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Ribosomes template piRNA formation from long non-coding RNAs

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piRNAs are small non-coding RNAs (24-35 nt) that form complexes with PIWI proteins to bind and cleave complementary RNAs. In mouse, piRNAs are highly expressed in testis and are essential for mouse spermatogenesis. However, what defines the sequence of a piRNA remains a mystery. The current model suggests that most piRNAs are generated from the fragmentation of long non-coding single-strand RNA precursors. piRNA precursors are conventional RNA polymerase II (Pol II) transcripts with 5´ m^{7}G caps and 3´ polyadenine tails, and unknown mechanisms mediate precursor recognition and fragmentation. Using germline-specific tagged-ribosome and ribosome profiling, we demonstrate that ribosomes bind to the piRNA precursors. We found that the ribosome footprints on piRNA precursors were distributed throughout the transcripts without restriction to open reading frames and did not show three nucleotides periodicity, implicating that precursor-bound ribosomes have other biological functions besides translation. The 5´ ends of ribosome footprints from piRNA precursors are already processed in vivo, and these ribosome footprints coincidentally shared 5´ ends with mature piRNAs. These observations indicate that ribosomes guide the precursor cleavage to generate the 5´ ends of mature piRNAs. This function of ribosomes in piRNA biogenesis, which also typifies rooster, likely predates the divergence of birds and mammals. Our results demonstrate an unconventional function of ribosome in processing non-coding RNAs, and fill the mechanistic void between the transcription of piRNA precursor and the generation of piRNA sequences that enable fertility.

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