Metabolic and Cardiovascular Disease Models and Services

MODELS AND SERVICES DESIGNED TO TAKE YOUR STUDY FURTHER
Metabolic and Cardiovascular Disease Models and Services

Diabetes, hypertension, heart disease and obesity have reached epidemic proportions, making research into cardiovascular and metabolic disorders a top priority.

Over 300 million people suffer from diabetes. Taconic assists researchers with models that mimic human disease for the study of different aspects of metabolic and cardiovascular disease.

The availability of predictive animal models is essential for the advancement of this vital research. To address this need, Taconic Biosciences offers a wide range of models and services including traditional and spontaneous mutants, transgenic models, and study-ready models such as the off-the-shelf diet-induced obesity model (DIO).
Taconic Transgenic Models™ (TTMs™) are important research models offered off-the-shelf in typical study quantities. TTMs™ carry a label license granting you the intellectual property right(s) to use the model in your research.
Apoe

CARDIOVASCULAR DISEASE MODEL
CONSTITUTIVE KNOCKOUT MOUSE
C57BL/6 BACKGROUND

- Contains a disruption of the endogenous murine apolipoprotein E gene.
- Homozygous ApoE mice are devoid of apoE protein.

Mice develop normally, but exhibit five times normal serum plasma cholesterol and spontaneous atherosclerotic lesions when maintained on a standard diet.

MODEL NUMBER APOE

APOE2

CARDIOVASCULAR DISEASE MODEL
TARGETED REPLACEMENT
C57BL/6 BACKGROUND

- Homozygous for a human APOE*2 gene through targeted replacement of the endogenous mouse Apoe gene.
- Expresses human apolipoprotein E2 isoform under the control of the murine Apoe regulatory sequences.

Develops hyperlipoproteinemia with elevated plasma cholesterol and triglyceride levels, decreased clearance of vLDL particles, and spontaneous atherosclerotic plaques on a normal diet, exacerbated by a high fat diet.

MODEL NUMBER 1547

APOE3

CARDIOVASCULAR DISEASE MODEL
TARGETED REPLACEMENT
C57BL/6 BACKGROUND

- Homozygous for a human APOE*3 gene through targeted replacement of the endogenous mouse Apoe gene.
- Expresses human apolipoprotein E3 isoform under the control of the murine Apoe regulatory sequences.

Exhibits an increased risk of atherosclerosis and hypercholesterolemia compared with wild type mice on a high fat diet, but not on a normal diet.

Useful for studying the role of human APOE3, which is the most common form of human APOE in diseases related to APOE isoforms.

MODEL NUMBER 1548
APOE4

CARDIOVASCULAR DISEASE MODEL
TARGETED REPLACEMENT
C57BL/6 BACKGROUND

- Homozygous for a human APOE*4 gene through targeted replacement of endogenous mouse Apoe gene.
- Expresses human apolipoprotein E4 isoform under the control of the murine Apoe regulatory sequences.
- Exhibits an increased risk of atherosclerosis compared with wild type and APOE3 targeted replacement mice.
- Useful for studying the role of human APOE polymorphism in atherosclerosis and lipid metabolism.
- On a high-fat diet, develops abnormal serum lipid profiles and atherosclerotic plaques that are more severe than the APOE3 model, with twice the cholesterol, ApoE, and ApoB-48 levels and larger plaques than the APOE3 model.

MODEL NUMBER 1549

ApoB100

CARDIOVASCULAR DISEASE MODEL
RANDOM TRANGENIC
C57BL/6 BACKGROUND

- Contains the human apolipoprotein B transgene.
- ApoB100 is the predominant human ApoB species found in plasma of ApoB100 mice.
- ApoB100 mice show elevated serum levels of LDL cholesterol.
- Develops atherosclerosis on a high fat, high cholesterol diet.
- Useful for identifying and evaluating compounds to reduce LDL levels and the risk of atherosclerosis.
- Also useful for studies of lipid transport and atherosclerosis.

MODEL NUMBER 1004

CETP-ApoB100

CARDIOVASCULAR DISEASE MODEL
RANDOM TRANGENIC
C57BL/6 BACKGROUND

- Carries both human cholesteryl ester transfer protein and human apolipoprotein B transgenes.
- Exhibits human-like serum HDL/LDL distribution.
- When fed a high fat, high cholesterol diet this mouse develops complex atherosclerotic lesions.
- Useful for evaluating compounds to treat hypercholesterolemia or HDL/LDL imbalance to reduce the risk of developing atherosclerosis.

MODEL NUMBER 3716
CETP

CARDIOVASCULAR DISEASE MODEL
RANDOM TRANSGENIC
C57BL/6 BACKGROUND

- Contains human cholesteryl ester transfer protein transgene.
- Exhibits dramatic reduction in serum HDL cholesterol.
- Useful for identifying and evaluating compounds that increase HDL levels.
- Serves as one control for the CETP-ApoB100 mouse model.

MODEL NUMBER 3715

Ppara

CARDIOVASCULAR AND METABOLIC DISEASE MODEL
CONSTITUTIVE KNOCK OUT MOUSE
C57BL/6 BACKGROUND

- Contains a disruption of the Ppara (peroxisome proliferator activated receptor α) gene.
- No profound hepatomegaly, peroxisomal proliferation or induction of fatty acid oxidation enzymes in response to classical peroxisome proliferators.
- Higher serum cholesterol and apoA-I concentrations than wild type controls.
- Altered fatty acid metabolism including lower β-oxidation of palmitic acid.
- β-oxidation of very long chain fatty acids is not altered.
- Useful in the study of lipid and glucose homeostasis, fatty acid metabolism and as a potential model for inborn errors of metabolism.

MODEL NUMBER 1640
EMERGING MODELS

LIGHT PRODUCING TRANSGENIC ANIMALS® (LPTA®)

Reporter models expressing luciferase under the control of various promoters, for use in bioluminescent imaging both in vivo and ex vivo.

LPTA® models relevant to the study of metabolic and cardiovascular disorders include:

**RIP-luc**
Useful for the study of transcriptional regulation of the insulin promoter, changes in insulin production (resulting from fasting, streptozotocin treatment etc.), and for pancreatic islet transplantation studies.

**Retn-luc**
Useful for obesity studies (including fasting, high-fat feeding, insulin resistance), and for adipose tissue transplantation studies.

**mIns2-luc**
Useful for the study of changes in insulin production (resulting from fasting, high-fat diet feeding, streptozotocin treatment etc.), and for pancreatic islet transplantation studies.

In this model, the mouse insulin promoter drives the expression of luciferase.

Visit [Taconic.com/lpta](http://Taconic.com/lpta) for a listing of all available LPTA® models.

* LPTA models are made available from Taconic under a license from Caliper Life Sciences and Promega Corporation. Other third party rights may apply. Refer to [Taconic.com/lpta](http://Taconic.com/lpta) for the LPTA® Conditions of Use.
**Black 6**

**AGING/DIET INDUCED OBESE MODEL INBRED MOUSE**

- The most widely used inbred strain for diet induced obesity research due to susceptibility to high fat diet.
- Popular in research applications of oncology, immunology, toxicology.
- Now available at the Germ-Free health profile in addition to Excluded Flora, Restricted Flora™ and Murine Pathogen Free™ health profiles.
- Taconic’s B6 sublines do not carry the known Nnt mutation.

**MODEL NUMBER B6**

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**Goto-Kakizaki Rat**

**DIABETES MODEL INBRED RAT**

- A non-obese model of Non-Insulin Dependent Diabetes Mellitus (NIDDM), type 2 diabetes.
- Exhibits similar metabolic, hormonal and vascular disorders to the human diabetes disease.
- Males typically develop type 2 diabetes at 14-16 weeks of age.
- Characteristics include fasting hyperglycemia, impaired secretion of insulin in response to glucose and polyuria and hepatic and peripheral insulin resistance.
- Late complications such as retinopathy, microangiopathy, neuropathy and nephropathy have been reported in the literature.
- Diet does play a role in onset and severity of phenotype development.

**MODEL NUMBER GK**

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**Non-Obese Diabetic Mouse**

**DIABETES MODEL INBRED MOUSE**

- Exhibits destructive autoimmune pancreatic insulitis as early as four weeks of age.
- Insulin-Dependent Diabetes Mellitus (IDDM), type 1 diabetes, is found in some females beginning at three months of age and in approximately 80% of females and 50% of males by six months of age.

**MODEL NUMBER NOD**
Spontaneously Hypertensive Rat

HYPERTENSION/CONGESTIVE HEART FAILURE DISEASE MODEL
OUTBRED RAT

• Males exhibit average systolic blood pressure greater than 200 mm Hg by 3-4 months of age.
• Generally used for studies in hypertension and cardiovascular research.

MODEL NUMBER SHR

Diabetic

DIABETES/OBESITY MODEL
SPONTANEOUS MUTANT MOUSE
BKS BACKGROUND

• A suitable model for the study of diabetic neuropathy and nephropathy.
• Also used in the study of the pathogenesis and prevention of Type 2 Non-Insulin Dependent Diabetes Mellitus (NIDDM).
• Experiences a hyperinsulinemic phase (Phase 1) followed by a hypoinsulinemic phase (Phase 2) at 2–3 months of age.
• Due to possible crossover of the misty (m) and Leprdb genes, a low percentage of DB-M could be heterozygous for the misty (m) gene.
• Only homozygotes are diabetic and obese, heterozygotes and wild types are non-diabetic and lean.

MODEL NUMBER DB

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Metabolic and Cardiovascular Disease
Diet Induced Obese DIO-B6 Mouse

OBESITY MODEL

- Taconic maintains an inventory of C57BL/6NTac male mice on 60% fat kcal irradiated diet. Taconic uses Research Diets industry standard high fat rodent diet, D12492. Control mice at the same age on the NIH-31M diet are also available.
- Mice are placed on an irradiated, sterility tested, high fat diet (RDI#12492) at 6 weeks of age.
- RDI D12492 is a 35% high fat and high carbohydrate diet. It is 35% fat by weight and 60% fat by kcal.
- Animals are maintained on diet up to 21 weeks of age.
- These mice exhibit similar metabolic, hormonal and vascular disorders to the human diabetes disease.
- Characteristics include fasting hyperglycemia, impaired secretion of insulin in response to glucose both in vivo and in isolated pancreatic cells, hepatic and peripheral insulin resistance and polyuria.

TESTING SOLUTIONS

MOLECULAR ANALYSIS SERVICES

Pre-validated genotyping assays
Taconic offers a variety of pre-validated genotyping assays to complement our portfolio of metabolic disease models. For example, the Obese spontaneous mutant mouse must be homozygous for the Lep<sup>ob</sup> allele to exhibit the obese phenotype. Taconic has a functional pyrosequencing assay that can screen for Lep<sup>ob</sup> homozygotes as well as genotyping assays for all Taconic Transgenic Models™ mentioned in this booklet.
Taconic uses both classic- and high- throughput, real-time PCR methods for genotyping.
Our comprehensive approach ensures our clients receive the best service in the industry.

Advantages of pre-validated assays:
- No initial set-up costs for assay development
- No time-lag for new assay development
- Great cost savings when genotyping multiple alleles using Taconic's real-time platform
- Spend more time on your research and less time genotyping

STUDY-READY OPTIONS

BLOOD COLLECTION AND TISSUE HARVESTING
Baseline, interim, and terminal (via cardiac puncture) blood samples can be collected and shipped to the client. Taconic’s expert staff have broad experiences with tissue dissections, and collections for a variety of purposes. Taconic also offers tissue RNA extraction which is performed with our strict quality control assessments.

CUSTOM DIET ADMINISTRATION
Taconic can administer custom-diets (medicated or non-medicated) to any rodent model based on your specifications.
Take Your Research Further

GEMS DESIGN
Taconic Biosciences GEMS Design empowers our clients to develop research models specifically suited to the unique needs of their discovery and development studies or therapeutic programs.

- Gene Inactivation
- Gene Mutation or Replacement
- CRISPR Gene Editing
- Transgene Expression
- miRNA Expression
- Cohort Production Packages

PRECISION RESEARCH MODELS
Research organizations demand precision tools that better reflect human physiology. Taconic Biosciences leads the field delivering innovative solutions to meet these continually evolving needs. Our core competencies include the delivery of complex strategies that both integrate human genetic sequences and engraft human cells and tissues into custom mouse and rat models.

- Human Gene Replacement
- Human Cell and Tissue Engraftment

GEMS MANAGEMENT
Taconic’s fully integrated GEMs Management brings innovative models from design to study-ready cohorts with unprecedented speed and transparency.

- Embryology
- Rapid Colony Expansion
- Contract Breeding
- Surgical Services
- Tissue Collection
- Genotyping and Molecular Analysis
- Microbiome and Germ-Free Research Models and Services

CHOOS...