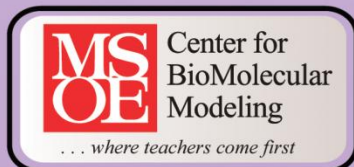


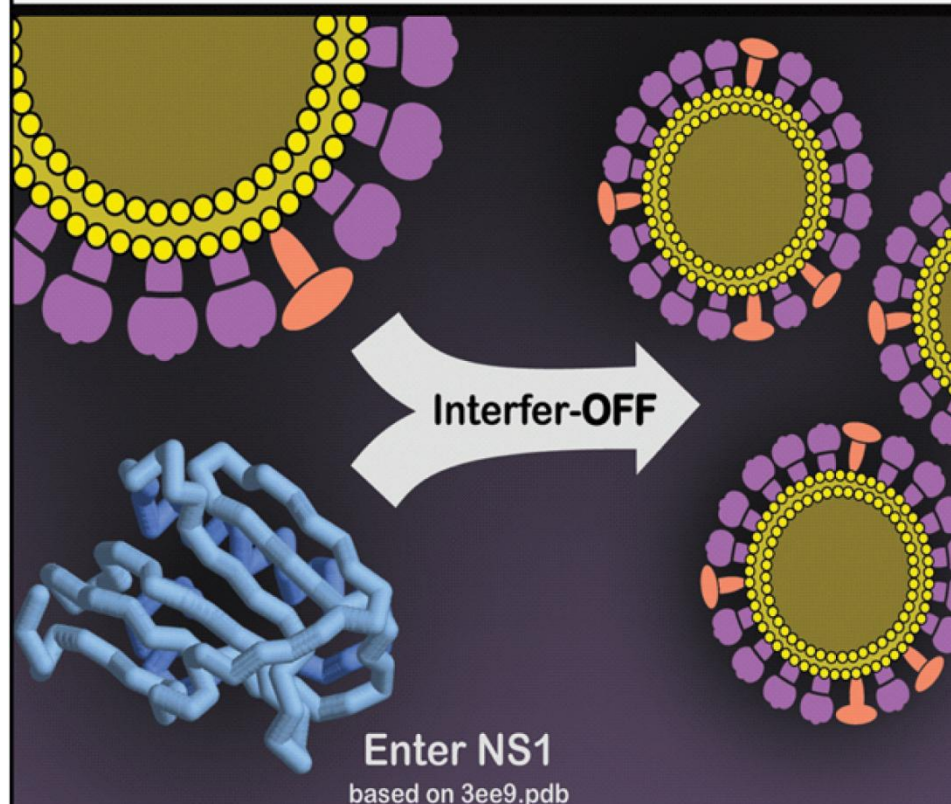
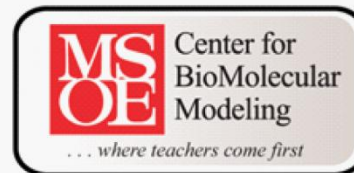


The Center for BioMolecular Modeling would like to acknowledge and thank the Science Education Partnership Award (SEPA; Grant #R25RR022749), a program sponsored by the National Institutes of Health (NIH) – National Center for Research Resources (NCRR), for their support in funding the SMART Team program.

The Center for BioMolecular Modeling would also like to thank the Medical College of Wisconsin for hosting the SMART Team Poster Session and Final Presentations.



SMART TEAMS
2009-10
Students Modeling A Research Topic



Final Presentations

March 27th, 2010

Medical College of Wisconsin
<http://cbm.msoe.edu>

Dear Teachers, Students, Mentors and Honored Guests,

Thank you for supporting the SMART Team program. We would not be able to continue to host this program without the teachers who donate their time, the students who commit themselves to the program, the mentors who work diligently with their teams, the administration who support their faculty, and family members who encourage their loved ones to excel in all that they pursue. We would not be here without all of you. A SMART Team is composed of several different members; it takes a team effort to accomplish all that you have this year. You have all worked very hard and we at the Center for BioMolecular Modeling would like to say thank you and congratulations to you all!

Center for BioMolecular Modeling

Shannon Colton, Ph.D.

Margaret Franzen, Ph.D.

Tim Herman, Ph.D.

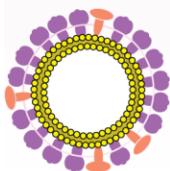
Mark Hoelzer

SMART Team Program Director

Program Director

CBM Director

Lead Designer



Special thanks for the time and effort of

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Julie Fangmann and Martin Volk

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Françoise Van den Bergh

Jung-Ja Kim

Shama Mirza

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Malathi Narayan and

Sally Twining

Sarah Kohler

Andrea Ferrante

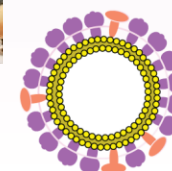
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Savannah Anderson

Bill Hoelzer

Cathy Weitenbeck

Ryan Wyss



HFE: An Iron Uptake Regulation Molecule

Brookfield Central High School

Authors: Yuhan Chen, Bryan Dongre, Justin Fu, Zach Gerner, Shariq Moore, Nick Nabar, Vick Nabar, Nikil Prasad, Joshua Speagle, Sai Vangala

Teacher: Louise Thompson

School: Brookfield Central High School, Brookfield, WI

Mentor: Andrea Ferrante, M.D., Blood Center of Wisconsin



Accumulation of excess iron results in a common hereditary disease, Hereditary Haemochromatosis (HH). There are various genetic mutations that lead to different forms of the disease. HH-I is a form of this disease in which iron accumulates in hepatocytes and intestinal epithelial cells and is associated with a mutation in the HFE (high iron protein) gene. The Brookfield Central SMART Team (Students Modeling A Research Topic) developed a model of HFE using 3D printing technology. The HFE gene encodes for a non-classical MHC class I protein. In physiological conditions, HFE is expressed and translocated to the cell surface where it may interact with a transferrin receptor (Tfr). The binding of the $\alpha 1/\beta 2$ domains of HFE to the Tfr allows for controlled release of iron bound to transferrin-transferrin receptor complex. A mutation (845G>A) causes the replacement of a cysteine with a tyrosine (C282Y). This replacement prevents the $\alpha 3$ subunit of HFE from folding properly and from interacting with $\beta 2$ microglobulin, abrogating the translocation of the HFE-microglobulin complex to the cell membrane and promoting its rapid degradation. This defect hinders the regulatory capability of HFE. Current treatments include phlebotomy to prevent organ damage from accumulated iron. Further study to increase understanding of the regulatory mechanism may lead to improved treatment design. *Supported by a grant from NIH-NCRR-SEPA.*

Order of Presentations

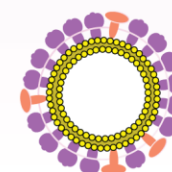
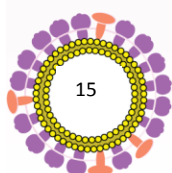
1st Session (9:00 – 11:30 AM)

Abstracts on Page

1. Introduction	
2. Brown Deer High School	1
3. Nathan Hale High School	2
4. Marquette University High School	3
5. Whitefish Bay High School	4
6. Wauwatosa West High School	5
7. Greenfield High School	6
8. Valders High School	7
9. St. Joan Antida High School	8

2nd Session (12:00-2:00 PM)

10. Introduction	
11. St. Dominic Middle School	9
12. Cedarburg High School	10
13. Kettle Moraine High School	11
14. Grafton High School	12
15. Messmer High School	13
16. Homestead High School	14
17. Brookfield Central High School	15



I'm a PC (Pyruvate Carboxylase)... ... and diabetes was not my idea!

Brown Deer High School

Authors: S. Andera-Cato, A. Arnold, S. Bach, J. DeSwarte, A. Faught, E. Frisch, A. Her, A. Keller, E. Kennedy, T. Martin, D. McMurray, C. Mitch, C. Orozco, C. Rice, B. Roberts, A. Rodgers, A. Sauer, A. Schulman, G. Sekhon, A. Suggs, K. Surfus, S. Tucker, T. Wray

Teacher: Gina Vogt

School: Brown Deer High School, Brown Deer, WI

Mentor: Martin St. Maurice, Ph.D., Marquette University

NIH estimates that 23 million Americans have diabetes, and 6.2 million are undiagnosed. If untreated, diabetes can cause complications, including heart disease and neuropathy. Type two diabetes patients cannot regulate glucose due to insulin resistance or deficiency. Pyruvate carboxylase (PC) plays an important role in insulin release from pancreatic β cells. Abnormal PC activity has been correlated with type two diabetes. PC is a dimer of dimers, each monomer a single chain with four domains: N-terminal biotin carboxylase (BC), central carboxyltransferase (CT), C-terminal biotin carboxyl carrier protein (BCCP), and allosteric domains. PC catalyzes the conversion of pyruvate to oxaloacetate (OAA). The process begins when biotin is carboxylated at the BC active site. The BCCP domain transfers the carboxybiotin to an active site in the CT domain. OAA is formed at the CT domain by adding a carboxyl group to pyruvate. Researchers concluded that the BCCP domain swings between active sites on opposite chains, instead of sites on the same chain. The Brown Deer SMART Team (Students Modeling A Research Topic), in collaboration with MSOE, built a model of PC using 3D printing technology illustrating this movement of the BCCP domain. Current research is focused on increasing PC activity through controlling a binding site in the allosteric domain, which may increase insulin production. *Supported by a grant from NIH-NCRR-SEPA.*



“Like a Boss”

The Role of FoxD3 in Pluripotency

Homestead High School

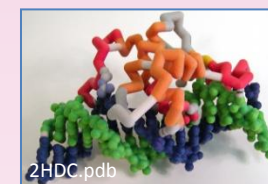
Authors: Laura Auiar, Claudia D'Antoine, Sophia D'Antoine, Lisa Liu, Sarah Lopina, Sahitya Raja, Nikhil Ramnarayan, Daniel Schloegel, Ross Schloegel, Claire Songkakul, Rahul Subramanian, Bryanna Yeh

Teachers: Chris Schultz and Rick Hubbell

School: Homestead High School, Mequon, WI

Mentor: Sarah Kohler, Ph.D., Medical College of Wisconsin

Stem cells play a major role in biological research due to their pluripotency, or ability to differentiate into various types of cells. Stem cells are essential for proper development and maintenance of systems. Therefore, it is imperative that adequate numbers of stem cells are produced during embryogenesis. During the initial stages of embryogenesis, differentiation must be suppressed until enough stem cells are produced. Several transcription factors, including FOXD3, help inhibit differentiation in order to produce the large numbers of cells required by the organism prior to differentiation. FOXD3 relies on a signaling pathway initiated by another transcription factor called Nanog to maintain the cell's pluripotency. Upon activation, the fork-head binding of domain of FOXD3 attaches to the DNA, causing the DNA to unwind and thereby making the DNA accessible to other transcription factors. This results in the activation of target genes, which are responsible for the maintenance of pluripotency in the stem cells. Once sufficient stem cells have been produced, FOXD3 is turned off, thus inhibiting the genes needed to maintain pluripotency and therefore allowing differentiation to occur. Determining how FOXD3 co-operates with other transcription factors, as well as how this protein is suppressed, could enhance understanding of stem cell development during embryogenesis. This research may be a source of new therapeutic treatments, such as using somatic cells that have been induced to a pluripotent state as a source for organ/tissue transplants, which would potentially eliminate host rejection during transplant procedures.



The Role of β -Catenin in Cell Division and Colon Cancer

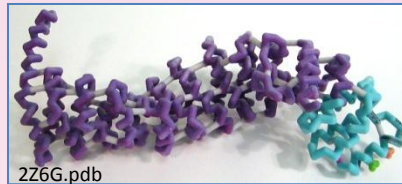
Messmer High School

Authors: Nancy Alba, Darrell Anderson, TeAngelo Cargille Jr., Sara Kujjo, Giovanni Rodriguez, Karla Romero

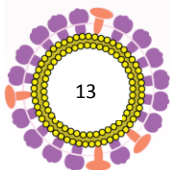
Teacher: Carol Johnson

School: Messmer High School, Milwaukee, WI

Mentors: Malathi Narayan and Sally Twining, Ph.D., Medical College of Wisconsin



Colon cancer is the fourth most lethal cancer in the U.S. As food passes through the colon, water and vitamins are absorbed and epithelial cells are sloughed off and replaced by a tightly regulated cell division process. Unregulated cell division can lead to the formation of polyps and tumors. β -catenin plays a role in regulating cell division and was modeled by the Messmer SMART Team (Students Modeling A Research Topic) using 3D printing technology. In non-dividing cells, a multi-protein complex of APC, GSK-3 and Axin phosphorylates β -catenin, signaling its degradation and preventing cell division. When cell division is needed, a Wnt signal cascade causes the complex to release β -catenin, stabilizing the protein for nuclear translocation and binding to TCF, a transcriptional activator, thus triggering cell division. Competitive binding of the inhibitor proteins, ICAT and Chibby, to β -catenin negatively regulates this process. In colon cancer, mutations in APC or Axin impede binding of the complex to β -catenin, preventing degradation, leading to increased nuclear localization, binding to TCF and deregulated cell division. Additionally, survivin, an anti-apoptotic protein that enables tumor cell survival, is upregulated. Understanding β -catenin's structure could help design drugs to promote binding of inhibitors to prevent the unregulated cell division of cancer. *Supported by a grant from NIH-NCRR-SEPA.*



APC: The Key to Colon Cancer

The APC protein and its role in controlling the cell cycle

Nathan Hale High School

Authors: Melissa Gall, Laenzio Garrett, Nick Goldner, Zach Koepp, Valerie Lamphear, Peter Nguyen, Vivek Patel, Stefan Pietrzak, Evan Rypel, Ajay Sreekanth, Kyle Tretow, Tyler Zajdel

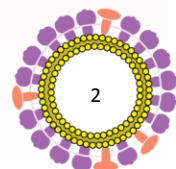
Teachers: Sue Getzel and Anne Xiong

School: Nathan Hale High School, West Allis, WI

Mentor: William Berger, M.D., VA Medical Center



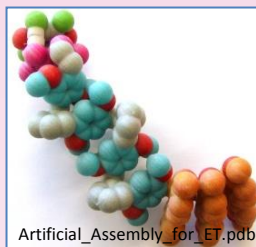
Colorectal cancer affects 1 in 18 Americans, and is linked to mutations in the Adenomatous Polyposis Coli (APC) gene. The rapid division of colonocytes is regulated by the Wntless Type (Wnt) signaling pathway, mediated by β -catenin. In the nucleus, β -catenin binds to Transcription Cell Factor (TCF) and initiates transcription of cell cycle proteins. Alternatively, β -catenin binds to the 20-amino acid repeat region of the APC protein with the help of the scaffold protein axin. The enzyme GSK-3 then phosphorylates threonine and serine residues of the APC protein and subsequently β -catenin. Phosphorylated β -catenin is degraded, slowing mitosis. Mutations in APC allow β -catenin to accumulate, resulting in hyperproliferation of colonocytes, an early step in colon cancer development. As such, better understanding of APC and its function could potentially lead to better diagnosis and treatment in colorectal cancer.



Cofacially-Arrayed Polybenzenoid Nano Structures

Marquette University High School

Authors: Zeeshan Yacoob, Caleb Vogt, Patrick Jordan, Jose Rosas, Kienan Knight-Boehm, Hector Lopez, Fernando Buchanan-Nogueron, Nicholas Zausch, Qateeb Khan, Judson Bro, Payton Gill, Jacob Klusman, Alexander Lessila, Jed Sekaran, Caden Ulschmid

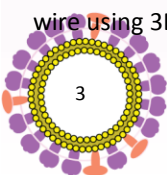


Teachers: Keith Klestinski and David Vogt

School: Marquette University High School, Milwaukee, WI

Mentor: Rajendra Rathore, Ph.D., Marquette University

Based on Moore's Law, every 18 months the number of transistors that can be placed per unit area on a microchip will double. However, by the year 2017 this trend will cease to exist due to the size restrictions imposed by silicon, the main component of microchips; this has led to the birth of molecular electronics. An organic molecule that has been extensively tested for its potential in molecular electronics is DNA. However, recent research has shown that DNA cannot function as a molecular wire due to its fragile nature. This is why Raj Rathore's group is developing organic molecular wires based on robust macromolecular structures. The specific assembly designed to study the wire behavior consists of a triad which is made up of polyfluorenes as an electron donor site, a spacer unit (or wire) made of polyphenylenes, and an electron donor-acceptor complexation site composed of hexamethylbenzene (HMB). A chloranil molecule—an electron acceptor—complexes with the HMB of the triad, and when a laser is shined on HMB/CA complex, a hole is introduced in the molecular wire which will travel 30 Å to the polyfluorene donor, via an electron hopping mechanism. The Marquette University High School SMART Team (Students Modeling A Research Topic) created a physical model of this molecular wire using 3D printing technology. *Supported by a grant from NIH-NCRR-SEPA.*

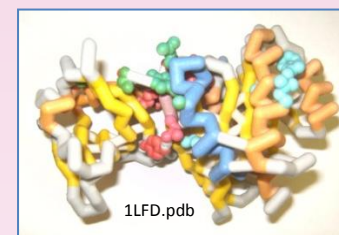


3

An OverRASsertive Mutation: The Uncontrolled Signaling in Cancer-Causing Ras

Grafton High School

Authors: Katie Best, Lisa Borden, Kelsi Chesney, Emily Dufner, Elizabeth Fahey, Matt Harter, Alex Konop, Gabi Kosloske, Kaleigh Kozak, Michaela Liesenberg, Sadie Nennig, Nick Scherzer

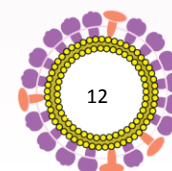


Teacher: Dan Goetz

School: Grafton High School, Grafton, WI

Mentor: Casey O'Connor, Medical College of Wisconsin

Ras is a signaling protein that acts to control certain cell functions, such as cell division, gene expression, or cell-to-cell communication. Ras is located in the cytoplasm near the cell membrane and is activated by the exchange of GDP for GTP. Ras deactivation is accomplished by hydrolysis of GTP to GDP. A mutation in Ras that prevents hydrolysis of GTP is found in a staggering number of cancerous cells and results in uncontrolled signaling of Ras-regulated pathways. Understanding the multiple structures and dynamics of RasGTP may lead to treatments for cancers with a permanently active Ras. When Ras is activated, it binds to other signaling proteins called effectors, which determine the cell functions to be carried out. The effector RalGDS is activated when bound to RasGTP, and leads to exchange of RalGDP for RalGTP. A single amino acid mutation in Ras permanently traps the protein in an active state with GTP, leading to increased association with RalGDS, resulting in an exchange of RalGDP for RalGTP. When Ral is activated, excessive signaling for cell proliferation and anti-tumor suppression is favored along with a change in cell shape. A critical step for developing possible anti-Ras cancer treatments lies within a complete understanding of the interaction between RasGTP and its effectors like RalGDS.



12

Plexin: Putting Together the Pieces

Kettle Moraine High School

Authors: Jacob Angst, Samantha Cinnick, Greg Dams, Allie Greene, Anna Henckel, Bronson Jastrow, Nick Merritt, Bradley Wilson, Aaron Zupan

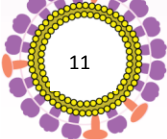
Teacher: Steve Plum

School: Kettle Moraine High School, Wales, WI

Mentor: Shama Mirza, Ph.D., Medical College of Wisconsin



The cause of Proteus Syndrome, characterized by uncontrolled cell division leading to tumor formations, is currently not understood. Recent work suggests that cells from Proteus Syndrome patients express a higher level of a protein called Plexin D1. Plexin D1 has been found in angiogenic vessels during embryogenesis and may play an important role during embryonic development. Exploring the structure and function of Plexin D1 may contribute to a further understanding of Proteus Syndrome. Mass spectrometry can be used to compare the types and amounts of proteins found in diseased and healthy cells. Using Trypsin, the proteins in a healthy control cell and a diseased cell can be cleaved at basic residue groups along the polypeptide chains, such as arginine and lysine. Performing trypsin digestion in presence of heavy water ($H_2^{18}O$) produces peptides with a +4 da mass shift. If ^{18}O labeled peptides from diseased cells are mixed with unlabeled peptides from control cells, the ratio of labeled : unlabeled protein can indicate a change in protein expression between the two samples. The molecular weight of peptides from Proteus cells can be found through the process of electrospray ionization mass spectrometry (ESI-MS). This process involves a fine spray of protein fragments that can be analyzed by a computer. The data is then recorded in order to find the molecular weight of the peptides. Comparing the observed masses to a database of known proteins allows researchers to identify the peptide fragments. Plexin D1 may be the key to unlocking the mystery of Proteus Syndrome; the higher frequency of Plexin D1 in Proteus cells versus healthy cells remains promising. By collecting and analyzing data through mass spectrometry the uncertainty surrounding this elusive protein and obscure disease could be dissolved.



The Dirt is Mightier than the Sword: Tetanus Toxin in the Human Body

Whitefish Bay High School

Authors: Cara Ahrenhoerster, Quinn Beightol, Gabe Drury, Xavier Durawa, Riley Gaserowski, Shirley Hu, Domi Lauko, Ciara Otto, Andrew Phillips, Helen Wauck

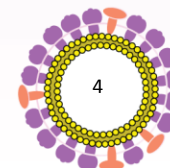
Teachers: Paula Krukar and Michael Krack

School: Whitefish Bay High School, Whitefish Bay, WI

Mentor: Joseph T. Barbieri, Ph.D., Medical College of Wisconsin



Tetanus neurotoxin (TeNT), one of the most potent toxins known to humans, causes paralytic death to thousands of humans annually. TeNT is produced by the bacterium, *Clostridium tetani*, an anaerobic bacterium usually found as spores in soil. *C. tetani* often infects humans through open wounds where the bacterium colonizes the infected tissues. There are two domains of TeNT: the A domain possesses catalytic activity, while the B domain is made up of two sub-domains: the translocation sub-domain and receptor-binding sub-domain. The SNARE protein contains VAMP-2, the target of the catalytic A domain of the TeNT. The SNARE protein regulates fusion of synaptic vesicles with the plasma membrane of the neuron, allowing the release of neurotransmitters that are responsible for relaying nerve signals such as inhibitory impulses to the body's muscle cells. TeNT binds to two gangliosides, on the presynaptic membrane of α -motor neurons. TeNT hijacks the trafficking machinery of the motor neuron and moves to the central nervous system, where it again binds to two gangliosides on the surface of neurons. Next, it enters the neuron by an endocytic mechanism to release the catalytic A domain into the host cell cytosol. The catalytic A domain cleaves the SNARE protein, which inhibits neurotransmitter fusion to the host cell membrane and the release of inhibitory neurotransmitter molecules. The loss of inhibitory impulses results in reflex irritability, autonomic hyperactivity, the classic large muscle spasticity and lockjaw associated with tetanus.



EnvZ: Triggering *Steinernema carpocapsae*'s Secret Weapon

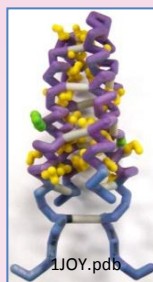
Wauwatosa West High School

Authors: Waj Ali, Jimmy Kralj, Jordan Llanas, Leah Rogers, Mariah Rogers

Teacher: Mary Anne Haasch

School: Wauwatosa West High School, Wauwatosa, WI

Mentor: Steve Forst, Ph.D., University of Wisconsin - Milwaukee



The bacterium *Xenorhabdus nematophilia* participates in an unusual and fascinating mutualistic relationship with the nematode, *Steinernema carpocapsae*, which could not complete its lifecycle without the bacteria's help. EnvZ, a kinase protein located in the cell membrane of the bacterium, is critical to both organisms' success. *Xenorhabdus* resides quietly in a specialized pouch in *Steinernema*'s intestines. To reproduce, the juvenile nematode enters an insect host via the anus or the mouth, and bores a hole through the intestine wall to get into the insect's blood. In response to the environmental signals in the blood, the nematode's pharynx begins to pump, forcing the *Xenorhabdus* out of the intestinal pouch and into the insect's blood. *Xenorhabdus* begins to act as an insect pathogen—killing the host insect, while simultaneously secreting antibiotics to eliminate its bacterial competitors. In killing the insect host, *Xenorhabdus* provides its symbiotic partner, *Steinernema*, with a carcass in which to reproduce. EnvZ helps *Xenorhabdus* sense the higher solute concentrations in the insect's blood through a currently unknown mechanism. EnvZ functions as a dimer. In response to appropriate environmental signals, a phosphate from ATP bound to the cytoplasm section of one EnvZ molecule is transferred to the HIS243 of another EnvZ. The phosphate group on HIS243 is then transferred to OmpR, a gene-regulating protein in *Xenorhabdus* that regulates genes that produce the antibiotics used to kill bacterial competitors. OmpR also regulates genes for exoenzymes that degrade insect tissues providing nutrients that help the nematode to reproduce.

Isovaleryl-CoA Dehydrogenase: Dehydrogenate This!

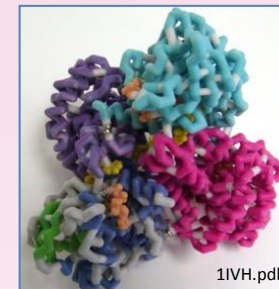
Cedarburg High School

Authors: Beth Bougie, Matt Cira, Colin Erovick, Anne Fahey, Nick Grabon, Kelsey Jeletz, Eleanore Kukla, Matt Murphy, Tim Rohman, Alyssa Sass, Michelle Sella, Laura Tiffany, Sam Wolff

Teacher: Karen Tiffany

School: Cedarburg High School, Cedarburg, WI

Mentor: Jung-Ja Kim, Ph.D., Medical College of Wisconsin



Although rare, isovaleric acidemia (IVA) is a potentially fatal metabolic disorder that affects one in every 250,000 people in the US. IVA results from lack of an enzyme, isovaleryl-CoA dehydrogenase (IVD), involved in the breakdown of leucine. Without this enzyme, leucine catabolism stops and organic acids accumulate within the body, causing symptoms of IVA, including vomiting, diarrhea, and fatigue. IVD belongs to a family of related enzymes called acyl-CoA dehydrogenases. IVD catalyzes the dehydrogenation, or removal of a pair of hydrogen atoms, of a small, branched-chain substrate, isovaleryl-CoA, during the third step of leucine catabolism. Glutamate 254 of IVD removes one hydrogen as a proton from the substrate, and flavin adenine dinucleotide, FAD, a cofactor of the enzyme, takes away the other hydrogen from the substrate. The three-dimensional structure of IVD, as determined through X-ray diffraction, illustrates how a small-branched chain substrate is able to fit into the active site of this enzyme and enables further investigation of how mutation of the IVD gene could affect IVD function, thus resulting in IVA. To further understand the structural impact on substrate specificity, a physical model of IVD has been designed and built by the Cedarburg High School SMART (Students Modeling A Research Topic) Team using 3D printing technology. Supported by a grant from NIH-NCRR-SEPA.

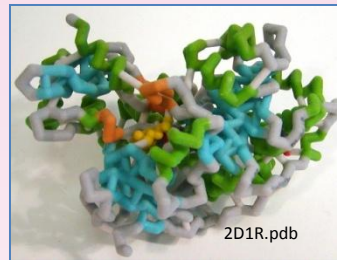
Lighting Up Science Firefly Luciferase St. Dominic High School

Authors: Elana Baltrusiatas, Allyson Bigelow, Rachel Brielmaier, Pamela Burbach, Jacob Dowler, John Fuller, Caroline Hildebrand, Teagan Jessup, Molly Jordan, Josh Kramer, Jenna Lieungh, Alex Mikhailov, Patrick O'Grady, Andrew Pelto, Quin Rowen, Rachelle Schmude, Robert Schultz, Katherine Seubert, Alex Sherman, Parker Sniatynski, Alex Venuti, Erin Verdeyen, Molly Wetzel

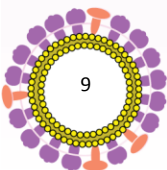
Teacher: Donna LaFlamme

School: St. Dominic Middle School,
Brookfield, WI

Mentors: Nathan Duncan and Françoise
Van den Bergh, Ph.D., Medical College of
Wisconsin



Luciferase is the generic name for an enzyme responsible for bioluminescence reactions and is commonly associated with fireflies. It is also found in many other organisms including bacteria, fungi, anemones, and dinoflagellates. Since the gene for the North American firefly (*Photinus pyralis*) luciferase was cloned in 1985, scientists have been genetically engineering the gene into living cells. The luciferase reaction is now widely used in scientific research to study protein production in cells, to analyze gene promoter activity, to study stem cell function *in vivo*, and in cancer studies, to trace the metastasis of cancer cells in living test animals. The scientific study of the luciferase enzymes themselves is also continuing. In recent research, single amino acid mutations to the active site cause the emission of different colored light in a predictable way. The uses of and improvements in bioluminescent imaging are increasing exponentially in cell biology, molecular biology, and in medical research.



9

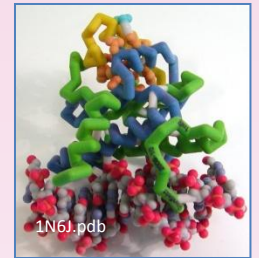
Cabin1's Control of MEF2 in the Developing Central Nervous System Greenfield High School

Authors: Robert Bhatia, Ellen Campbell, Chelsea Herr, Leticia Gonzalez, Alohani Maya, Danielle Murphy, Tiann Nelson-Luck, Kara Stuiber, and Jordan Tian

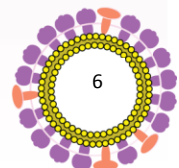
Teachers: Julie Fangmann and Martin Volk

School: Greenfield High School, Greenfield, WI

Mentors: Dena Hammond and Ava Udvadia, Ph.D.
University of Wisconsin - Milwaukee, WATER Institute



Cabin1 (calcineurin binding protein) is predicted to play an important role in maintaining the nervous system, which regulates important functions such as breathing, heart rate, thinking, and movement. Mice lacking Cabin1 die early in development, and other Cabin1 malfunctions have been linked to cancer. As the nervous system develops, neurons require guidance to determine their growth. The expression of specific proteins influences this neuronal growth. Transcription factors, proteins that bind to DNA and other proteins, regulate the production of these neuronal growth proteins. MEF2 (myocyte enhancer factor 2), a protein known to bind to Cabin1, is involved in nervous system development. MEF2 is a transcription factor necessary for neuronal growth and survival. MEF2 activates transcription when it binds to DNA, causing proteins involved in neural development to be made. MEF2 has a hydrophobic binding pocket that attracts four amino acids found on Cabin1: Ile106, Thre110, Ile116, and Leu119. When Cabin1, a transcription repressor found in the nucleus, binds to MEF2's hydrophobic binding pocket, transcription is turned off. This prevents the proteins from being produced and causes neurons to stop growing or to potentially die. Since cell death and survival are both necessary for nervous system development, Cabin1 is hypothesized to play a major role in this process. Current research is examining what happens to neuronal growth and survival when there is a shortage or an excess of Cabin1, eventually leading to a better understanding of the precise way Cabin1 functions.



6

Inhibiting Dihydrofolate Reductase as a Treatment for Tuberculosis

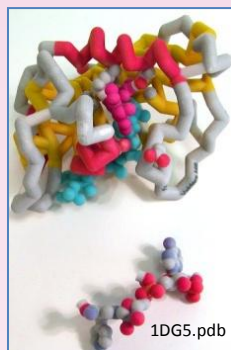
Valders High School

Authors: Corrine Brandl, Kaylin Kleinhans, Emily Weyker, Nicole Maala, Lauren Brandl, Grace Ebert, Paige Neumeyer, Ryan Jirschele, Gavin Schneider, Luke Schuh

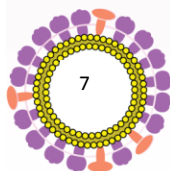
Teacher: Joe Kinscher

School: Valders High School, Valders, WI

Mentors: Andrew Olson and Dan Sem, Ph.D., Marquette University



One-third of the world's population is infected by *Mycobacterium tuberculosis* (*M.tb*). Two million people die each year from tuberculosis (TB), the disease caused by this bacterium. TB primarily affects the lungs and is easily transmitted. One way to kill *M. tb* might be to inhibit the enzyme dihydrofolate reductase (DHFR). DHFR catalyzes the production of tetrahydrofolate by transferring a hydrogen ion (H^+) from NADPH to dihydrofolate, thereby releasing tetrahydrofolate and $NADP^+$. Tetrahydrofolate is essential to the bacteria's survival, and is a cofactor that is needed for the synthesis of the DNA base thymine. Isoniazid is one antibiotic already used to treat TB by targeting several TB proteins that are necessary for building *M. tb* cell walls and inhibiting DHFR. Unfortunately, strains of *M. tb* are evolving resistance to isoniazid, so next generation antibiotics are needed. A variation of isoniazid could be designed to avoid resistance, and to inhibit DHFR, thereby targeting bacterial DNA synthesis. The Valders SMART Team (Students Modeling A Research Topic), using 3D printing technology, created a physical model of DHFR and a possible inhibitor of tetrahydrofolate production. *Supported by a grant from NIH-NCRR-SEPA.*



7

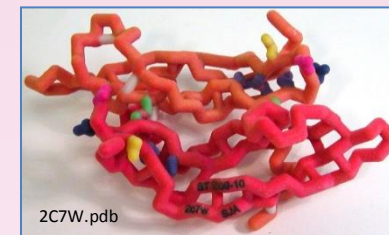
Go with the Flow The Importance of VEGF-B St. Joan Antida High School

Authors: Beanca Buie, Maritza Campos, Brianna Castanon, Kateri Duncklee, Jagnoor Grewel, Monica Harris, Neli Jasso, Meghan Krause, Malayia Roper, Shinny Vang, Sukaina Yacoob

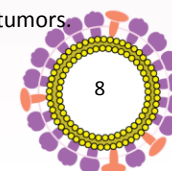
Teachers: Linda Krause and Cynthia McLinn

School: St. Joan Antida High School, Milwaukee, WI

Mentor: Mary Holtz, Ph.D., Medical College of Wisconsin



Blood vessels are such a vital part of our body that without them we would not progress from the embryo stage in the womb and our wounds would never heal. In addition, they are extremely helpful for the transportation of nutrients and oxygen and the removal of waste from cells in our body. In order for blood vessels to function correctly, Vascular Endothelial Growth Factor Type-B [VEGF-B] needs to be present. Unlike VEGF-A, which controls the development of blood vessels, VEGF-B controls the functions and prevents apoptosis. Though this protein does not make the blood vessels, VEGF-B stops apoptosis, or cell death, of endothelial cells, making it one of the main factors to the survival and development of blood vessels. VEGFs are a family of secreted glycoproteins, critical for development and function of blood vessels. The structure of VEGF-B consists of two cysteine knots, meaning two monomers, each of which contains eight cysteine residues and four disulfide bonds. The monomers are attached to form the dimer known as VEGF-B. VEGF-B promotes blood vessel survival by blocking apoptosis, in three kinds of cells that make up blood vessels: endothelial cells, smooth muscle cells, and pericytes. VEGF-B is sent between vascular endothelial cells (VEC) in the vessel connecting to the target cell in a locking fashion, assessing whether cells need to migrate, proliferate, specialize, or survive. Further understanding of the role that VEGF-B plays in vessel formation could be potentially used therapeutically against tumor formation. Tumors require angiogenesis, the production of new blood vessels, to enable blood transport to the tumor cells for continued growth. As a result, VEGF-B's abilities are taken advantage of by invading malignant tumors. Knowing more about VEGF-B is potentially life-saving and can be used to help maintain healthy blood vessels without encouraging vessel growth in tumors.



8