

We've got your KO mice
and ES Clones
CLICK ON IT



TIGM.org
Texas Institute for Genomic Medicine

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Texas Institute for Genomic Medicine Newsletter

July 2007 - 3rd Quarter

Dear Jennifer Pursley,

TIGM has great news and new services we would like to share with you. You may browse our newsletter or click on a link below to go straight to the information you would like to read. If you would like information on how TIGM can help you access your knockout mice or clones please call, toll free (888) 377-TIGM or +1-713-677-7401, or you may visit our website at www.TIGM.org.

Kind regards,

Jennifer Pursley

Business Development

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In This Issue

[100,000 New Clones Available in C57BL/6](#)

[TIGM Submits Sequence Tags to GenBank®](#)

TIGM1 Is Almost Done

100,000 NEW CLONES AVAILABLE IN C57BL/6

TIGM has added **100,000 new clones** to its **C57BL/6** gene trap library. TIGM now has access to over **300,000** clones in the **C57BL/6** mouse strain and over **270,000** clones in the 129SvEvBrd strain. The genes that are interrupted in these new clones have been added to our database. Our gene trap database is fully searchable at <http://tigm.org/database/>. If you were previously unsuccessful in finding your gene, please take another look. TIGM provides breeding pairs of heterozygous knockout mice or ES cells.

TIGM SUBMITS SEQUENCE TAGS TO GenBank®

TIGM has submitted insertion sequence tags for over 250,000 clones from our C57BL/6 library to the GSS division of GenBank®. For more information or to search GenBank®, please visit <http://www.ncbi.nlm.nih.gov/Genbank/>.

TIGM'S NEW MOUSE FACILITY IS RUNNING AHEAD OF SCHEDULE

Completion of TIGM1, the first of several planned animal facilities is ahead of construction schedule and should be fully operational in September, 2007. This facility was designed with a Class A barrier that has sufficient space to house over 8,800 cages. It also has a Class B clean area capable of holding over 6,500 cages.



ABSTRACTS OF NOTE

Below are just a few abstracts from recent publications describing genes of high scientific interest. TIGM has these genes trapped in ES cell clones, and we are ready to produce the knockout mice for your research needs. The gene names have

been linked to the updated TIGM database for your browsing convenience.

If you have a recent publication you would like to present in our quarterly newsletter, please send the abstract to jpursley@tigm.org.

Frayling, T. et al. A Common Variant in the *FTO* Gene Is Associated with Body Mass Index and Predisposes to Childhood and Adult Obesity. *Science*. 11 May 2007; Vol. 316. no. 5826, pp. 889 - 894.

Obesity is a serious international health problem that increases the risk of several common diseases. The genetic factors predisposing to obesity are poorly understood. A genome-wide search for type 2 diabetes-susceptibility genes identified a common variant in the [FTO](#) (fat mass and obesity associated) gene that predisposes to diabetes through an effect on body mass index (BMI). An additive association of the variant with BMI was replicated in 13 cohorts with 38,759 participants. The 16% of adults who are homozygous for the risk allele weighed about 3 kilograms more and had 1.67-fold increased odds of obesity when compared with those not inheriting a risk allele. This association was observed from age 7 years upward and reflects a specific increase in fat mass.

Tahiliani, M. et al. The histone H3K4 demethylase SMCX links REST target genes to X-linked mental retardation. *Nature*, 31 May 2007; 447(7144):601-5.

Gene transcription is critically influenced by chromatin structure and the modification status of histone tails. Methylation of lysine residues in histone tails is dynamically regulated by the opposing activities of histone methyltransferases and histone demethylases. Here we show that JARID1C/SMCX, a JmjC-domain-containing protein implicated in X-linked mental retardation and epilepsy, possesses H3K4 tri-demethylase activity and functions as a transcriptional repressor. An SMCX complex isolated from HeLa cells contains additional chromatin modifiers (the histone deacetylases HDAC1 and HDAC2, and the histone H3K9 methyltransferase G9a) and the transcriptional repressor REST, suggesting a direct role for [SMCX](#) in chromatin dynamics and REST-mediated repression. Chromatin immunoprecipitation reveals that SMCX and REST co-occupy the neuron-restrictive silencing elements in the promoters of a subset of REST target genes. RNA-interference-mediated depletion of SMCX derepresses several of these targets and simultaneously increases H3K4 trimethylation at the sodium channel type 2A (*SCN2A*) and synapsin I (*SYN1*) promoters. We propose that loss of SMCX activity impairs REST-mediated neuronal gene regulation, thereby contributing to SMCX-associated X-linked mental retardation.

Beales, P. et al. IFT80, which encodes a conserved intraflagellar transport protein, is mutated in Jeune asphyxiating thoracic dystrophy. *Nature Genetics*, June 2007; 39(6):727-9.

Jeune asphyxiating thoracic dystrophy, an autosomal recessive chondrodysplasia, often leads to death in infancy because of a severely constricted thoracic cage and respiratory insufficiency; retinal degeneration, cystic renal disease and polydactyly may be complicating features. We show that [IFT80](#) mutations underlie a subset of Jeune asphyxiating thoracic dystrophy cases, establishing the first association of a defective intraflagellar transport (IFT) protein with human disease. Knockdown of *ift80* in zebrafish resulted in cystic kidneys, and knockdown in *Tetrahymena thermophila* produced shortened or absent cilia.

Steinthorsdottir, V. et al. A variant in CDKAL1 influences insulin response and risk of type 2 diabetes. *Nature Genetics*, June 2007; 39(6):770-5.

We conducted a genome-wide association study for type 2 diabetes (T2D) in Icelandic cases and controls, and we found that a previously described variant in the transcription factor 7-like 2 gene (*TCF7L2*) gene conferred the most

significant risk. In addition to confirming two recently identified risk variants, we identified a variant in the [CDKAL1](#) gene that was associated with T2D in individuals of European ancestry (allele-specific odds ratio (OR) = 1.20 (95% confidence interval, 1.13-1.27), $P = 7.7 \times 10^{-9}$) and individuals from Hong Kong of Han Chinese ancestry (OR = 1.25 (1.11-1.40), $P = 0.00018$). The genotype OR of this variant suggested that the effect was substantially stronger in homozygous carriers than in heterozygous carriers. The ORs for homozygotes were 1.50 (1.31-1.72) and 1.55 (1.23-1.95) in the European and Hong Kong groups, respectively. The insulin response for homozygotes was approximately 20% lower than for heterozygotes or noncarriers, suggesting that this variant confers risk of T2D through reduced insulin secretion.

*Look for our ads in Science and Nature