CONCLUSION

We conclude from our studies that cholinergic system through muscarinic M1 and M3 receptors play an important role in the regulation of pancreatic β-cell proliferation and insulin secretion. Cholinergic activity as indicated by acetylcholine esterase, a marker for cholinergic system, decreased in the brain regions - hypothalamus, brain stem, corpus striatum, cerebral cortex and cerebellum during pancreatic regeneration. The functional changes in the muscarinic receptors studied in the brain regions and it showed that the total muscarinic receptors decreased at the time of regeneration. Increased central cholinergic activity cause hyperglycaemia as well as increase in sympathetic stimulation. So the decrease in the muscarinic receptor function maintains the normoglycaemic level. Central muscarinic M1 and M3 receptors showed reciprocal changes during regeneration. Muscarinic M1 receptors decreased at time of regeneration while M3 receptors showed an increase in the function. Gene expression studies also showed a similar change in the mRNA level of M1 and M3 receptors. These alterations in the muscarinic receptors regulate sympathetic activity and maintain glucose level during pancreatic regeneration. Pancreatic muscarinic M1 and M3 receptor activity increased during proliferation indicating that both receptors are stimulatory to β-cell division. Acetylcholine dose dependently increase EGF induced DNA synthesis in pancreatic islets in vitro, which is inhibited by muscarinic antagonist atropine confirming the role of muscarinic receptors. Muscarinic M1 and M3 receptor antagonists also block acetylcholine induced DNA synthesis suggesting the importance of these receptors in regeneration. Acetylcholine also stimulated glucose induced insulin secretion in vitro which is inhibited by muscarinic M1 and M3 receptor antagonists.
Central muscarinic M1 and M3 receptor subtypes functional difference regulates sympathetic and parasympathetic systems, which in turn control the islet cell proliferation and glucose homeostasis. Pancreatic muscarinic M1 and M3 receptors play a major role in regulating the pancreatic regeneration and insulin secretion. Thus the muscarinic receptors activity and their functional balance in the brain and pancreas exert a profound influence in the insulin secretion and also regeneration of pancreas.