

A multidisciplinary approach to defining the identity and dynamics of adult gastric isthmus stem cells

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Abstract

The gastric corpus epithelium is the thickest area of the gastro-intestinal tract, with turnover fuelled by rapidly cycling progenitors in the isthmus region of the gland. Several markers have been proposed for gastric corpus cells with stem cell function in both the isthmus and base regions. However, it is not understood how these two populations cooperate to maintain normal homeostatic turnover. Here, based on unbiased random genetic labelling, we used lineage tracing measurements to resolve the dynamics and fate behaviour of epithelial stem cells in the gastric corpus epithelium. The gastric corpus glands displayed compartmentalised lineage tracing patterns, with distinct clones spanning either the pit-isthmus-neck or the base region of individual glands. Isthmus clones showed rapid initial expansion and long-term maintenance, while base clones grew slowly achieving a much smaller clone size. Statistical analysis of the data indicated that the vast majority of durable isthmus clones are derived from actively cycling stem cells in the isthmus region. Using the Fucci cell cycle reporter mouse, expression profiling of these rapid cycling isthmus cells identified two selective markers for proliferating cells, Ki67 and Stathmin1. Lineage tracing experiments based on these two independent markers provided further support for our conclusion that the pit-isthmus-neck region of corpus glands are maintained long-term by rapidly cycling isthmus stem cells. Finally, single-cell RNA-seq analysis is used to define the molecular nature and sub-lineage relationship of a single, cycling isthmus stem cell population. These observations define the identity and functional behavior of gastric isthmus stem cells.

Keywords: *Gastric corpus isthmus stem cells, unbiased genetic labelling, biophysical modelling, single cell analysis*

Biography

Dr. Seungmin Han has worked as a research associate in the WT-CRUK Gurdon Institute of the Univ. of Cambridge since 2016. He obtained his BSc degree in the Department of Mathematics of Pohang University of Science and Technology (POSTECH) in 2006 and received his Ph.D. degree in the Interdisciplinary School of Bioscience and Bioengineering in the same university in 2013. After PhD program, he performed his research in Prof. Sung Ho Ryu's lab in POSTECH as a postdoctoral researcher by 2015.