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Biography

Sarah Ferber is graduated at the Technion under the supervision of Prof. Hershko and Prof. Ciechanover on revealing the Biology of the ubiquitin system for protein degradation (Nobel Prize in 2004). She completed her post-Doctoral studies at Harvard Medical School on the regulation of insulin secretion and moved to Diabetes Cell Therapy in UTSW-Dallas TX. She established her own research lab at Sheba Medical ctr. Israel and was the first to demonstrate liver to pancreas trans differentiation *in vivo* and in human tissues *in vitro* for generating an autologous insulin producing tissue. She has since published in leading journals, and her papers were cited >2700 times. She has been serving as an editorial board member of reputed journals and on the Israeli and the European boards of Gene and Cell Therapy Societies. She serves as Orgenesis' CSO and founder and is the inventor of >10 patents on adult cells reprogramming.

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AUTOLOGOUS CELL REPLACEMENT THERAPY FOR DIABETIC PATIENTS BY LIVER TRANSDIFFERENTIATION

Trans differentiation is the direct reprogramming of adult cells into alternate cell types with different function. Liver to pancreas transdifferentiation (TD) induced by ectopic expression of pancreatic transcription factors (pTFs) was first described by our group both *in vivo* and in human liver cells *in vitro*. The keynote lecture will disclose our understanding of the mechanism of liver to pancreas TD and will describe this approach's industrial implementation as an autologous cell replacement therapy for diabetic patients. Our data suggest that TD occurs in predisposed liver cells that display specific characteristics. Moreover, TD-propensity can be extended to most of the cells by epigenetic manipulations, hence, increasing the trans differentiation efficiency. Using primary cultures of liver derived from >20 human donors we have identified a sub-population of human liver cells that are persistently predisposed to undergo TD (5-15% of the cells). Upon ectopic pTFs expression, 70% of the predisposed liver cells produced and secreted the processed hormone in a glucose-regulated manner. Epigenetic analyses suggested that pancreatic genes' chromatin is more transcrpition-permissive in TD-predisposed than in recalcitrant liver cells. TD-predisposed liver cells display a reduced level of DNA methylation which further decreases upon the induction of reprogramming. Using epigenetic modifiers, we could convert TD-resistant liver cells into TD-permissive cells. Moreover, *in vitro* culturing of the AIP cells in a 3D organoid manner, and their exposure to a suitable and relevant niche, increased the transdifferentiated liver cells maturation insulin production. In summary, pancreatic TD is restricted to a specific cell population within the adult liver tissue, which harbors obligatory signaling patterns and specifically permissive epigenome. The extension of TD-propensity to most of the cells in culture/tissue, is expected to dramatically increase this process efficiency bringing it closer to its therapeutic implementation, as an autologous cell replacement therapy for diabetic patients.

Note: