Chapter 2

Objectives

Rationale and Objectives:

ATMs are significant mediators in pathogenesis of obesity and IR contributing to chronic low-grade inflammation that drives metabolic dysfunction. Several animal and cellular models have been used to investigate the development of metabolic diseases and identifying potential therapeutic targets. Several cellular models have been developed for basic and preclinical research, for example, Min-6 cells to study pancreatic β-cells, 3T3-L1 and OP9 cells to study adipocytes, etc.

Traditionally, investigations to explore the functions and roles of ATMs during obesity, have primarily utilised macrophages isolated from AT, primary monocytes and / or animal models. While these models have provided valuable insights, they present several challenges, including ethical concerns associated with animal use, high variability in isolating primary macrophages, and the need for invasive biopsies to obtain human adipose tissue samples. Additionally, these approaches presents challenges in carrying out research and quick drug screening.

In our approach we are using THP-1 cells, a well-established monocytic cell line, to study the characters and its interaction with adipocytes. This is an easier approach and will eliminate the need of biopsies and invasive methods. Moreover, it aligns with ethical research practices by reducing reliance on animal models.

Objectives:

1. Establishing and characterising *in vitro* model of MMe: Inflammatory, surface, ER stress and autophagy markers
2. Metabolism of Macrophage subtypes: Metabolic characters, effect of 2DG, etomoxir and GW9662 on inflammation
3. Effect of macrophages on adipocytes
4. Discovery proteomics and unique protein profile of macrophage subtypes