NUS National University of Singapore

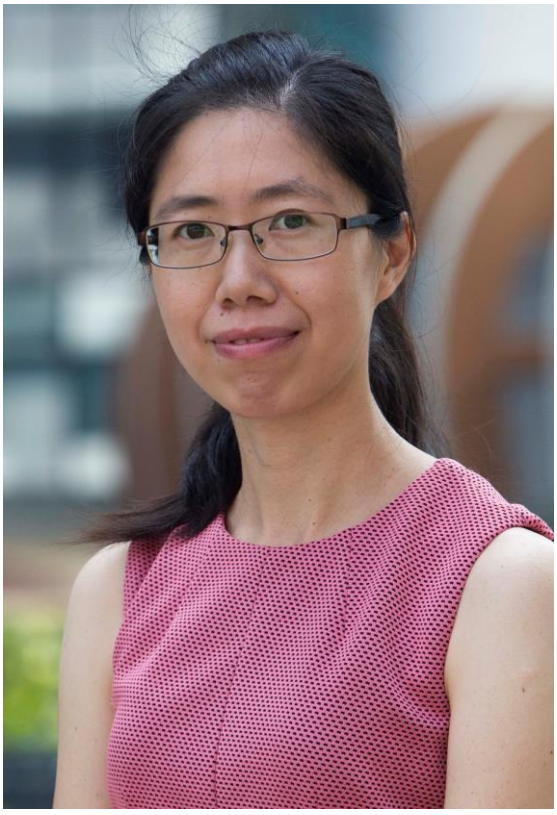
Department of Biological Sciences
Faculty of Science

SEMINAR

Thurs 21 Feb 2019 | 10am | DBS Conference Room 1

Hosted by Prof Gong Zhiyuan

Silencing the genome during development



By **Shifeng Xue**

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During embryonic development, genes need to be turned on and off at the right time. SMCHD1 is an epigenetic regulator required for silencing genes. In mammals, SMCHD1 has a critical role in X inactivation, and in the maintenance of imprinting. SMCHD1 haploinsufficiency has been previously associated with facioscapulohumeral muscular dystrophy type 2 (FSHD2). By studying patients that were born without a nose, we unexpectedly found that missense mutations in SMCHD1 cause a different disease, Bosma arhinia microphthalmia syndrome (BAMS). Here we show that overexpression of BAMS but not FSHD2 mutations in Xenopus embryos was able to cause craniofacial abnormalities. Biochemical assays also show that BAMS mutations were able to increase the activity of the ATPase domain in SMCHD1. We conclude that in contrast to FSHD2 mutations in SMCHD1, BAMS mutations are gain of function. Lastly, by using a smchd1 null zebrafish, we discover a previously unknown role of Smchd1 in silencing key autosomal genes during early development for proper body plan formation. Together, our results identify a critical role for accurate gene silencing in various aspects of physiology.

Artwork by Ann Nee, DBS, NUS