In vitro expansion and redifferentiation of adult human islet cells

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Beta-cell replacement represents the ultimate cure for type 1 diabetes, however it is limited by availability of organ donors. Adult human islets are difficult to propagate in culture, and efforts to expand them result in loss of beta-cell phenotype. We have recently shown that cells from adult human islets of multiple donors can be significantly expanded in tissue culture in a simple medium for at least 16 population doublings, without a change in replication rate or noticeable cell mortality, representing an expansion of over 65,000-fold. Microarray studies revealed extensive changes in gene expression in the expanded cells, compared with normal islets. Indirect evidence suggested that a significant fraction of the replicating cells were derived from dedifferentiated β cells. However, genetic lineage-tracing studies in mouse models failed to document expansion of cultured beta cells. We are currently developing lineage-tracing tools for studying cultured human beta cells. In a screening of compounds capable of inducing redifferentiation of the expanded cells we have shown that betacellulin restores β-cell gene expression and insulin content in cells from part of the donors. These methods may allow transplantation of functional islet cells from single donors into multiple recipients.