



ANIMAL MODELS OF HUMAN DISEASE

Overview

Animal models are extensively used for PK/PD and pharmacology studies as they provided systemic data on drug efficacy, biodistribution, metabolism and toxicity. Additionally, modeling disease in animal models is a mainstay for preclinical research and evaluation of therapeutic efficacy and toxicity. Rodent models are most commonly used to model human disease states and are developed using genetic engineering or specific stimuli to induce the disease phenotype.

Biomere has expertise in evaluating animal models for different disease areas including obesity, cardiovascular disease, diabetes (type I and II), autoimmune disease and ocular disease. Our team is continuously testing models of disease states independently or in collaboration with drug developers to evaluate new models.

Contact us at bd@biomere.com to connect with our client services and scientific operations teams.

Models of Metabolic Disease

Obesity and related complications are of high interest largely due to the clinical and commercial success of GLP-1 based therapies and there is high interest in testing next-generation therapies in preclinical animal models. Metabolic disease models are typically classified into induced and engineered models – for example, diet is the primary stimulus to induce an obese phenotype while genetically modified mice such as ApoE variant mice develop obesity when exposed to high fat diets. Biomere has validated the following models for obesity and related complications.

Disease Indication	Model	Species
Obesity	Diet-induced Obesity (DIO) ob/ob mice	Mouse Mouse
Hyperlipidemia & hypercholesterolemia Atherosclerosis	High-Fat, High-Calorie (HFHC) diet in ApoE mice	Mouse

Models of Diabetes and Diabetic Complications

Mouse models are widely used to study both type I and type II diabetes and related complications and are either genetically engineered or induced. For example, Streptozotocin (STZ) destroys pancreatic beta-cells that produce insulin mimicking type I diabetes. Type II diabetes models include ob/ob and db/db mice that are engineered to be leptin deficient and leptin receptor deficient respectively. Since these mouse models recapitulate many hallmarks of diabetes, they are used to study related complications such as delayed wound healing and kidney damage. More recently, these models are being used to study protective effects of GLP-1 therapies. Biomere has experience with the following models for diabetes & related complications

Disease Indication	Model	Species
Type I Diabetes Mellitus	STZ-induced Diabetes	Mouse, Rat
Type II Diabetes Mellitus	ob/ob mice db/db mice Zucker Diabetic Fatty (ZDF) Rat	Mouse Mouse Rat
Diabetic Nephropathy	STZ induction +nephrectomy + high salt load	Mouse, Rat
Delayed diabetic wound healing	STZ induction (Type I Diabetes) + skin excision	Rat
	Type II Diabetes (db/db mouse or ZDF rat) + skin excision	Mouse, Rat

Models of Autoimmune Disease

Rodent models of autoimmune disease are valuable tools to understand disease onset and development and evaluate changes in the immune system such as the development of autoantibodies and activated lymphocytes. While there are about 100 identified autoimmune diseases, Biomere has evaluated rodent models for commonly studied diseases listed below.

Disease Indication	Model	Species
Rheumatoid Arthritis	CFA (Complete Freund's Adjuvant) induced arthritis Collagen induced arthritis	Mouse, Rat
Systemic Lupus Erythematosus (SLE)	MRL/Lpr mice that combines a spontaneous strain (MRL) and Fas mutation	Mouse
Graft vs Host Disease (GvHD)	PBMC transplants in immune-deficient mice	Mouse
Ulcerative Colitis	TNBS-induced colitis	Rat
	DSS (dextran sulfate sodium) induced colitis	Mouse
Psoriasis	Imiquimod induced (topical application)	Mouse

Models of Blood Disorders

Chemotherapy-induced blood disorders are commonly observed clinically so it is important to evaluate if specific therapies induce blood disorders such as anemia and thrombocytopenia. Additionally, mouse models such as the Factor VIII knockout model are used to evaluate if novel therapeutics including viral and nonviral gene therapies cause spontaneous bleeding or other blood issues. Biomere has used the F8KO model as well as multiple species to evaluate blood disorders caused by chemotherapeutic agents.

Disease Indication	Model	Species
Coagulation Disorders	Hemophilia in F8KO (Factor VIII) mice	Mouse
Granulocyte/thrombocytopenia	Chemotherapy-induced	Mouse
Anemia	Chemotherapy-induced	Mouse, Rat

Models of Kidney Disease

Kidney disease can be induced through multiple methods including surgery (5/6 nephrectomy), ischemia triggered by tubule damage or drugs such as cisplatin. Additionally, diabetic mouse models can be induced via surgical ablation to develop kidney disease. Biomere has used large and small animal models for acute kidney injury and chronic kidney disease.

Disease Indication	Model	Species
Acute kidney injury Granulocyte/Thrombocytopenia	Unilateral renal ischemia and reperfusion	Rat
	Cisplatin-induced injury	Mouse, Rat
Chronic kidney disease	5/6 nephrectomized	Rat

Models of Skin Conditions

Rodent and large animal models are popular preclinical models to study skin conditions. . While swine are popular models for skin conditions due to similar tissue architecture, thickness and permeability as human skin, primate models can also be used for erythema studies.

Disease Indication	Model	Species
Wound healing	Skin excision	Mouse, Rat
Erythema	UV or inflammation induced skin redness	Primate

Models of Ocular Disease

Several species are useful to study ocular diseases including rodents, primates and rabbits. Primate eyes have similar anatomy and physiology as human eyes and are a highly translational model for ocular diseases. Rabbits are widely used due to the large eye size that lack tear ducts ensuring that topically applied drugs do not wash out. Additionally, rabbits have similar tissue architecture including vasculature as humans. Similarly, rodent models are valuable tools for ocular studies. Biomere has a dedicated ocular team that is proficient in doing specialty dosing (eg. subretinal, intravitreal, intracameral, subconjunctival) or topical dosing and are continuously evaluating new models of ocular diseases using advanced methods such as qualitative and quantitative imaging analysis (OCT, Fundus, corneal imaging), Electroretinography (ERG), and Visual Evoked Potential (VEP) recording.

Disease Indication	Model	Species
Corneal Wound	Chemical or mechanical wounds	Rabbit
Choroidal Neovascularization (CNV)	Laser induced CNV	Mouse, Rat
Acute & Chronic Glaucoma	Silicon Oil Acute Glaucoma Trabecular Meshwork Laser Chronic Glaucoma	Mouse, Primate
Wet & Dry AMD	Sodium Iodate	Rat
Retinal Neovascularization (RNV)	DL-AAA (DL-2-aminoadipic acid) Induced	<i>Rabbit (in progress)</i>

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