Role of GATA4 in Early Gastrointestinal Tract Development

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GATA4 is a transcription factor critical in the developmental process and early differentiation of the gastrointestinal tract. Studies using genetically modified mouse models have shown GATA4 is necessary in hindstomach epithelium development, however its role in humans is unknown. The differentiation of human induced pluripotent stem cells into stomach organoids was utilized to recapitulate the stages of human development in a dish. Two cell lines were created, one was the mutant, possessing a knockdown of the GATA4 gene, and the other was the control, expressing normal levels of GATA4. At day three, the endoderm stage, GATA4 was knocked down by about 70% within the mutant cell line, as shown by qRT PCR and western blot analysis. The GATA4 depleted cells were still capable of generating endoderm properly, indicating GATA4 is not imperative for endoderm. At day six, buds formed in the control cell line and were propagated into stomach organoids. In contrast, the knockdown cell line produced little to no budding spheroids at day six. To determine why budding morphogenesis was not occuring efficiently in the knockdown cells, the expression profile of other markers known to be expressed in spheroids at this time were evaluated. HNF1b levels did not change compared to the control, however SOX2 levels decreased. From preliminary data it can be deduced that GATA4 levels have an effect on SOX2 quantities. This study adds to the basis that patient derived iPS cells may be utilized to more effectively examine disease development and drug screening.

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