Scientists find a new beta cell maturation step triggered by weaning from milk to chow

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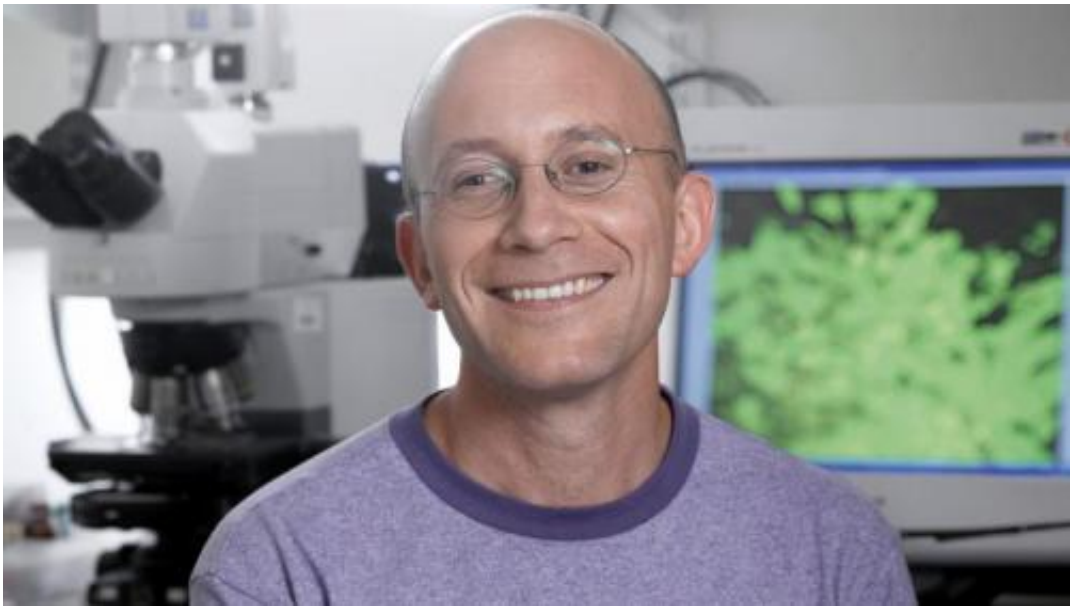

Discovering a new developmental step is professor Yuval Dor at the Hebrew University's Institute for Medical Research Israel-Canada (IMRIC). Credit: Yoram Aschheim for Hebrew University

A long-standing puzzle in the diabetes field has been the fact that only a small subset of insulin-producing beta cells in the pancreas of adult organisms can replicate (and hence contribute to beta cell regeneration in diabetes). Furthermore, this subset of replicating cells continues to decline with advancing age.

Young animals demonstrate a superb potential for tissue regeneration.

Because this tissue regeneration deteriorates with age, it is generally assumed that the younger the animal, the better it compensates for tissue damage.

In a new study appearing in *Developmental Cell*, Prof. Yuval Dor and research associate Dr. Miri Stolovich-Rain at the Hebrew University of Jerusalem's Institute for Medical Research Israel-Canada (IMRIC), in collaboration with Prof. Benjamin Glaser from the Hadassah Medical Center, set out to understand the age-related decline of beta cell regeneration.

To do this, they examined the ability of beta cells in young mice to replicate in response to hyperglycemia, a condition in which excessive glucose circulates in the blood.

Expecting to find a superb regenerative response that declines with age, the researchers were surprised to discover that young mice don't begin to possess the cellular machinery that allows them to regenerate after they are done weaning.

Examining the production of pancreatic beta cells in suckling mice, the researchers found that in these young mice, beta cells failed to enter the cell division cycle in response to high levels of glucose. In addition, insulin secretion in response high levels of glucose was much reduced compared with the situation in adult mice.

Thus the researchers concluded that compensatory proliferation (the ability to replicate in response to physiologic stimuli such as a high level of glucose in the blood) is a trait of the mature beta cell, which requires a discrete maturation step associated with the dietary change once the mice stop suckling.

Similarly, the full potential to secrete proper amounts of insulin in

response to elevated levels of glucose is acquired only post-weaning.

The results reveal a new discrete developmental step in the process of beta cell maturation, brought about by the change of diet from high-fat milk to high-carbohydrate chow.

According to Prof. Dor, "The data suggest that regenerative potential is a trait of mature tissues, which has to develop actively, similar to functional maturation, rather than an innate feature of newly born cells."

The findings further indicate that the dietary transition from fat-rich milk to carbohydrate-rich food enhances the ability of beta cells to secrete insulin in response to glucose, and allows glucose to stimulate beta cell replication.

The exact molecular signal that sets off these events is still to be determined, but further research to identify it could help advance our understanding and treatment of diabetes. For example, the maturation step associated with weaning can be relevant for attempting to direct the differentiation of embryonic stem cells to fully functional beta cells for transplantation to patients with diabetes.

Next, the researchers plan to study how premature weaning in mice and in humans may affect the long term health of beta cells and the chances to develop diabetes.

The research paper, "Weaning Triggers a Maturation Step of Pancreatic Beta Cells," is published in the March 9 issue of *Developmental Cell*.

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