Objectives

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1. **To assess the efficacy of melatonin, GABA and combination therapy in amelioration of diabetic manifestations in streptozotocin induced T1D mouse model.**
   (a) Assessment of glucose tolerance.
   (b) Assessmentof β-cell regeneration by β-cell proliferation, islet neogenesis and α to β-cell trans-differentiation.
   (c) Assessment of β-cell apoptosis.

2. **To assess the efficacy of melatonin, GABA and combination therapy in amelioration of diabetic manifestations in high fat diet (HFD) induced T2D mouse model.**
   (a) Evaluation of glucose tolerance and insulin sensitivity.
   (b) Estimation of plasma melatonin, leptin and insulin levels.
   (c) Estimation of mRNA expression and enzyme levels of glucoregulatory enzymes (*GCK, G6Pase, FBPase, PEPCK, GP* and *GS*) in liver.
   (d) Estimation of mRNA expression of mitochondrial biogenesis markers (*SIRT1* & *PGC1α*) in skeletal muscle.
   (e) Estimation of mRNA expression of *MTNR1B, GLUT4* and lipid metabolism genes (*ACC1* & *ATGL*) in adipose tissue.
   (f) Estimation of Oxygen Consumption Rate (OCR) of mitochondrial complexes in skeletal muscle.
   (g) Estimation of protein expression of insulin signaling pathway in skeletal muscle.
   (h) Determination of β-cell mass.

3. **To assess genotype-phenotype correlation of leptin (LEP) and its receptor (LEPR) in Gujarat T2D patients and controls.**
   (a) Study the association of following *LEP* and *LEPR* polymorphisms with T2D:
   - *LEP* -2548 G/A (rs7799039)
   - *LEP* 5' UTR +19 G/A (rs2167270)
   - *LEPR* Q223R A/G (rs1137101)
   - *LEPR* K656N G/C (rs8179183)

   (b) Estimation of *LEP* & *LEPR* mRNA expression in PBMCs of T2D patients and controls.
   (c) Estimation of plasma LEP and sOb-R levels in T2D patients and controls.
   (d) Study the possible genotype-phenotype correlation of LEP and LEPR in T2D.