Biological Sciences Seminar

D'Ambra Auditorium ~ Life Science Building ~ University at Albany

February 13, 2012 ~ 2:00pm

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From dsRNA to ssRNA: Unwinding the mystery of RISC maturation

The mammalian RNA induced silencing complex (RISC) contains a single-stranded RNA derived from a duplex miRNA/siRNA and one-of-four Argonaute (Ago) proteins. The process of how small RNA duplexes associate with different Agos and subsequently become single-stranded in vivo is not well established. The Agos contain an evolutionary conserved PAZ (Piwi/Argonaute/Zwille) domain believed to bind the 3'-end of small RNAs. We found that Ago2-Paz domain disrupted proteins are still able to bind small RNAs and induce transgene silencing because the slicer activity allowed for cleavage and removal of the passenger strand RNA. In contrast, in the absence of slicer activity or slicer substrate duplex RNAs, Paz-disrupted Agos bound duplex siRNAs but were unable to unwind and eject the passenger strand. Thus, the Paz domain plays an important role in RISC maturation. These results have implications for si/shRNA designs with reduced off-target effects.

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