Establishment of *in vitro* models of insulin resistance

Insulin resistance (IR) is the inability of cells to respond normally to insulin. IR is a cardinal feature of Type 2 diabetes (T2D), a disease characterized by hyperinsulinaemia, hyperglycaemia, hyperlipidaemia and chronic inflammation. All these “insults” are reported to contribute to IR, although hyperinsulinaemia occurs first in the progression to T2D, and it is suggested to be the main driver of IR. We have successfully set up an *in vitro* model of insulin-induced insulin resistance to evaluate how chronic high levels of insulin impair insulin signalling. We have established such model in multiple cell systems including: SGBS (human adipose cell line), 3T3-L1 (mouse adipose cell line) and primary human hepatocytes, where we observed a consistent decrease in the insulin pathway activation (measured by phosphorylation of Akt) upon chronic treatment with insulin. We have also assessed glucose uptake in adipose cell lines by using a 2DG6P detection luminescence kit, where insulin resistant 3T3-L1 cells showed a higher baseline and a strong reduction of insulin-induced glucose uptake compared to insulin sensitive 3T3-L1. Differently, insulin resistant SGBS did not show any difference in glucose uptake compared to insulin sensitive SGBS. In conclusion, we have established and characterized *in vitro* models of insulin-induced insulin resistance and these represent a powerful tool to test novel insulin sensitizing agents for the treatment of IR and T2D.