"UNVEILING MOLECULAR MECHANISMS OF piRNA PATHWAY FROM SMALL SIGNALS IN BIG DATA"

piRNA is a group of 23–35 nucleotide short RNAs that protect animal gonads from transposon activities and ensure the faithful transfer of genetic information from generation to generation. My thesis research focused on the biogenesis of piRNA by analyzing sequencing data of piRNAs and transposon transcripts.

In *Drosophila* germ line, piRNAs are categorized into two different categories—primary and secondary—based on their origins. Primary piRNAs are released from piRNA cluster transcripts by endonuclease Zuc. They mainly associate with Piwi and Aub proteins and can initiate the production of secondary piRNA in the “Ping-Pong cycle”—reciprocal cleavages of transposon transcripts by Aub and Ago3. We discover that the majority of the primary piRNAs are actually produced from the cleavage products by Ago3 in the Ping-Pong cycle by Zuc, which cleaves those piRNA precursors processively in a periodicity of ~26 nucleotide. On the other hand, the cardinal function of Ago3 is to produce antisense piRNAs that direct transcriptional silencing by Piwi, instead of amplifying Aub-associated piRNAs that slice transposon mRNA in the cytoplasm.

piRNAs bound to Aub typically begin with uridines (1U), while piRNAs bound to Ago3 often have adenines at their 10th (10A). The Ping-Pong model proposes that the 10A is a consequence of 1U. However, we discover that 10A is not directly caused by 1U. Instead, it is a consequence of Aub having an intrinsic preference for adenine at that position. On the other hand, Ago3-associated 10A piRNAs generate cleavage products with uridines at their 5′ ends, maximizing their efficiency to be loaded into Aub to initiate the next Ping-Pong cycle.

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