

SMART Teams 2014-2015

Research and Design Phase

Brown Deer High School SMART Team

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Human Argonaute-2: For All Your RNA Slicing Needs

PDB: 4F3T

Primary Citation: Elkayam, E., Kuhn, C., Tocilj, A., Haase, A. D., Greene, E. M., Hannon, G. J., Joshua-Tor, L. (2012). The Structure of Human Argonaute-2 in Complex with miR-20a, *Cell* 150: 100-110

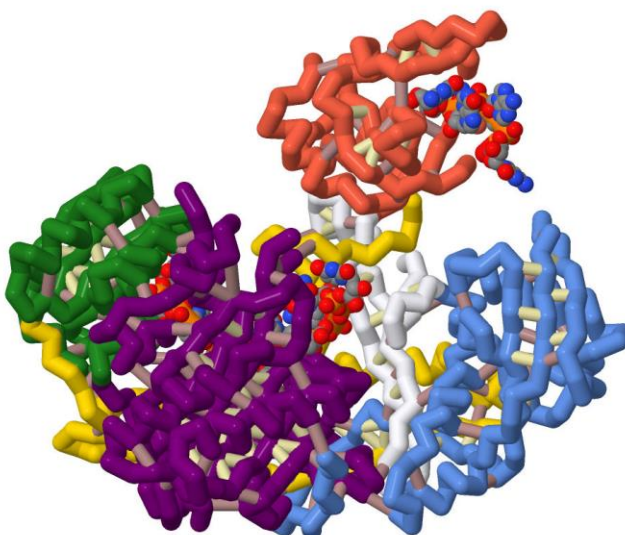
Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

Human cells have the remarkable capability to regulate protein production by degrading target mRNA by two pathways: RNA interference (RNAi) and micro RNA (miRNA). Central to these pathways is the protein Argonaute-2 (Ago-2). In the RNAi pathway, small RNAs derived from viruses are used by Ago-2 to slice virus mRNA, protecting the cells from infection. In the miRNA pathway, Ago-2 utilizes naturally occurring miRNA to slice cellular mRNAs to control protein production. Ago-2 works by binding small (~22 nucleotide) regulatory RNAs (siRNA and miRNA) to target mRNA by base pairing.

Ago-2 attaches to the phosphate backbone of the regulatory RNA, that guides Ago-2 to the target RNA. The RNase domain of Ago-2 (containing His807, Asp669, Asp597, and Glu637 in its active site) then "slices" the target to initiate degradation. Scientists can reduce the level of disease-causing proteins (for example, in breast cancer) using the siRNA pathway. Determining the structure of Ago-2 allowed researchers to understand how this enzyme functions in the siRNA/miRNA pathways. The Brown Deer High School SMART (Students Modeling A Research Topic) Team has designed a model of Ago-2 using 3D printing technology to investigate its structure-function relationship. SMART Team programs are supported by a grant from NIH-CTSA.



Specific Model Information:

- | | |
|---|----------------|
| • Amino Acids 1-174 (the N domain): | CornFlowerBlue |
| • Amino Acids 175-225 (the Linker 1 domain): | GhostWhite |
| • Amino Acids 226-346 (the PAZ domain): | Tomato |
| • Amino Acids 347-449 (the linker 2 domain): | Gold |
| • Amino Acids 450-572 (the MID domain): | ForestGreen |
| • Amino Acids 573-859 (the PIWI domain): | Purple |
| • H bonds: | PaleGoldenRod |
| • Struts: | RosyBrown |
| • RNA: | CPK |
| • Active site (His807, Asp669, Asp597, Glu637): | CPK |

<http://cbm.msoe.edu/smartTeams/index.php>

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