14th International Conference on
Clinical Gastroenterology and Hepatology
August 29-30, 2018 | Toronto, Canada

Uncovering the role of planar cell polarity during intestinal morphogenesis

Abilasha Rao-Bhatia[1,2], Sabrina Coquenlorge-Gallon, Wen-Chi Yin, Xiaoyun Zhang, Min Zhu, Chi-Chung Hui, Sevan Hopyan, Helen McNeill[1,3] and **Tae-Hee Kim[1,2]**

[1]The Hospital for Sick Children, Canada
[2]University of Toronto, Canada
[3]Washington University School of Medicine, USA

The mammalian intestine is lined with millions of finger-like projections, termed villi. These villi are critical for maximizing nutrient absorption, digesting food and serving as a barrier from the harsh luminal environment. As such, compromised villi can lead to serious diseases including malabsorption, short bowel syndrome, celiac, and others. Although villi are precisely patterned by a network of signaling pathways during embryogenesis, it remains unclear as to how these signals translate into distinct morphogenetic transformations. Previous studies attribute the formation of mesenchymal clusters distinguished by Hedgehog (Hh) activation, as critical for epithelial rearrangement into villi. However, the mechanisms of Hh-mediated clustering remain unknown. Our RNA-seq analyses coupled with *GLI2* (Hh-transcriptional activator) ChIP-seq reveal that planar cell polarity (PCP) genes such as *Fat4, Dchs1* and *Vangl2* are putative direct targets of Hh in the gut mesenchyme. Notably, mice deleted and/or mutated for these genes exhibit severe villus fusions and fail to form mesenchymal clusters, demonstrating for the first time the importance of PCP in villification. Furthermore, genetic interaction studies reveal that the core PCP axis (*Vangl2*) acts in parallel to the atypical cadherin axis (*Fat4, Dchs1*) in maintaining PCP. Additionally, ongoing live-imaging of mutant villification *ex vivo* will uncover the types of mesenchymal cell behavior that is required for clustering and subsequent villus formation. Together, we introduce Hh-activated stromal PCP as novel mechanisms required for the morphogenetic events seen during villification.

Biography

Abilasha Rao-Bhatia is currently a PhD candidate under the supervision of Dr Tae-Hee Kim, Scientist at The Hospital for Sick Children and Assistant Professor of the Molecular Genetics Department at the University of Toronto. She is part of an interdisciplinary team dedicated to understanding developmental and stem cell biology of the gastrointestinal system. Prior to this, she completed her undergraduate studies at the University of Waterloo with a degree in Honour's Biology Co-operative studies. Her passion for biomedical research began here as a Co-op student in Dr John Dick's laboratory studying the stem cell origins of acute myeloid leukemia relapse.

abi.rao@mail.utoronto.ca

Notes: