Understanding ε-mediated inhibition of bacterial F-type ATP synthase to develop drugs against *Mycobacterium tuberculosis* in the Duncan Lab

*Mycobacterium tuberculosis* (MTB) is an infectious pathogen that causes Pulmonary Tuberculosis and kills over one million people every year. It is also a major cause of death in HIV patients. Evolution of extreme drug-resistant strains in MTB poses a serious problem towards its treatment. As a result, there is an ongoing need to develop novel drugs that can effectively fight the resistant strains. The F-type ATP synthase is responsible for energy production in living organisms and was recently identified as a drug target for treatment of MTB. It is a unique rotary motor enzyme that can synthesize as well as hydrolyze ATP depending on its direction of rotation.

The ATP synthase is often called F₀F₁. It has a membrane embedded F₀ complex that transports protons by rotation of its c subunits and an external catalytic F₁ complex that is composed of 5 subunits with the stoichiometry of α₃β₃γδε. The ε subunit is involved in inhibition of many bacterial ATP synthases wherein its C-terminal domain inhibits both ATP synthesis and hydrolysis whereas the N-terminal domain is necessary for functional assembly of the enzyme. Work in the Duncan lab is focused on understanding of ε-mediated inhibition of bacterial ATP synthase. Recently, the Duncan lab determined the first high resolution crystal structure of F₁ in *Escherichia coli* (EF₁) in an autoinhibited conformation. The structure showed ε’s CTD in a highly extended conformation (ε_CTD) that engaged in interaction with rotor and stator subunits inside the central cavity of EF₁. These interactions of ε with other subunits are responsible for inhibition of the enzyme.
PUBLICATIONS:


http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0059094

Cherry Mae Ignacio wrote an opinion article for The Scientist, a popular science magazine, entitled "Open Access for the 3rd World," where she describes her own experience with the lack of journal access in third world countries and calls on scientists around the world to advocate for open-access policies.  

Brian Haarer, Lei Mi-Mi, Jessica Cho, Matthew Cortese, Susan Viggiano, Daniel Burke, and David Amberg  
http://www.g3journal.org/content/3/3/553.long

AWARDS AND RECOGNITION RECEIVED:

Steven Hanes gave a talk at the Science and Math Colloquium, Houghton College, Houghton, NY. "Use of Model Organisms in Biomedical Research" on March 5, 2013.

Huimei (Janet) Zheng’s manuscript entitled “Protein Fragment Exchange (FREX): a Novel Approach for Converting a Ligand-Binding Protein into a Biosensing Conformational Switch” has been chosen to be the College of Graduate Studies’ winner of the 2013 John Bernard Henry, M.D., Endowed Scholarship Award.

Stephan Wilkens was selected by the College of Graduate Studies’ Graduate Student Association to receive the Outstanding Teacher Award for 2013.

Makandiwa Shoniwa, Patty’s Graduate Student, was the Honorable Mention for her poem “Homecoming” in the 2013 Bruce Dearing Writing competition.

David Jarvis, Sandy’s husband, won the BMB 2013 NCAA basketball tournament, with David Amberg coming in second. Graduate Assistant, Cherry Mae Ignacio, won the coveted last place award this year that happened to be a pink rubber worm.

Notable mention—Penny was actually beating Stewart for a good portion of the tournament, but in the end Stewart pulled off a third place position (just out of the money) for a second year in a row. Poor Stewart—“Always a bridesmaid, but never a bride”.

http://www.g3journal.org/content/3/3/553.long
PERSONAL NEWS:

Sandy Jarvis is proud to announce that her son, David, has enlisted into the United States Marines and will be heading to boot camp in Parris Island, South Carolina, on June 3rd. After boot camp, he will head to North Carolina to begin his training in the School of Infantry. He hopes to eventually become a member of the Marine Special Forces.

Rich and Donna Cross report that their daughter Emily married Alan Marin in Rome, Italy on March 13, 2013. The ceremony took place in an ancient structure on the Appian Way that now houses a popular Roman restaurant. Incidentally, the wedding was on the same day that the new Pope was elected, so there were two major events in Rome on March 13th. You may well ask “why was the wedding held in Italy”. The answer is not that the groom was from Rome. The story is that a year earlier while Rich, Donna, Emily, and Alan were vacationing in Sorrento, Alan proposed. The couple decided it would be very romantic to return to Italy for the wedding. The small group of relatives and family friends that made the long trip was rewarded by a great week. Side events included attending a day-long class at the Cooking School of Rome where they ate what they cooked, and tours of The Roman Forum and other sites guided by a very entertaining historian. The accompanying picture shows Emily and Alan on their honeymoon in Florence. The happy couple lives in San Diego.