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Redifferentiation of expanded human islet β cells by inhibition of ARX

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Ex-vivo expansion of adult human islet β cells has been evaluated for generation of abundant insulin-producing cells for transplantation; however, lineage-tracing has demonstrated that this process results in β-cell dedifferentiation. Redifferentiation of β-cell-derived (BCD) cells can be achieved using a combination of soluble factors termed Redifferentiation Cocktail (RC); however, this treatment leads to redifferentiation of only a fraction of BCD cells. This study aimed at improving redifferentiation efficiency by affecting the balance of islet progenitor cell transcription factors activated by RC treatment. PAX4 and ARX are transcription factors which play key roles in directing pancreas endocrine progenitor cells into the β/δ or α/PP developmental pathways, respectively. Blocking ARX activation in BCD cells treated with RC elevated insulin mRNA levels 11-fold, and more than doubled the number of insulin-positive BCD cells. These findings confirm the hypothesis that ARX is misactivated in some BCD cells treated with RC, and that its downregulation promotes the differentiation of additional β cells. The combination of RC and ARXshRNA treatment may facilitate the generation of abundant insulin-producing cells for transplantation into patients with type 1 diabetes.

Biography

Friedman Orr has completed her BSc Cum Laude from Ben Gurion University, Israel and MSc studies *Magna Cum Laude* from The Hebrew University Faculty of Medicine, Israel. She is a PhD student in the Department of Human Molecular Genetics and Biochemistry in Tel Aviv University Faculty of Medicine, Israel. She has contributed several papers in reputed journals.

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