

P005 *Ngn3* expression in the adult pancreas contributes to sufficient endocrine function

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Ngn3 is both necessary and sufficient to induce endocrine islet cell differentiation. Because most studies have shown that *Ngn3* is only detected in pancreatic cells that do not express endocrine hormones, and most, if not all *Ngn3*⁺ cells adopt endocrine cell fate, it is regarded as an endocrine progenitor cell marker. Here we present several pieces of evidence that suggest the sustained *Ngn3* expression in the adult islet cells and its possible involvement in functional maintenance. First, we found that the *Ngn3* locus is haploinsufficient. In the *Ngn3*^{+/-} animals, both islet mass and glucose tolerance ability of the animals are compromised. This finding suggests that a high *Ngn3* protein level within each pancreatic cell is critical for initiating endocrine differentiation. Second, *Ngn3* mRNA and protein could be detected in wild type adult islets by RT-PCR and Western blot, respectively. Third, conditional *Ngn3* inactivation in the adult pancreas compromises endocrine function. Fourth, by using a *Ngn3*-CreER mouse line, in which the CreER coding region is knocked into the *Ngn3* locus, we showed that *Ngn3* transcription indeed occurs in the adult pancreas. Interestingly, the number of cells that express detectable level of CreER increases under conditions that favor regeneration, for example, with pancreatectomy. These findings revealed a formerly unrecognized *Ngn3* function in differentiated islet cells.