

Microsymposium

MS93.O06

Structural basis for post-transcriptional gene silencing by human Argonaute-2

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Argonaute proteins are a unique class of RNases that degrade substrate RNAs in a sequence-specific manner. Argonaute proteins acquire substrate specificity by binding to a small RNA (21 nucleotide), termed the guide RNA, and use the encoded sequence to locate target message RNAs (mRNAs) through base-pairing complementarity. We have determined crystal structures of human Argonaute-2 (Ago2) bound a guide RNA and a variety of complementary target RNAs. The structures reveal how Ago2 uses discrete regions of the guide to scan for targets and the conformational changes associated with target recognition. Using free phenol as a probe, we also identified a constellation of hydrophobic cavities on the surface of Ago2 that we suggest are involved in the recruitment of additional protein factors to target mRNAs upon recognition by Ago2.

Keywords: Argonaute, RNA interference, RNA Silencing