Project 2: Metabolic Reprogramming in the Offspring of Insulin Resistance Parents

Project Goals: the main goals of this internship at the Joslin Diabetes Center (JDC) are 1) to understand the impact of *in utero* insulin resistance on physiology in the adult offspring 2) to understand paternal-induced metabolic changes in the offspring of insulin resistant fathers.

Summary of background and importance of diabetes studies: Diabetes mellitus is a metabolic disease that is mainly characterized by an abnormal raise in plasma glucose concentration. The etiology of the disease is vast and the complications lead to morbidity. Type-1 diabetes (T1D), or insulin- dependent diabetes, is acute, progresses quickly and is characterized by a complete insulin deficiency due to the loss of pancreatic beta cells by various factors (e.g., virus, environmental). Type-2 diabetes (T2D), or non-insulin-dependent diabetes, which was reported to be restricted to adults and elderly individuals, is now also recognized in adolescents due to undetermined factors [1]. Diabetes mellitus is increasing worldwide and by 2030 is expected to affect 366 million people [2]. During 2012 the total estimated cost of diabetes care in USA was 220 billion euros and represented more than 20% of the total health care budget [3]. On the other hand, 12.4% of the Portuguese population lived with diabetes in 2009. This resulted in an estimated total annual cost of 1.3 billion euros, representing 11% of the Portuguese healthcare budget [4]. Despite the identification of more than 100 genes conferring risk of diabetes, only a small portion of the disease risk can be ascribed to the genes. As progression to T2D is largely due to insulin secretory dysfunction and significant beta-cell loss, further research in understanding the epigenetic modifications in offspring beta-cells of insulin resistant parents, will likely play an important role in determining how elevated levels of insulin and glucose itself, influences the expression of important genes in beta cell function and survival.