Adipose tissue derived mesenchymal stem cells (ADSCs) is the easy source of isolation of mesenchymal stem cells (MSCs) and hence this area of research has flourished lately. Human ADSCs can be isolated from the lipoaspirate of the subject and can be further expanded in vitro for the autologous or allogenic transplantation. The focus of our study was to investigate the role of human ADSCs in ameliorating insulin resistance in type 2 diabetes employing in vitro and in vivo models. The investigation carried out in the present study gathers the information about the role of ADSCs in the treatment of obesity induced metabolic disorders both in in vitro and in vivo models.

Firstly, we developed an in vitro model of Insulin Resistance (IR) to understand the role of ADSCs Conditioned Media (ADSCs CM) in improving the diseased condition especially in adipose and muscle cells (both being the primary organ affected during IR). Our data demonstrates that ADSCs CM treatment leads to enhancement of glucose uptake in diseased 3T3L1 and C2C12 cells by upregulating GLUT4 gene expression. Our data also suggests that treatment with ADSCs CM in vitro leads to reduction of adipogenesis in 3T3L1 cells with concomitant decrease in triglycerides within C2C12 cells. Moreover, ADSCs CM treatment in the diseased cells led to reduction in inflammatory genes expression viz. Il-6 and Pai-1. The data collected in vitro was further validated by in vivo study.

Taken a lead from the in vitro data, we were interested to know if ADSCs/ ADSCs CM treatment reduces inflammation in vivo. Hence, we developed carrageenan induced model of acute inflammation in db/db mice. We found that both ADSCs and ADSCs CM were able to reduce inflammation significantly when compared to the untreated control as evidenced by reduction in paw volume, serum interleukin-6.
This led us to investigate the role of different forms of ADSCs in ameliorating insulin resistance in Diet Induced Obesity (DIO) model of mice. The comparison of the three different forms of ADSCs viz. the cell suspension (CS), conditioned medium (CM) and cell lysate (CL) was investigated to pin down the best possible form of stem cells to reverse obesity induced metabolic dysregulation. Since the gold standard for the treatment of IR is metformin, we used it as a positive control. Amongst the three forms of ADSCs used, CS was found to be the best in improving the insulin resistant state and the next was CM. CL showed the least correcting effect. It is very well known that MSCs work mainly through the paracrine secretions. We inferred that the reason behind CS being the best of all is the continuous supply of cytokines from the intramuscularly injected cells which facilitates slow and sustained release for a longer period of time resulting in the recovery from the diseased state. However, CM injection offers limited supply of the cytokines and would exhaust soon unless subsequent injection are given frequently. Treatment with CS normalised hyperglycemia, hyperinsulinemia, hypertriglyceridemia and related parameters. However, there was no reduction in the body weight. Metformin showed significant reduction in the body weight of the mice.

Since metformin showed significant reduction in body weight wherein stem cell treatment failed to do the same, we thought of combining ADSCs and metformin for the management of DIO induced hyperglycemia. Fasting glucose levels drastically reduced with the combination treatment within four weeks as compared to eight weeks in ADSCs alone. Few weeks after injection, there was a significant reduction in all the elevated basic parameters of the diseased state which includes body weight too.

It can be concluded from the data presented in the thesis that both stem cells and its secretome are equally good in the management of diet induced obesity and diabetes as they target inflammation, a key factor in progression of the disease.