Poster

Role of the transcription factor Gata4 in the identification of the gastric epithelium

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ABSTRACT

Motivation:

Previous studies from the host lab have shown that GATA4 and GATA6 play redundant roles in mouse pancreas organogenesis. Using the Cre/loxP technology, we inactivated GATA4 in the Pdx1 domain, which includes the pancreatic progenitors, hindstomach and duodenum. As previously reported, pancreas development appears to be normal in the absence of GATA4. However, a detailed analysis of Gata4 KO stomach revealed altered epithelial glands differentiation and presence of heterotopic pancreas in the subserosa layer of the stomach. Base don this result, we hypothesize that GATA4 is to maintain epithelial glandular differentiation and identity. In this project, we aim to analyze at a histological and molecular level the glandular epithelial cells of Gata4 KO mice. We will also investigate the potential of GATA4 to maintain the gastric phenotype of AGS cell line by using RNA interference to knockdown Gata4.

Methods:

The gastric epithelium of GATA4-deficient mice was analyzed by histology, immunohistochemistry and immunofluorescence techniques from paraffin-embedded stomach tissues. AGS cells were transfected with small interfering RNA (siRNA) against Gata4 to specifically interfere with its translation. Analysis of gastric and pancreatic markers were performed in Gata4-knockdown AGS cells to study the potential role of GATA4 in the maintenance of gastric identity.

Results:

The gastric epithelium of GATA4 KO mice displays abnormal morphology from embryonic stage e17.5. Analysis of differentiation markers, including H+/ATPase and Mucin5 reveal defects in gastric differentiation in the absence of GATA4. Pancreatic tissue derived from the abnormal gastric epithelium is observed in the subserosa layer of GATA4 KO stomach. Heterotopic pancreas comprised well-differentiated acinar cells (amylase positive) and endocrine cells (insulin and glucagon positive cells).

Conclusions:

Our data shows that GATA4 is essential for the development of the gastric epithelium, and to maintain its identity. Loss of GATA4 during stomach development leads to changes in the gastric phenotype towards a pancreatic phenotype. The transfection of SiRNA GATA4 in AGS cells produces 70% reduction of GATA4 expression by qPCR. Evaluation of AGS phenotype upon GATA4 inactivation is still under study.

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