Abstract

Diabetes mellitus is characterized by the dysfunction and reduction of insulin-producing cells, resulting in hyperglycemia, which in long term harms the organism. For future therapy, it is crucial to understand the function of various factors participating in the differentiation and maturation of endocrine pancreatic cells. The aim of this study was to unravel the functional role of ISL1 during the development of the pancreas. ISL1 is expressed in all endocrine cells of the islets of Langerhansbut its function remains unclear, especially during early pancreatogenesis. As the global deletion of this gene is embryonically lethal, we used the tissue specific deletion of *Isl1* in *Neurod1* possitive cells using the Cre-loxP system. In this work we studied the effect of this deletion on the structure of islets of Langerhans, the formation of endocrine cell types and relative expression of genes during early pancreatic development. A defective achitecture of islets together with postnatal absence of α-cells was found in the *Isl1* deletion mutant. Also, the expression of genes important for the specification of α-cell lineage and their subsequent function was decreased. The secondary outcome was the optimalization of a protocol for effective sorting of endocrine cells using fluorescent flow cytometry, which will enable molecular biological analyses in the future. Using this mouse model the importance of ISL1 in development of endocrine cells and the architecture of Langerhans islets was demonstrated.

Key words

Pancreas, *diabetes mellitus*, transcription factor ISL1, endocrine cells, mouse model