SMART Teams 2013-2014
Research and Design Phase

Hartford Union High School SMART Team

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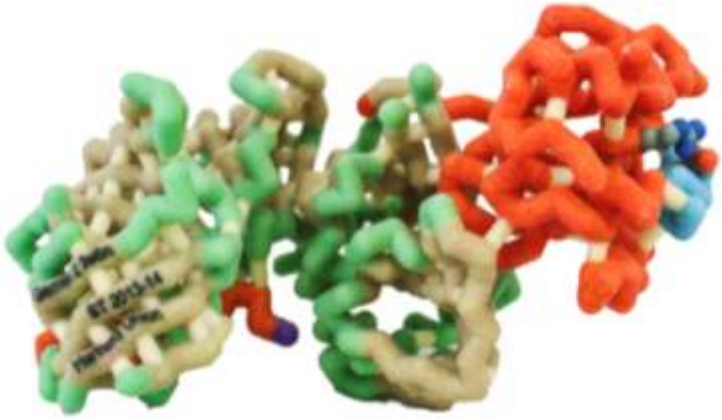
Correct Splicing: The Desolation of SMA
Spinal Muscular Atrophy and the Survival Motor Neuron Complex

PDB: 3S6N

Primary Citation: Zhang, R., So, B. R., Li, P., Yong, J., Glisovic, T., Wan, L., & Dreyfuss, G. (2011). Structure of key intermediate of the SMN complex reveals genin2's crucial function in snRNP assembly. *Cell* 146: 384-395.

Format: Alpha carbon backbone

RP: Zcorp with plaster



Description:

Spinal muscular atrophy (SMA) is a genetic disorder usually leading to death before age two. This is caused by the degeneration of motor neurons in the spine and affects one in six thousand babies yearly (Families of SMA, 2013). It is unknown why a point mutation or deletion of the SMN1 gene, which produces survival motor neuron (SMN) protein, causes this degeneration. The SMN complex, found in the cytoplasm, is made of SMN and smaller units called Gemin proteins. In a normally functioning system, the SMN1 gene codes for SMN proteins that are part of the SMN complex that forms small nuclear ribonucleoproteins (snRNPs) from SM proteins and sRNA. The SMN protein binds to Gemin-2 which holds five of the seven SM proteins, the smaller units in snRNPs, in place until the target snRNA sequence is located. The final SM proteins are added when the N-terminus of Gemin-2 is moved. The snRNPs have many functions in cells, and five of them are involved in RNA splicing. The knowledge that is available on normal interactions of SMN and Gemin-2 allow modeling of these proteins to be completed through 3D printing by the Hartford Union SMART (Students Modeling a Research Topic) Team. In children with SMA, the SMN protein cannot to bind to Gemin-2 because Asp44 is replaced by valine, causing a break in the ionic bond holding the helices together. While this situation still produces normally operating snRNPs, there are too few to correctly splice the pre-mRNA, leading to SMA.

Specific Model Information:

- Gemin-2 protein alpha carbon backbone is colored red.
- Survival of Motor Neuron protein (SMN) alpha carbon backbone is colored aqua.
- The pentameter is highlighted in pale green.
- Beta sheets are highlighted in tan.
- Amino acids Asp 44 and Arg 213, displayed in ball and stick and colored in cpk, form a salt bridge that holds the SMN protein and the Gemin-2 protein together.
- The N-terminus of Gemin-2 is highlighted in purple.
- Hydrogen bonds are colored papaya whip.
- Structural supports are colored lemon chiffon.

http://cbm.msoe.edu/smartTeams/

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