Joint SGCC-CSI Gastric Cancer Seminar

Lgr5+ Stem Cells in Gastric Epithelial Homeostasis and Cancer

Speaker: Dr. Marc Leushacke
Date: 7 April 2015 (Tuesday)
Time: 5-6PM
Venue: NUS Centre for Translational Medicine, Block MD6, #01-02
Moderator: Dr. Nicholas Barker

Marc Leushacke,
Senior Research Fellow,
Epithelial Stem Cells Laboratory,
A*STAR Institute of Medical Biology,
Singapore

The epithelium of the adult glandular stomach is constantly renewed throughout life. Limited reservoirs of adult stem cells located within numerous gastric units resembling flask-shaped tubular glands fuel the process of repetitive tissue regeneration. Multiple Lgr5+ cells reside at the base of each pyloric gland. In-vivo lineage tracing analysis characterized these cells as self-renewing, multipotent adult stem cells involved in long-term renewal of the pyloric epithelium. In addition, we demonstrate that numerous Lgr5+ cells routinely contribute to epithelial renewal in the pyloric gland and, similar to what was previously observed in the intestine, a balanced homeostasis of the glandular epithelium and stem cell pools is predominantly achieved via neutral competition between symmetrically dividing Lgr5+ stem cells. Using the Lgr5-DTR-eGFP knock-in mouse model, we identified individual cell populations residing at the gland base of the pylorus and corpus epithelium that present high levels of Lgr5 driven DTR-eGFP expression. Such Lgr5-driven expression of DTR-eGFP selectively confers diphtheria toxin (DT) sensitivity on Lgr5+ cells. To evaluate the contribution of Lgr5-expressing cells to long-term epithelial homeostasis in the stomach, we specifically ablated those cells in Lgr5-DTR-eGFP transgenic mice. Ablation of Lgr5-DTR-eGFP-expressing cells in vivo caused severe tissue damage in a large proportion of the glandular epithelium. Interestingly, however, we also identified a minority of glands with an intact morphology, indicating a negligible effect of Lgr5+ stem cell loss within such glands. These findings represent a major advance in our basic understanding of tissue homeostasis in the stomach and form the foundation for identifying altered stem cell behaviour during gastric disease and cancer.

JOINTLY ORGANISED BY:

SGCC Singapore Gastric Cancer Consortium

CSI SINGAPORE

To register, please contact Bryan Choo at mdccpb@nus.edu.sg