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### ***Ex-vivo* generation of insulin-producing cells for beta-cell replacement**

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**B**eta-cell replacement represents an attractive prospect for diabetes therapy. Given the shortage of human pancreas donors, *ex-vivo* expansion of adult human beta cells has been considered, however it results in loss of beta-cell phenotype. Lineage tracing has shown that human beta cells survive, dedifferentiate and undergo epithelia-mesenchymal transition (EMT), and significantly replicate *in vitro*. Epigenetic analyses suggest that the dedifferentiated cells preserve the beta-cell epigenome. Recent findings demonstrate that these cells can be redifferentiated *in vitro* into insulin-producing cells. Our current efforts focus on improvement of redifferentiation efficiency by manipulating signaling pathways involved in EMT. Using the lineage tracing system we also generated induced pluripotent stem (iPS) cell lines from human beta cells, termed BiPS. The reprogrammed pluripotent cells maintained open chromatin structure at key beta-cell genes. BiPS cells demonstrated an increased ability to differentiate into insulin-producing cells *in vitro* and *in vivo*, compared with other pluripotent stem cells, suggesting that their epigenetic memory may predispose them to differentiation into beta cells. These findings demonstrate that human iPS cell phenotype may be influenced by their cell of origin, and suggest that their skewed differentiation potential may be advantageous for cell replacement therapy. This work may enable the generation of an abundant source of human insulin-producing cells for transplantation into patients with type 1 diabetes, given adequate immune protection means, as well as into type 2 diabetic patients. In addition, these human insulin-producing cells can be used in basic research, toxicology studies, and drug screening.

### **Biography**

Shimon Efrat received his Ph.D. in molecular biology in 1984 from the Hebrew University in Jerusalem. In 1989 he joined the Department of Molecular Pharmacology and the Diabetes Research Center at Albert Einstein College of Medicine in New York, where he raised to full professorship and worked until 1999. He joined the staff of Tel Aviv University in 1995, and since 1999 also holds a Visiting Professor appointment at Albert Einstein. He has published more than 100 papers in reputed journals.

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