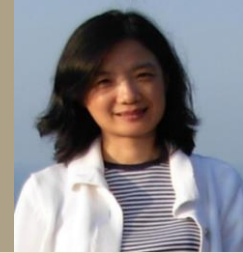


CANCER SCIENCE INSTITUTE OF SINGAPORE SEMINAR ANNOUNCEMENT

Yang Yingzi

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Regulation of Hedgehog signaling by GPCR/Gas/ signaling in bone formation

Date: Monday, 26 May 2014

Time: 11am – 12pm

Venue: #01-01A Active Learning Room @ MD 6
 14 Medical Drive, Singapore 117599

Host: Prof Fu Xin-Yuan

Abstract:

Bone formation is exquisitely controlled in space and time. Heterotopic ossification (HO), the pathologic formation of extra-skeletal bone, occurs as a common complication of trauma or in genetic disorders and can be disabling and lethal. However, the underlying molecular mechanisms are largely unknown. Here we demonstrate that Gas restricts bone formation to the skeleton by inhibiting Hedgehog (Hh) signaling in mesenchymal progenitor cells. In progressive osseous heteroplasia (POH), a human disease caused by null mutations in GNAS that encodes Gas, HH signaling is upregulated in ectopic osteoblasts and progenitor cells. Ectopic Hh signaling is sufficient to induce HO, while Hh signaling inhibition blocks HO in animal models. As our previous work has shown that GNAS gain of function mutations upregulate Wnt/b-Catenin signaling in fibrous dysplasia (FD), our findings identify Gas as a critical regulator of osteoblast differentiation by maintaining a balance between two key signaling pathways: Wnt/b-catenin and Hh. HH signaling inhibitors developed for cancer therapy may be repurposed to treat HO and other diseases caused by GNAS inactivation.

Biography:

Dr Yang completed her Ph.D in Molecular Biology at the Weill Medical College of Cornell University, New York. After which she continued her postdoctoral studies at the Department of Molecular and Cellular Biology, Harvard University, under the mentorship of Dr Andrew McMahon. She is currently a tenured Senior Investigator at the National Institutes of Health (NIH) since 2006. A recipient of numerous honours such as the US Government Service Award, NIH Award of Merit and SCBA Young Investigator Award, Dr Yang has also held various editorial positions including those in the Journal of Molecular Cell Biology and Developmental Biology.