Poster

The iINS-4F mouse: A novel tool to explore the regenerative effect of partial reprogramming in the pancreas

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ABSTRACT

Type 1 diabetes mellitus is a metabolic disease caused by autoinmmune destruction of pancreatic β-cells. Although current therapies allow glycemic control, they do not restore the function of these cells, underscoring the need for innovative therapeutic approaches. In this context, partial reprogramming by transient overexpression of Yamanaka factors (OSKM) has emerged as a promising strategy in regenerative medicine (Chondronasiou et al., 2022).

In this study, we introduce the iINS-4F murine model, designed to induce partial reprogramming specifically in pancreatic β-cells. This model combines the TetOn system with Cre recombinase, allowing controlled activation of OSKM exclusively in β-cells following doxycycline administration. To evaluate its potential, we implemented a partial reprogramming protocol based on short induction cycles in both young and old animals.

We have performed a comprehensive characterization of the iINS-4F model, analyzing the specificity and expression level of OSKM as well as its impact on key β-cell identity markers. Our results reveal an initial phase of transient dedifferentiation, marked by the reversible loss of insulin and Glut2. The ability to recover after a rest period indicates a remarkable flexibility of the system. Furthermore, our data suggest that although age does not subtantially limit reprogramming and recovery, sex could influence the process.

These findings position the iINS-4F model as a valuable tool for the study of partial reprogramming in pancreatic β-cells and open new possibilities for its application in innovative diabetes therapies.

REFERENCES

Chondronasiou, D. et al. (2022) 'Deciphering the roadmap of in vivo reprogramming toward pluripotency', Stem Cell Reports, 17(11), pp. 2501–2517. doi:10.1016/j.stemcr.2022.09.009.