

## E0043

**GCN5, A Key To Opening DNA.** K. Bauer, A. Benz, B. Berg, L. Breu, B. Brophy, M. Dougherty, A. Limbach, M. Masterson, D. Miller, K. Moakley, T. Mueller, D. Polaski, A. Puzach, D. Rayburn, M. Ruka, A. Solberg, L. Spaits, D. Tighe, B. Tushaus, K. Volbrecht, R. Widmann, D. LaFlamme, St. Dominic School SMART Team, Brookfield, WI 53005, Mentor: Dr. Vaughn Jackson, Medical College of Wisconsin, Milwaukee, WI 53226-0509.

GCN5 is an important enzyme in the cell because it is involved in making the DNA in the nucleus of cells available for replication (copying) and transcription (reading of genes). Histone acetyltransferases were first isolated in the mid-1990s. Scientists noticed that very active DNA was associated with highly-acetylated histones in nucleosomes.

This molecule is also interesting because histone acetyltransferases have been associated with several cancers including leukemia. This enzyme is overactive in some cancer cells causing them to keep dividing out of control. The scientists (A.N. Poux *et al*, *PNAS*, October 2002) who determined the structure of GCN5 also designed an inhibitor to stop the molecule from working. They made an inhibitor using Coenzyme A bonded to a piece of histone 3. This inhibitor stops the molecule from working by making it impossible for acetyl CoA to fit into the enzyme's active site and then to acetylate histone 3. This is exciting because inhibitors could be used to stop cancer cells from reproducing.

Our model design is based on the 1M1D pdb file and includes the sidechains listed in the A.N. Poux paper and the *Nature* (Rojas, et.al) paper because of their importance in binding the inhibitor and the normal substrates.