

Diabetes mellitus is the **most common endocrine disorder** of humans and **Type 2 diabetes (T2D)** is currently the 6<sup>th</sup> leading cause of death. Diabetes is characterized by abnormalities of carbohydrate and lipid metabolism and long-term complications including retinopathy, nephropathy, neuropathy, and premature atherosclerosis. More than 90 percent of the patients with this disease are categorized as having non-insulin-dependent diabetes mellitus (**NIDDM**), **adult onset or type II diabetes (T2D)**. NIDDM is a disorder resulting from varied degrees of **insulin resistance**, which is often associated with impaired insulin secretion. The incidence of NIDDM increases with age and approximately 80 percent of type II diabetic patients are overweight. Insulin-dependent diabetes mellitus (IDDM) or **Type I diabetes (T1D)** is a disorder caused by the destruction of insulin-producing endocrine cells within the pancreas and currently considered to be the result of an autoimmune process. As a result of the insulin production deficit, long-term complications, especially cardiovascular disease and kidney failure, invariably occur to some extent in most patients.

The lack of suitable large animal models has hindered investigations in the field of diabetes, particularly in the study of NIDDM (**T2D**) and the complications of diabetes. Miniature swine have many characteristics similar to humans that make them suitable to model human diseases (Bellinger et al., 2006). Miniature swine are omnivores, easy to handle, raise fewer ethical considerations, offer similar size to adult humans, have several organ systems very similar to humans in term of anatomy, physiology and metabolism, and test compounds can be administered through all routes of delivery, including trans-cutaneous delivery systems (patches). Swine also have similar metabolic lipoprotein profile, have tendency to obesity, have phenotypic susceptibility to coronary atherosclerosis and can be trained for exercise, make them attractive species to identify causative mechanisms.

Insulin dependent diabetes or **T1D** can be induced in miniature swine using streptozotocin or alloxan. The induced IDDM closely mimics the type 1 diabetes of humans. Because of the similarities between swine and humans, the induced diabetes can be monitored and controlled using the same protocols as in humans. Alternatively, pancreatectomized miniature swine have been recognized as an excellent model for studying the vascular changes associated with type 1 diabetes. Miniature and domestic swine are also very involved in investigations aiming at permanently curing type I diabetes using whole pancreas or islet cell allo and xenograph transplantation. Xenotransplantation may represent a solution to human organ shortage, and pig pancreases may be a suitable source because of the similarities between human and porcine insulin.

Sinclair offers a dietary high fat-high cholesterol (HFHC) induced model of **T2D** with dyslipidemia in miniature swine (Dixon et al., 1999; Roberts et al., 2001). The dyslipidemia observed is very similar to the one of diabetic humans and early atherosclerosis lesions have also been detected. The similarities of the lipid metabolism, vascular anatomy, capacity and collateral circulation of the coronary arteries between swine and humans make this animal model even more attractive. Miniature swine have been used extensively for research in diabetes, hypertension, hypercholesterolemia and atherosclerosis in humans. Sinclair can conduct your diabetic pig study design at our AALAC accredited, GLP compliant facility or sell and deliver induced, stabilized and confirmed diabetic miniature swine (T1D or T2D) and normal control animals directly to your facility.

Sinclair is experienced in developing and using large animal models in a contract research environment. We guarantee absolute confidentiality, emphasize open and timely communication with clients, and provide quick response and rapid turnaround times. Sinclair, Yucatan and micro-Yucatan miniswine are available for these studies. Bellinger et al. (2006) have stated "Pigs have great potential as a relevant animal model of insulin-resistant type 2 DM to identify mechanisms that lead to the development of diabetic complications and to develop and test novel therapeutic compounds."

Bellinger DW et al. Swine Models of Type 2 Diabetes Mellitus: Insulin Resistance, Glucose Tolerance, and Cardiovascular Complications. *ILAR Journal*, Vol 47, No. 3, 2006: 342-258.

Dixon JL et al. Increased atherosclerosis in diabetic dyslipidemic swine: Protection by atorvastatin involves decreased VLDL triglycerides but minimal effects on the lipoprotein profile. *J Lipid Res* 43, 2002: 1618-1629.

Roberts TM et al. Alterations in the oxidative metabolic profile in vascular smooth muscle from hyperlipidemic and diabetic swine. *Mol Cell Biochem* 217, 2001: 99-106.