

Wednesday, October 2nd, 2013

LSC 3 - Life Sciences Centre

2350 Health Sciences Mall

12-1pm



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“Set7 at the intersection of Hippo and Wnt signalling in intestinal homeostasis, regeneration and cancer”

One of the key processes in the body is the ability to regenerate and repair damaged tissue. In the intestine, intestinal epithelial cells (IECs) are constantly turning over, with a complete renewal of the epithelium every three to five days. However, due to its high regenerative capacity, the intestine is susceptible to dysregulated growth, resulting in the development of cancers. Indeed, colorectal cancers account for over 5% of all cancer deaths world-wide. Thus, cellular proliferation, differentiation and survival must be tightly regulated. Despite the importance of these processes, the molecular mechanisms that regulate intestinal homeostasis, regeneration and tumourigenesis are not well defined. The Hippo/Yap and Wnt/b-catenin pathways have emerged as critical, interrelated regulators of intestinal physiology by regulating cell proliferation, differentiation and apoptosis. We have recently identified a novel methylation-dependent checkpoint that regulates intestinal homeostasis by controlling activation of the Hippo/Yap pathway in IECs. The methyltransferase Set7 directly methylates Yap and regulates its subcellular localization. We now have extensive new data that extends these findings to the regulation of Wnt/b-catenin signaling, with direct effects on intestinal regeneration and tumourigenesis. The regulation of the Hippo/Yap and Wnt/b-cat pathways by Set7 in the intestine and the implications for intestinal health and disease will be discussed.

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