Mutated in Colorectal Cancer (MCC): A Novel Centrosomal Protein Involved in Adult Intestinal Homeostasis and Disease

Catherine Yu ’21, Molecular Biology
A*Star Institute of Medical Biology, Singapore
Funded by CHW under the IIP program

Introduction
Mutated in colorectal cancer (MCC) is a candidate tumor suppressor gene reported to be somatically mutated in Familial Adenomatous Polyposis (FAP). However, more than 25 years since its discovery, the mechanisms by which MCC functions during normal intestinal tissue homeostasis remain unknown. Thus far, The Ray Dunn lab has determined that MCC is a centrosomal protein expressed in the proliferative cells of the mouse intestinal epithelium. As intestinal cells undergo differentiation, MCC re-localizes from the centrosome within the crypt compartments to the apical membrane of differentiated cells; therefore, MCC is potentially involved in the establishment and maintenance of epithelial integrity. We intend to elaborate the role of MCC in vivo by characterizing the intestinal phenotype of MCC mouse mutants.

Objective and Internship Responsibilities
- To investigate the subcellular localization and function of the mouse MCC homolog in the intestinal epithelium
- To generate clinical relevant insights into the involvement of a novel centrosome component in intestinal tissue homeostasis and disease.
- My main responsibilities included 3D in vitro intestinal organoid culture and mouse model genotyping, as well as immunofluorescence and confocal microscopy analysis. I mainly focused on the former.

Results

Discussion, Conclusion and Future Work
- The homozygous mutant for MCC causes serious proliferation defects in intestinal organoid growth, as well as a difference in appearance of the whole-mount duodenum phenotype.
- Future work: How does MCC play a role and affect phenotype in the earlier stages of development (embryo, neonate, etc.)

Acknowledgements and Reflection on Experience Aboard
I would like to thank Dr. Ray Dunn for allowing me to intern at his lab in IMB this summer. I would also like to thank Lucian Tomaz, who served as my mentor for the summer. My experience in Singapore has been overwhelmingly positive and I am grateful for it.