

Biomere Proprietary Diabetes Models

In addition to the commonly used animal models for diabetes, Biomere has proprietary rat models of Type 1 and 2 Diabetes including spontaneous and induced disease models. Our expertise managing complex clinical care of these animals is derived from years of experience performing both short and long-term studies. Our standard studies are easily adapted for the testing of novel compounds to prevent diabetes and associated complications.

Type 1a Diabetes (T1D)

	Human	BBDP Rat	NOD Mouse
MHC	Multiple	RT1B/D ^u	I-Ag ⁷
Other Loci	~18	>5	≥27
Gender	M=F	M=F	F>M
Insulinitis	+	+	+
DKA	+	+	-
IDDM	+	+	-
AutoAbs	+	+	+

Rat models of T1D

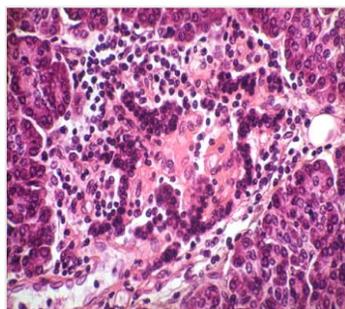
The BB/Wor and MAD (Multiple Autoimmune Disease) rats develop spontaneous and/or TLR-induced syndromes of autoimmune diabetes. According to the FDA Guidance for Industry; these are considered to be the best rat models for human Type 1 diabetes.

Diabetes Mellitus: Developing Drugs and Therapeutic Biologics for Treatment and Prevention (2008).

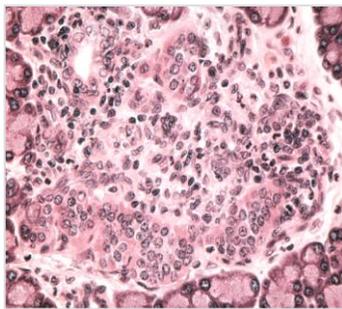
Salient features include:

- Genetic predisposition
- Abrupt onset of insulin dependent, ketosis-prone diabetes
- Autoimmune destruction of pancreatic Beta-cells (pictured below)
- Their inbred status (>140 generations of sib matings)
- High (80-95%) incidence of diabetes among both genders
- Average age of onset of diabetes at 79 days

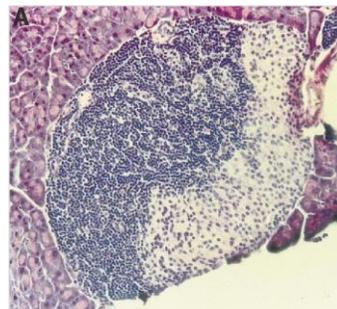
The BBDP/Wor rats develop more severe and more human like complications of diabetes when compared to other models such as NOD mice, STZ or alloxan induced diabetes models.



Human Pancreas Insulinitis



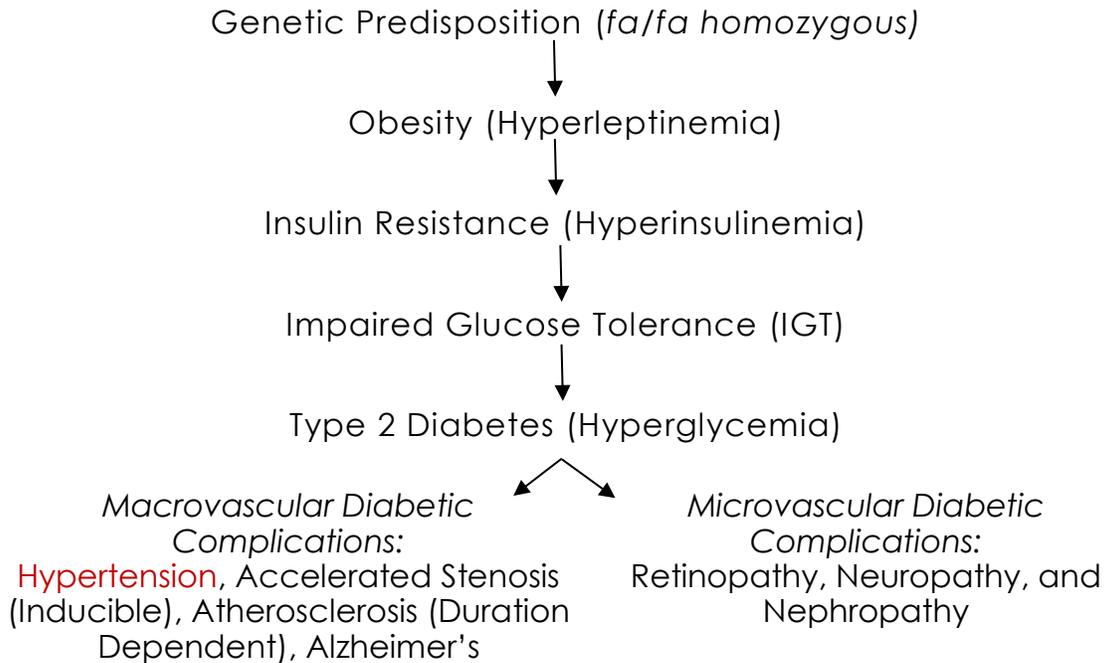
BBDP Rat Insulinitis



NOD Mouse Peri-insulinitis



Biomere's Type 2 diabetic rat (T2D) - clinical characteristics



T2D

BBZDR/Wor Rat Model

Biomere has a proprietary rat model for Type 2 diabetes, BBZDR/Wor. This rat is a well-established model system used to study Type 2 diabetes and resulting diabetic complications. Obese diabetics, obese females with impaired glucose tolerance, and lean animals of both genders provide an ideal system to study diabetes and the progression to diabetic complications. Our highly qualified staff can design and implement experimental protocols to test the efficacy of novel compounds in this model system.

Saline features:

- Pancreatic Islets are hyperplastic
- Diabetics rats have diminished GLUT- 2 transporters within the islets
- Animals have obesity and insulin resistance
- >95% of the obese males become hyperglycemic at ~84 days of age
- BBZDR rats are the only diabetic rat model with Hypertension strikingly similar to human with T2 diabetes
- Diabetic complications included atherosclerotic, heart disease, retinopathy, neuropathy, nephropathy and Alzheimer's

Atherosclerotic Features	Human	BBZDR/Wor Type 2 Diabetic	BBZDR/Wor Lean Control
SMC Proliferation	+++++	+++++	+++++
Inflammatory Cells	+++++	+++++	+++++
Lipid Deposits	+++++	+++++	+/-
Cholesterol Crystal	+++++	+++++	+/-
Foam Cells	+++++	+++++	-
Cell Debris	+++++	+++	-
Rupture	+++	+++	+
Thrombosis	+++	+++	+/-
Calcification	+++++	++	+

