Diabetes mellitus affects an estimated 150 million people worldwide. This disease is characterized by hyperglycemia resulting from the inability of pancreatic beta cells to function normally. Treatments for diabetic patients are inadequate because they do not prevent complications associated with the disease; therefore, considerable efforts are focused on the derivation of beta cells from embryonic stem cells or understanding the molecular control of beta cell expansion in vivo. Mouse models are commonly used to study beta cell expansion, but beta cell proliferation in healthy adult mice is rare except when mice are metabolically challenged, such as during pregnancy. Changes in pregnant mutant and control mice can be studied to analyze mechanisms of beta cell expansion in vivo, providing information that will facilitate the manipulation of beta cell progenitors for cell therapies. The transcription factor Foxd3 is expressed in the pancreatic primordium beginning at 10.5 dpc and is localized predominantly to beta cells after birth. Mice carrying a deletion of Foxd3 from the pancreatic epithelium appear normal during development and adult life, but mutants have impaired glucose tolerance during pregnancy. Preliminary data show that these mice have defects in beta cell proliferation. Because Foxd3 is required for survival, self-renewal and multipotent nature of multiple progenitor cell lineages, it may be a critical gene for molecular control of in vivo beta cell expansion. Understanding the molecular mechanisms of beta cell mass expansion in vivo may provide insight to developing treatments for diabetes.

doi:10.1016/j.ydbio.2009.05.305

Program/Abstract # 279
Foxd3 is required to maintain glucose tolerance during pregnancy
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Diabetes mellitus affects an estimated 150 million people worldwide. This disease is characterized by hyperglycemia resulting from the inability of pancreatic beta cells to function normally. Treatments for diabetic patients are inadequate because they do not prevent complications associated with the disease; therefore, considerable efforts are focused on the derivation of beta cells from embryonic stem cells or understanding the molecular control of beta cell expansion in vivo. Mouse models are commonly used to study beta cell expansion, but beta cell proliferation in healthy adult mice is rare except when mice are metabolically challenged, such as during pregnancy. Changes in pregnant mutant and control mice can be studied to analyze mechanisms of beta cell expansion in vivo, providing information that will facilitate the manipulation of beta cell progenitors for cell therapies. The transcription factor Foxd3 is expressed in the pancreatic primordium beginning at 10.5 dpc and is localized predominantly to beta cells after birth. Mice carrying a deletion of Foxd3 from the pancreatic epithelium appear normal during development and adult life, but mutants have impaired glucose tolerance during pregnancy. Preliminary data show that these mice have defects in beta cell proliferation. Because Foxd3 is required for survival, self-renewal and multipotent nature of multiple progenitor cell lineages, it may be a critical gene for molecular control of in vivo beta cell expansion. Understanding the molecular mechanisms of beta cell mass expansion in vivo may provide insight to developing treatments for diabetes.

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