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The College of Graduate Studies and the College of Science Cordially Invite You to a

Master Thesis Defense

Entitled

THE ROLE OF VITAMIN D RECEPTORS IN GASTRIC EPITHELIAL HOMEOSTASIS

by

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Date & Venue

10:00 AM
Thursday, 19 April 2018

Room 020, Building F3

Abstract

The gastric epithelium consists of different types of cells, which are involved in gastric homeostasis by balancing cell proliferation and differentiation. This process involves several signaling molecules such as growth factors and vitamins. Vitamin D_3 (VD_3) plays a role in cell differentiation, cell proliferation and calcium homeostasis. The biological activities of VD_3 are mediated by vitamin D receptor (VDR). Target tissues of VD_3 in the gastrointestinal tract were identified earlier in intestine and gastric cancer tissues; however, the normal expression of VDR in stomach is poorly studied. The main objectives of this thesis are: 1) to investigate the normal expression of VDR in gastric epithelium and 2) to study the possible role of VDR and VD_3 in maintaining gastric epithelial homeostasis by establishing and analyzing mouse model deficient in VD_3. PCR analysis showed that VDR is expressed in different regions of normal mouse stomach. Co-immunostaining analysis showed specific expression of VDR in parietal cells and the different mucus secreting cells. The results suggested that parietal cells and mucous cells are targets for VD_3 signaling. To examine the role of VD_3 on gastric homeostasis, wild type mice were put on VD_3 deficient diet for 3 months. Using Real-Time PCR, stomachs of mice deficient of vitamin D showed significant decrease in expression of parietal cell specific genes (HKα and HKβ) and increase gastrin gene expression. Moreover, quantification for cells in the S-phase of the cell cycle showed significant increase in their number in vitamin D deficient mic. Gene expression analysis of VDR signaling genes showed significant decrease in PTHLH, but not other target genes like TRPV6 and p21. This work will add value to the field of stomach biology by providing better understanding of how VD_3 and VDR are involved in maintaining gastric epithelial homeostasis.

Keywords: Vitamin D3, VDR, Gastric epithelium, Stem cell, Proliferation, Differentiation.