SMART Teams
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FINAL PRESENTATIONS

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Center for BioMolecular Modeling
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**S.W.A.T., Starches with Attitudes**  
The Mary Ryan Boys and Girls Club

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**Teacher:** Amanda Lavoe

**Mentors:** Will Allen, Growing Power; Tim Herman, Jon Knopp, Justin Snowden, and Jennifer Morris, MSOE Center for BioMolecular Modeling

**Function:** Glucose is a carbohydrate produced by plants and is an important energy source for humans, animals, and plants.

**Abstract:** We are the Mary Ryan Boys and Girls Club S.W.A.T Team, Starches With Attitudes. We have been working with Will Allen at Growing Power, an example of agriculture in the city using recyclable organic wastes. Will Allen uses hydroponics and vermiculture to break down the organic wastes into nitrogen and carbon which helps plants grow. We have been working on understanding how plants capture the energy of the sun, carbon dioxide, water, and create carbohydrates. This process is called photosynthesis and produces oxygen and glucose. Glucose is one of the most important carbohydrates and is used as a good source of energy in animals and plants.

**Sir2 Histone H4 Deacetylase: A Key to Controlling DNA**  
St. Dominic Middle School

**Students:** Mike Beining, Katie Benz, Brian Borges, Ana Caballero, Ryan Cisler, Tyler Cobb, Jimmy Delforge, Meredith Dentice, Megan Farley, Drew Fink, Kevin Kallinger, John Lambert, Jesse Mark, Alex Mattern, Jim Mirda, Sarah Misna, Becca Moore, Ben Robey, John Selas, Joe Sladky, Sam Sladky, Stephen Varnum, David VonRuden, Jon Weisse

**Teacher:** Donna LaFlamme

**Mentor:** Dr. Vaughn Jackson, Medical College of Wisconsin

**Function:** Regulates DNA expression by removing acetyl groups from lysine 16 of the histone H4 tails of the nucleosome. (continued on the next page - St. Dominic Abstract)
Abstract: The purpose of the St. Dominic SMART Team project was to design a physical model of the enzyme yHst2 Histone H4 Deacetylase using data deposited in the Protein Data Bank and a molecular visualization program called RasMol. The designing process helped us to learn about this important enzyme's structure, its function in the cell, and also about the chemical reaction it catalyzes. Our mentor, Dr. Vaughn Jackson, helped us understand how yHst2 controls DNA expression by removing acetyl groups from the lysine 16 of the histone H4 tails of nucleosomes. Removing an acetyl group from lysine changes its charge from neutral to positive. This positively charged histone tail is attracted to the negatively charged backbone of the DNA wrapped around the histones. Scientists have known for some time that acetylated histone tails are associated with active DNA and deacetylated tails with inactive or silent DNA.

Our enzyme, yHst2, belongs to an important family of enzymes called sirtuins. yHst2 is the yeast homologue of human Sir two 2. All Sir2 deacetylases have amino acid sequences that are very similar in all organisms from bacteria to humans. They all remove acetyl groups from acetyllysine sidechains on the proteins that they target. They all use NAD+ to accomplish this.

Sir2 proteins are very important to cells because they are involved in essential activities such as turning off genes, promoting the repair DNA, maintaining genome stability, and in cell metabolism. They have even been linked to increased lifespan. For example, scientists have discovered that restricting calories can extend the life of several research organisms. They noticed that calorie restriction causes cells to have very active Sir2 enzymes. Maybe, in the future, drugs that activate Sir2 deacetylases may become a way to stay young! Doctors are already using Sir2 activators in research trials to treat the cancers, lymphoma and leukemia.

The Effect of 2,3 Diphosphoglycerate (DPG) on Hemoglobin
Marquette University High School

Students: Fritz Bartel, Matthew Clark, Jason Carr, Patrick Carter, Thomas Fleming, Creston Flemming, Raman Kutty, Evan Lloyd, Ashim Singh

Teacher: Keith Klestinski

Mentors: Dr. George Phillips and Mr. Roman Aranda, University of Wisconsin-Madison; Dr. Michael Patrick, MSOE Center for Biomolecular Modeling

Function: Interaction of DPG with hemoglobin promotes the movement of oxygen from red blood cells to body tissues.

Abstract: Hemoglobin is among the most important molecules in biology, for it facilitates a complex, efficient transfer of oxygen which distinguishes the higher organisms. Hemoglobin is an allosteric (continued on next page - Marquette Abstract)
protein; that is, it undergoes conformational changes that affect its function. The two primary allosteric states of hemoglobin are the "tense" (T) state, which is characteristic of a hemoglobin molecule without oxygen, and the "relaxed" (R) state, which is favored when the molecule is oxygenated.

The tendency of hemoglobin to assume either the T or R state is mediated by a number of environmental and molecular factors termed "allosteric effectors." One such molecule is 2,3-diphosphoglycerate, or DPG. DPG binds to hemoglobin within the molecule's central cavity, and forms rigid salt bonds with hemoglobin subunits that "lock" hemoglobin in the T-state. Because the T-state has lower oxygen affinity than the R-state, DPG-induced hemoglobin tends to release more oxygen at tissue-level than R-state hemoglobin, which holds on to oxygen more tightly.

DPG plays an important role in the body's adaptation to varying environmental conditions. At high altitude, DPG production is accelerated, allowing for an increase in hemoglobin's release of oxygen that counterbalances the lower oxygen concentration of mountain air. Human fetuses have a modified hemoglobin molecule that prevents the binding of DPG, thus giving fetal hemoglobin a great affinity for oxygen than maternal hemoglobin and allowing for oxygen transfer across the placenta. Increased DPG is also associated with diseases such as emphysema and congenital heart disease that reduce the efficiency of the body's oxygenation mechanisms.

Eukaryotic Peptide Chain Release Factor (ERF3)
St. Joan Antida

Students: Lina AbdulKarim, Nadia Ali, Elisa Krause, Pamela Xiong

Teacher: Mary Carlson

Mentor: Dr. Anita Manogaran, University of Illinois-Chicago Laboratory for Molecular Biology, Illinois

Function: ERF3 plays a role in the termination of protein synthesis and has been known to misfold in yeast, leading to protein aggregates, or prions.

Abstract: The building blocks of the entire human body-proteins-play many important roles in everyday processes. Proper folding of proteins is important to their function. In some cases, proteins misfold and cannot properly function. The misfolding of a protein can lead to the formation of prion disease. Prion disease is (continued on next page - St. Joan Antida Abstract)
Acceptance of the Influenza Pathogen into Class II MHC
Whitefish Bay High School

**Function:** The immune response to viral and bacterial diseases is mediated by Class II MHC molecules. These molecules present peptide fragments to the T cells in order to mount an immune response against foreign particles.

**Abstract:** The class II major histocompatibility complex (MHC II) molecule is involved in immune responses to viral and bacterial diseases. When a peptide fragment of a protein is "loaded" into the molecule, the alpha helices of the Class II MHC unwind and the peptide is inserted in the gap. The class II MHC molecule is critical in the production of antibodies to fight illness and prevent future infections. The class II MHC helps the body identify antigens by presenting antigen fragments to helper T-cells. The helper T-cells then instruct B-cells to produce antibodies, which in turn alert other cells to the presence of a pathogen and instruct them to fight the intruder. We are focusing on influenza and the way in which a fragment of the influenza protein fits into the class II MHC molecule. In the case of influenza, macrophages ingest the virus, producing peptide fragments that the MHC molecules collect. We have designed a physical model of the class II MHC protein and a peptide fragment of influenza in the PDB file DR1HATCR.pdb. Researchers like Dr. Gorski are working to understand how the MHC molecule opens for the peptide to be inserted. Understanding this peptide loading process is important for rational vaccine design, as vaccines should optimize the ability to load the class II MHC with pathogen-derived peptide fragments.
**FcRN: From Mother to Fetus**  
West Bend East High School

**Students:** Logan Riemer, Christine Anhalt, and Megan Petri  
**Teacher:** Trish Strohfeldt  
**Mentor:** Dr. Jason A. Bubier, Post-doctoral researcher, Jackson Laboratory

**Function:** Transfer of IgG across placenta

**Association of the Molecule with Disease:** FcRn can be used as a possible therapeutic agent in the treatment of diseases.

**Abstract:** Fc Receptor Neonatal or FcRn is a protein in mammals by which immunity is passed from mother to fetus before birth. FcRn is a heterodimer that consists of three identical beta-2-microglobulin chains and three Fc Receptor chain. FcRn binds to Immunoglobin G (IgG) and aides in transport of IgG across the placenta. FcRn's function is regulated by pH and is involved in the transport of IgG through transport vesicles. FcRn binds to IgG at a pH of 6.0 in the vesicles and releases at a pH of 7.4 in the fetal blood stream. FcRn is also important in the control of the catabolism of IgG. It prevents degradation of IgG, substantially increasing the half-life of IgG. IgG lasts 22-23 days in humans. Since FcRn has the ability to increase the half-life of IgG, research is being done with coupling of therapeutic agents to IgG to increase the stability of the therapeutic agent. Research on FcRn and IgG is currently being done on mice and rat models.
**Neonatal Alloimmune Thrombocytopenia**  
Wauwatosa High School

**Students:** Shazia Ali, Danielle Perszyk, Ben Schrank  
**Teacher:** Donnie Case  
**Mentors:** Drs. Debra and Peter Newman, Blood Research Institute

**Function:** Integrins are a family of molecules on the surface of cells that mediate cell-matrix and cell-cell interactions. The PSI domain contributes to activation of integrin and genetic variation in the PSI domain is associated with NATP.

**Abstract:** Platelets, also called thrombocytes, are required to control bleeding. Alloimmune thrombocytopenia is a disease that results when an individual makes antibodies that bind to proteins on another individual's platelets. Neonatal Alloimmune Thrombocytopenia (NATP) occurs when a mother makes antibodies that bind to her baby's platelets. In this disease, the mother's antibodies on the fetal platelets can cause them to be cleared by the immune system or prevent them from working properly, resulting in severe bruising and hemorrhaging. Once the antibodies are gone, the baby's platelets will then function properly and initiate clotting. The baby is in danger when the antibodies are present at or before birth because of the possibility of intracranial bleeding can lead to severe brain damage.

A major target for antibodies in NATP is the glycoprotein IIb-IIIa, (GPIIb-IIIa), which is made up of two subunits, GPIIb and GPIIIa, and is expressed only on platelets. NATP most commonly occurs when a mother has the amino acid proline (Pro or P) and her baby has a leucine (Leu or L) at position 33 of the GPIIIa subunit.

Scientists have struggled for years to solve the structure of the region within the GPIIIa subunit that contains the L33P polymorphism. They have recently determined that it folds into a structure called a PSI domain. We have built a model of the PSI domain of GPIIIa, which possesses a leucine at position 33. The ability to visualize the structure adopted by the PSI domain of GPIIIa will hopefully enable scientists to use their knowledge of that structure to find successful treatments for NATP.
Caspace: And the Death of a Cell
Kettle Moraine High School

Students: Becca Denison, Ian Flaws, Claire Gannon, Chris Pierzchalski, Heather Rusk, Tony Schuler

Teacher: Karen Deboer and Pete Nielsen

Mentor: Dr. Jean-Yves Sgro, University of Wisconsin - Madison

Function: Caspaces are involved in the process of apoptosis, or programmed cell death.

Abstract: "For every cell, there is a time to live and a time to die". Apoptosis, or programmed cell death, is a naturally occurring process that is vital to normal life and development. This cellular pathway eliminates damaged, dangerous or unwanted cells in organisms. Triggers can include radiation, poison, and viral infection. After a cell dies, surrounding cells engulf it to prevent the spread of its infected contents. A genetically controlled form of cell suicide, it is initiated by normally inactive enzymes, called caspases. These proteases and apoptosis can also play a role in many diseases including cancer, autoimmune disorders, viral infections, Alzheimer's disease, ischemic injuries, and osteoporosis.

Located in all cells, whether eukaryotic or prokaryotic, caspaces are highly conserved and show little variation between species. The caspase involved in our study of baculoviruses is SF-caspase-1, located in Autographa californica. The baculoviral p35 protein blocks apoptosis in two distinct steps of caspase inhibition. Before cleavage, the p35 recognizes the caspase and then cleaves the protein leaving an irreversible complex. The N terminus of p35 bonds with the active site cysteine of the caspase that is opened during cleavage to prevent hydrolysis and the continuation of the reaction.
COX-1 and COX-2 Enzymes Catalyze Prostaglandin Synthesis and Are Inhibited by Nonsteroidal Anti-inflammatory Drugs

Madison West High School

Students: Audra Amasino, Yuting Deng, Samuel Huang, Iris Lee, Adeyinka Lesi, Yaoli Pu, Peter Vander Velden

Teacher: Gary Graper, Teacher Emeritus, University of Wisconsin-Madison

Mentors: Dr. David Nelson, University of Wisconsin-Madison, and Basudeb Bhattacharyya, Student, University of Wisconsin-Madison

Function: COX-1 and Cox-2 are enzymes that synthesize prostaglandins, which are proteins responsible for fever, pain and inflammation, as well as maintaining the stomach lining and preventing ulcer formation.

Abstract: Prostaglandin Hormone Synthases (COX-1 and COX-2) are enzymes embedded in cell membranes that produce prostaglandins responsible for fever, pain, and inflammation, but also maintenance of the lining of the stomach and prevention of ulceration. COX is short for CYCLOOXYGENASE meaning that it is an enzyme that oxidizes a substrate. Prostaglandins are modified fatty acids attached to a 5-membered ring that act as local messengers near their site of synthesis, and are metabolized very rapidly. COX-1 is found mainly in the gastrointestinal lining, and COX-2 at sites of inflammation. NSAIDS (Nonsteroidal anti-inflammatory drugs) such as aspirin, naproxen, ibuprofen, and flurbiprofen inhibit both COX-1 and COX-2, and are taken regularly by over 33 million Americans for pain and inflammation. Some 10%-50% of these users suffer gastrointestinal side effects such as abdominal pain, diarrhea, bloating, heartburn, and ulcers. Thus, recent efforts to inhibit only COX-2 have resulted in COX-2 inhibitors such as Celebrex, Vioxx, and Bextra which do not have the unwanted side-effects, but have been linked to increased numbers of heart attacks and strokes. We are studying the interaction of the COX enzymes with NSAIDS and COX-2 inhibitors to see how the enzymes are inhibited from catalyzing prostaglandins, as well as the structural differences between COX-1 and COX-2. We are designing models of the active sites of COX-1 and COX-2 using pdb files 1Q4G and 1PXX, as well as models of the normal COX substrate, arachidonic acid, and NSAIDS and COX-2 inhibitors to better understand the actions and side-effects of NSAIDS and COX-2 inhibitors.
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