Objectives

1. **Investigation of genotype-phenotype correlation of *TNF-α* and *MTNR1B* polymorphisms with T2D susceptibility in Gujarat population.**
   (a) To assess *TNF-α* polymorphisms: promoter -238 G/A (rs361525), -308 G/A (rs1800629), -857 C/T(rs1799724) and -863 C/A (rs1800630).
   (b) To assess *MTNR1B* polymorphisms: promoter -1193 C/T (rs4753426), 5' UTR G/C (rs10830962) and intron C/G (rs10830963).
   (c) To monitor plasma TNF-α, FFA, melatonin levels, and *TNFA* transcript levels in PBMCs.

2. ***In vitro* effect of sitagliptin, melatonin and combination treatment on β-cell proliferation in mouse pancreatic islets.**
   (a) To study dose and time dependent effect of melatonin, sitagliptin and combination treatment on mouse pancreatic β-cell proliferation.
   (b) To study effect of melatonin, sitagliptin and combination treatment on mouse pancreatic β-cell proliferation under glucotoxicity.
   (c) To study effect of melatonin, sitagliptin and combination treatment on mouse pancreatic β-cell proliferation under gluco-lipotoxicity.

3. **Effect of sitagliptin, melatonin and combination treatment on pancreatic β-cell regeneration in Streptozotocin (STZ)-induced T1D mouse model.**
   (a) To establish STZ-induced T1D mouse model.
   (b) To evaluate glucose tolerance.
   (c) To study β-cell regeneration by β-cell proliferation, neogenesis and trans-differentiation.
   (d) To assess β-cell apoptosis.

4. **Effect of sitagliptin, melatonin and combination treatment on High Fat Diet (HFD)-induced T2D mouse model.**
   (a) To establish HFD-induced T2D mouse model.
   (b) To evaluate glucose tolerance and insulin sensitivity.
   (c) To estimate of plasma insulin, leptin, melatonin levels and lipid profile.
   (d) To monitor transcript levels and activity of glucoregulatory enzymes in liver.
   (e) To assess transcript levels of genes involved in lipid metabolism in adipose tissue and mitochondrial biogenesis in skeletal muscle.
   (f) To study the expression of proteins involved in insulin signalling pathway in skeletal muscle.
   (g) To study mitochondrial respiration in skeletal muscle.
   (h) To assess pancreatic β-cell mass and islet number.

5. **Effect of sitagliptin and melatonin combination treatment on β-cell proliferation in humanized euglycemic mouse model of islet transplantation.**