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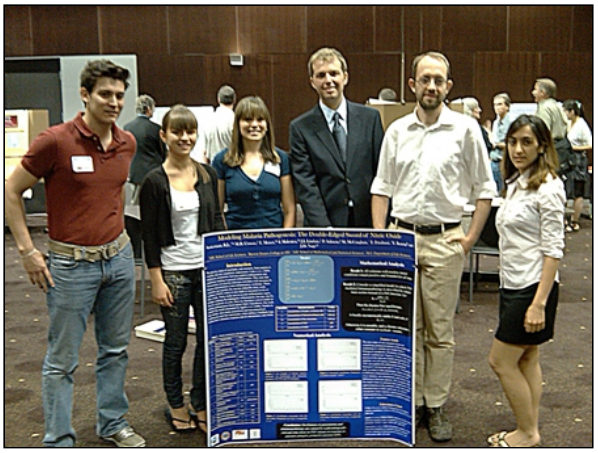
SCC Students Present Research Project at ASU Symposium

Scottsdale Community College / ASU Student Biology Team Presents Research Project at ASU's Undergraduate Research Symposium April 27

~ Students present: "Modeling malaria pathogenesis: the double-edged sword of nitric oxide" ~

Scottsdale, AZ (May 12, 2009) – A team of undergraduate research students from SCC and ASU presented their research project, *Modeling Malaria Pathogenesis*, at ASU's College of Liberal Arts and Sciences Undergraduate Research Symposium on April 27. The presentation continues a collaboration between ASU's School of Mathematical and Statistical Sciences, the ASU School of Life Sciences, and the SCC Department of Life Sciences.



Team members included SCC students Michael Crusoe and Josh "Ian" Lindsay, former SCC/current ASU students R.J. Austerman and Tanaz Farahani, and ASU students Pablo Salmon, Ivana Malenica, Tasha Moyer and Megan McCaughan.

"The team did an excellent job and received a lot of positive feedback from faculty, graduate researchers and other undergraduate research students," said Dr. John Nagy, SCC and ASU biology faculty member and advisor of the project.

According to Nagy, the project team set out to develop a mathematical model that expresses a hypothesis developed by Ian Clark, professor of biochemistry and molecular biology at The Australian National University, and his colleagues, which suggests that the major symptoms and even death from malaria are caused as much by the body's response to the infection as from the infection itself. It is thought that the body's immune response alone may be the main cause of death.

Nagy describes that the body naturally responds to infection by producing certain chemicals that cause inflammation. In malaria, this inflammation is a double-edged sword. On one hand, it helps kill the invading parasites. On the other hand, the inflammation directly and indirectly causes many of malaria's symptoms, including fever, chills, headache, sweats, fatigue, nausea and vomiting.

To calm the inflammation, the body also produces a gas called nitric oxide. Nitric oxide, however, is

"In a malaria patient this can be deadly because anemia--an inability of the blood to carry oxygen--is a frequent complication of the disease," said Nagy. "To repair the damage the body needs more oxygen precisely when oxygen is less available."

The research project gave the students the chance to evaluate the balance between the therapeutic and pathological effects of inflammation and nitric oxide in the bloodstream, understanding that too little allows the parasite to survive, while too much can damage and even kill the patient.

Yet not all malaria is the same, explains Nagy. The disease is caused by a variety of similar parasites, all called *Plasmodium*. Most cases of malaria are typically caused by a parasite called *Plasmodium vivax*, which is also referred to as "benign" because this parasite rarely causes death. Another strain, called *Plasmodium falciparum*, is the "malignant" form which is associated with most malaria deaths.

The research team explored the idea that Clark's hypothesis may help explain the difference in death rates between vivax and falciparum malaria. "The problem is very complex, and there are many known differences between the two parasites that complicate the picture," said Nagy. "Because of this complexity the students chose to work with a mathematical model because such models are ideally suited to these kinds of intricate issues."

After much investigation and testing, the students landed on a model which has already yielded a major prediction – suggesting that a time delay between when the body senses the parasite and when it reacts by secreting a chemical called TNF, causing other cells in the body to produce nitric oxide, can generate instability in the parasite/immune system interaction.

This time delay, the team discovered, may be the key to understanding the patterns of symptoms seen in malaria. In particular, symptoms of malaria sometimes oscillate--that is, they come and go every 2 to 3 days, depending on the strain involved. The team showed that their model reproduces such oscillations, and that the oscillations are caused by the time delay.

"In essence, once the parasite population begins to expand, the body tries to kill it off by secreting TNF and nitric oxide," said Nagy. "The parasite density in the blood will fluctuate in a precise pattern, and so, therefore, will the immune response and the nitric oxide in the blood."

Although patients typically suffer continuous fever and other symptoms throughout the course of the disease, Nagy describes that malarial episodes can occasionally resemble the fluctuations observed in the model. "Classical malaria, in fact, has this property, with fevers and other symptoms coming in waves every two to three days, depending on the type of parasite causing the disease."

According to Nagy, the models have shown that, under certain conditions, the body can clear the parasite that causes malaria, even the most deadly strain. While the body is clearing itself of the disease, the patient would experience symptoms of the disease until it eventually disappears. In other cases, a chronic infection is established, which can last indefinitely until conditions in the body change. Nagy explains that in the case of chronic infection, the model predicts conditions under which the infection will oscillate.

"We know that the body responds differently to the two parasites, vivax and falciparum," said Nagy. "In particular, we have reason to suspect that the pattern of nitric oxide production differs depending on the parasite involved. We hope our modeling shows that these differences either cannot explain the different clinical behaviors of the two parasites, or that it can explain it. If the latter, then the

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Students pictured are, from left to right: Pablo Salmon, Ivana Malenica and Tasha Moyer (all ASU students), R.J. Austerman (lead author, current ASU and former SCC student), Michael Crusoe (current SCC student) and Tanaz Farahani (current ASU, former SCC). Not pictured is current SCC student Ian Lindsay and ASU student Megan McCaughan.

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