvegicus Zinc Finger With Ufm1-Specific Peptidase	
ILMN_1350927	Domain (Zufsp)	Zufsp
ILMN_1370492	Rattus Norvegicus Tetraspanin 2 (Tspan2)	Tspan2
	Predicted: Rattus Norvegicus Similar To Lrrg00135	
ILMN_1371120	(Loc501637)	Loc501637
	Predicted: Rattus Norvegicus Similar To Cdna Sequence	
ILMN_1365562	Bc024479 (Loc500974), Misc Rna.	Loc500974
ILMN_1368776	Predicted: Rattus Norvegicus Loc498674 (Loc498674)	Loc498674
	Predicted: Rattus Norvegicus Similar To Orf2 Consensus	
	Sequence Encoding Endonuclease And Reverse Transcriptase	
ILMN_1363227	Minus Rnaseh (Loc499554)	Loc499554
	Predicted: Rattus Norvegicus Kinesin Family Member 5B	
ILMN_1354288	(Kif5B)	Kif5B
ILMN_1376454	Rattus Norvegicus Tar Dna Binding Protein (Tardbp)	Tardbp
	Predicted: Rattus Norvegicus Zinc Finger Ccch Type	
ILMN_1364779	Containing 7 A (Predicted), Transcript Variant 2 (Zc3H7A)	Zc3H7A
	Predicted: Rattus Norvegicus Similar To Lrrgt00082	
ILMN_1361017	(Loc500398)	Loc500398
	Rattus Norvegicus Heterogeneous Nuclear Ribonucleoprotein	
ILMN 1369798	F (Hnrnpf), Transcript Variant 2	Hnrnpf

# Appendix G

#### COMMON GENES FROM PND5 DBP100 SAM AND PND5 DBP500 SAM ANALYSES

ILMN_1350792	Phd Finger Protein 20-Like 1	Phf20L1
ILMN_1351553	Similar To Acyl-Coenzyme A Binding Domain Containing 5	Loc682593
ILMN_1354105	Similar To Riken Cdna 2810403A07	Rgd1565775
ILMN_1354288	Kinesin Family Member 5B	Kif5B
ILMN_1355423	Prp39 Pre-Mrna Processing Factor 39 Homolog	Prpf39
ILMN_1355694	Similar To Ac1262	Loc363492
ILMN_1359410	Krit1, Ankyrin Repeat Containing	Krit1
ILMN_1361017	Similar To Lrrgt00082	Loc500398
	Similar To Orf2 Consensus Sequence Encoding Endonuclease	
ILMN_1363227	And Reverse Transcriptase Minus Rnaseh	Loc499554
ILMN_1363928	Polypyrimidine Tract Binding Protein 2	Ptbp2
ILMN_1364779	Zinc Finger Ccch-Type Containing 7A	Zc3H7A
ILMN_1366649	Similar To Lrrgt00057	Rgd1562999
ILMN_1369444	Similar To Orf4	Loc361942
ILMN_1370492	Tetraspanin 2	Tspan2
ILMN_1371063	Similar To Orf4	Loc498048
ILMN_1371120	Similar To Lrrg00135	Loc501637
ILMN_1376515	Origin Recognition Complex, Subunit 2	Orc2L
ILMN_1650840	Cyclin L2	Ccnl2
ILMN_1350927	Zinc Finger With Ufm1-Specific Peptidase Domain	Zufsp
ILMN_1365562	Similar To Cdna Sequence Bc024479	Loc500974
ILMN_1368776	Loc498674	Loc498674
ILMN_1369798	Heterogeneous Nuclear Ribonucleoprotein F	Hnrpf
ILMN_1376454	Tar Dna Binding Protein	Tardbp

# Appendix H

#### COMMON GENES FROM PND5 DBP100 SAM AND PND5 DBP500 LIMMA ANALYSES

ILMN_1350792	Phd Finger Protein 20-Like 1	Phf20L1
ILMN_1351226	Cbl Proto-Oncogene, E3 Ubiquitin Protein Ligase B	Cblb
ILMN_1351553	Similar To Acyl-Coenzyme A Binding Domain Containing 5	Loc682593
ILMN_1354105	Similar To Riken Cdna 2810403A07	Rgd1565775
ILMN_1354288	Kinesin Family Member 5B	Kif5B
ILMN_1355423	Prp39 Pre-Mrna Processing Factor 39 Homolog	Prpf39
ILMN_1355694	Similar To Ac1262	Loc363492
ILMN_1359410	Krit1, Ankyrin Repeat Containing	Krit1
ILMN_1361017	Similar To Lrrgt00082	Loc500398
	Similar To Orf2 Consensus Sequence Encoding Endonuclease	
ILMN_1363227	And Reverse Transcriptase Minus Rnaseh	Loc499554
ILMN_1363928	Polypyrimidine Tract Binding Protein 2	Ptbp2
II MN 1364770	7 The Finance Could The Countering 74	
11.10111 1304//9	Zinc Finger Cccn-Type Containing /A	Zc3H7A
ILMN_1366649	Similar To Lrrgt00057	Zc3H7A Rgd1562999
ILMN_1366649 ILMN_1369444	Similar To Orf4	Zc3H7A Rgd1562999 Loc361942
ILMN         I366779           ILMN         I366649           ILMN         I369444           ILMN         I370492	Similar To Orf4 Tetraspanin 2	Zc3H7A Rgd1562999 Loc361942 Tspan2
ILMN 1366649 ILMN 1369444 ILMN 1370492 ILMN 1371063	Similar To Lrrgt00057 Similar To Orf4 Tetraspanin 2 Similar To Orf4	Zc3H7A Rgd1562999 Loc361942 Tspan2 Loc498048
ILMN 136649 ILMN 1366649 ILMN 1369444 ILMN 1370492 ILMN 1371063 ILMN 1371120	Similar To Lrrgt00057 Similar To Orf4 Tetraspanin 2 Similar To Orf4 Similar To Lrrg00135	Zc3H7A Rgd1562999 Loc361942 Tspan2 Loc498048 Loc501637
ILMN 136649 ILMN 1366649 ILMN 1369444 ILMN 1370492 ILMN 1371063 ILMN 1371120 ILMN 1376515	Similar To Lrrgt00057 Similar To Orf4 Tetraspanin 2 Similar To Orf4 Similar To Lrrg00135 Origin Recognition Complex, Subunit 2	Zc3H7A Rgd1562999 Loc361942 Tspan2 Loc498048 Loc501637 Orc2L
## Appendix I

## COMMON GENES FROM GD20 DBP500 SAM AND PND5 DBP500 SAM ANALYSES

ILMN_1369444	Predicted: Rattus Norvegicus Similar To Orf4 (Loc361942)	Loc361942
ILMN_1355694	Predicted: Rattus Norvegicus Similar To Ac1262 (Loc363492)	Loc363492
	Rattus Norvegicus Origin Recognition Complex, Subunit 2-	
ILMN_1376515	Like (Yeast) (Orc2L)	Orc2L
ILMN_1371063	Predicted: Rattus Norvegicus Similar To Orf4 (Loc498048)	Loc498048
ILMN_1650840	Predicted: Rattus Norvegicus Cyclin L2 (Predicted) (Ccnl2)	Ccnl2
	Predicted: Rattus Norvegicus Similar To Riken Cdna	
ILMN_1354105	2810403A07 (Rgd1565775)	Rgd1565775
	Predicted: Rattus Norvegicus Prp39 Pre-Mrna Processing	
ILMN_1355423	Factor 39 Homolog (Yeast) (Predicted) (Prpf39)	Prpf39
	Predicted: Rattus Norvegicus Similar To Acyl-Coenzyme A	
ILMN_1351553	Binding Domain Containing 5 (Loc682593)	Loc682593
	Rattus Norvegicus Polypyrimidine Tract Binding Protein 2	
ILMN_1363928	(Ptbp2)	Ptbp2
	Rattus Norvegicus Zinc Finger With Ufm1-Specific Peptidase	
ILMN_1350927	Domain (Zufsp)	Zufsp
ILMN_1370492	Rattus Norvegicus Tetraspanin 2 (Tspan2)	Tspan2
	Predicted: Rattus Norvegicus Similar To Lrrg00135	
ILMN_1371120	(Loc501637)	Loc501637
	Predicted: Rattus Norvegicus Similar To Cdna Sequence	
ILMN_1365562	Bc024479 (Loc500974), Misc Rna.	Loc500974
ILMN_1368776	Predicted: Rattus Norvegicus Loc498674 (Loc498674)	Loc498674
	Predicted: Rattus Norvegicus Similar To Orf2 Consensus	
	Sequence Encoding Endonuclease And Reverse Transcriptase	
ILMN_1363227	Minus Rnaseh (Loc499554)	Loc499554
	Predicted: Rattus Norvegicus Kinesin Family Member 5B	
ILMN_1354288	(Kif5B)	Kif5B
ILMN_1376454	Rattus Norvegicus Tar Dna Binding Protein (Tardbp)	Tardbp
	Predicted: Rattus Norvegicus Zinc Finger Ccch Type	
ILMN_1364779	Containing 7 A (Predicted), Transcript Variant 2 (Zc3H7A)	Zc3H7A
	Predicted: Rattus Norvegicus Similar To Lrrgt00082	
ILMN_1361017	(Loc500398)	Loc500398
	Rattus Norvegicus Heterogeneous Nuclear Ribonucleoprotein	
ILMN_1369798	F (Hnrnpf), Transcript Variant 2	Hnrnpf