a place of mind

THE UNIVERSITY OF BRITISH COLUMBIA

Department of Cellular and Physiological Sciences

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Faculty of Medicine

Division of Gastroenterology

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****CPS SEMINAR TIME****

12:30 PM Thursday, Feb. 14, 2019

Location: LSC3

Hosted by Drs. Rideout and Kopp

"Inflammation and an intestine-like differentiation programme underlie the cellular origins of esophageal adenocarcinoma"

Esophageal cancer patients suffer one of the poorest survival rates (14%) of all cancer types. Esophageal squamous cell carcinoma (ESCC) and the now predominant esophageal adenocarcinoma (EAC) differ dramatically in their cell of origin deriving from either squamous or intestinal metaplasia associated lineages respectively. This transition to the intestinal metaplasia known as Barrett's esophagus (BE) parallels the differentiation pathways of the lower intestine but carries an increased life time risk of dysplasia and is commonly observed in those presenting with EAC. Underlying the development of both BE and EAC is a history of gastro-esophageal reflux disease (GERD) leading to inflammation and ulceration that, when combined with as yet ill-defined genetic propensities, is proposed to alter the reparative or regenerating esophageal epithelium towards this metaplastic intestine-like lineage. However, anatomical differences between humans and model organisms have hampered supportive direct evidence. In this seminar I will discuss and demonstrate the routes through which GERD, inflammation, intestinal metaplasia and somatic variation contribute to the development of EAC through genomic and functional studies of the intestinal-like nature of BE, single cell sequencing of stem cell derived "mini gut" or organoids of BE, functional genomic screening of EAC cells and cancer genome atlas data of esophageal cancers. Collectively these studies suggest the possibility of a GERD driven positive selection of intestine-like cellular lineages and clonal cell populations with GATA factor amplifications during both BE and EAC development with implications for patient outcome and treatment.

While the esophagus is largely composed of stratified squamous epithelial cells, ESCC and EAC differ dramatically in their cell of origin deriving from either squamous or intestinal metaplasia associated lineages respectively. This transition to the intestinal metaplasia known as Barrett's esophagus (BE) carries an increased life time risk of progression and is commonly observed in those presenting with EAC. Underlying the development of both BE and EAC is a history of gastro-esophageal reflux disease (GERD) leading to inflammation and ulceration that, when combined with as yet ill-defined genetic propensities, alter the reparative or regenerating esophageal epithelium towards a metaplastic lineage. In this seminar I will discuss and demonstrate the routes through which GERD, inflammation, intestinal metaplasia and somatic variation contribute to the development of EAC through genomic and functional studies of the intestinal-like nature of BE, single cell sequencing of stem cell derived "mini gut" or organoids of BE, functional genomic screening of EAC cells and cancer genome atlas data of esophageal cancers. Collectively these studies suggest the possibility of a GERD driven positive selection of intestine-like cellular lineages and clonal cell populations with GATA factor amplifications during both BE and EAC development with implications for patient outcome and treatment.

Join us for coffee and cookies at Noon in LSC 1416!!!

For more information please contact Dr.Rideout<elizabeth.rideout@ubc.ca>, Dr.Kopp<janel.kopp@ubc.ca>