



**THE HONG KONG UNIVERSITY OF SCIENCE & TECHNOLOGY**  
**Division of Life Science**

***LIFS Seminar Series***

**Ribosome-mediated fragmentation determines nascent  
piRNA sites on long intergenic RNAs in mouse testis**

by

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**Abstract:**

PIWI proteins and their associated piRNAs are essential for gamete production and provide a window into the causes of infertility. In adult mouse testis, most piRNAs derive from long intergenic non-coding RNAs ranging from 500 to 80,000 nt. Their precursors, which are RNA polymerase II transcripts containing 5' caps, spliced exons, and poly(A) tails, are cleaved into tens of thousands of fragments that are loaded into PIWI proteins and eventually become piRNAs. Fragmentation requires enzymes found on the outer membrane of mitochondria that generate the piRNA 5' ends. piRNA 5' ends determine piRNA seed sequences that guide PIWI proteins to recognize and degrade base-pair complementary RNA targets. How piRNA precursors are fragmented and whether the choice of piRNA 5' ends is dictated by biased fragmentation or preferential PIWI loading are unknown. Using sucrose gradients to separate mouse testis lysates without destroying mitochondria, we found that piRNA precursors co-sediment with mitochondria and polysomes, and that most steady-state piRNA precursors are fragmented with a 5' monophosphate end. Using a mouse strain expressing epitope-tagged ribosomal protein, end sequencing of 5' monophosphorylated RNAs, and ribosome profiling, we show that 80S ribosomes are bound to piRNA precursor-derived fragments at their 5' extremities, and that these *in vivo* ribosomal footprints mark the sites of nascent piRNA production. In mutant mice in which PIWI loading is blocked, fragmentation still occurs, ribosome-bound piRNA precursor-derived fragments accumulate, and these ribosomes occupy nascent piRNA sites despite the lack of mature piRNA production. Our results indicate that piRNA identity is pre-determined by ribosome-mediated fragmentation prior to PIWI loading. This ribosome-mediated piRNA biogenesis is also found in rooster, and thus likely predates the divergence of birds and mammals. Our results demonstrate an unconventional function for ribosomes beyond protein synthesis, and fill a mechanistic void between the synthesis of piRNA precursors and the generation of piRNA sequences that enable male fertility.

**Date** : **23 June 2017 (Friday)**  
**Time** : **4:00 p.m.**  
**Venue** : **Lecture Theatre D**  
**The Hong Kong University of Science & Technology**  
**Clear Water Bay, Kowloon**

*(Host faculty: Prof. Bik Tye)*

***All are Welcome!!***