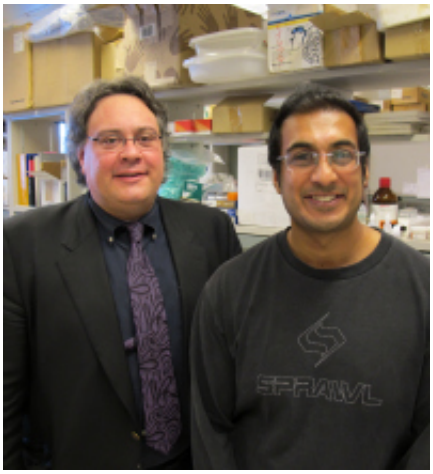
Researchers move closer to a cure for a deadly cardiovascular disease

June 24 2011, By Quinn Phillips



Evangelos Michelakis and Gopinath Sutendra

(Medical Xpress) -- A multidisciplinary research team in the Faculty of Medicine & Dentistry at the University of Alberta has taken a big step towards understanding the cause and potential cure for a deadly cardiovascular disease.

Evangelos Michelakis, a cardiologist, and his graduate student Gopinath Sutendra in the Department of Medicine, along with fellow researchers in the faculty and collaborators from Laval and Yale universities, found that a protein called Nogo is critical in the development of pulmonary arterial hypertension.

This condition causes high blood pressure in the arteries of the lungs and leads to heart failure and death. Available therapies may alleviate some symptoms but they cannot reverse the disease and prolong survival of the patients.

“Mice with pulmonary arterial hypertension had very high levels of Nogo in their lung arteries, but animal models that were genetically lacking Nogo were completely resistant to developing the disease,” said Michelakis. “New therapies are planned in other diseases where Nogo is important, like spinal-cord injury. Such therapies could be applied to pulmonary arterial hypertension.”

In addition to work done in laboratory models, the research team found that the level of Nogo was also high in arteries of patients with pulmonary arterial hypertension. Michelakis took samples from 41 patients at his pulmonary hypertension clinic and compared it to 26 patients who didn’t have the disease.

“We showed that Nogo levels were higher in pulmonary arterial hypertension,” said Michelakis. “We also found the sicker the patient was, the higher the levels. This might be an important biomarker for the disease. A lab test could show us how severe the disease is or whether the disease is going to get worse.”

This is a “very satisfying” step forward, according to Sutendra, because it creates a platform on which several experimental therapies might be developed because many scientists are studying Nogo.

“We believe that by bringing along these [spinal cord and neurology] colleagues into the field of pulmonary hypertension, we’ll contribute to accelerating knowledge and discovery of new therapies in this disease,” said Michelakis.

For Sutendra personally, this research is significant as he works towards his PhD.

“This is personally very exciting, because under Dr. Michelakis’s supervision I was able to have my name put on some really good papers that will really change the way doctors in this field will look at treating their patients,” said Sutendra.

Currently the Michelakis lab is testing molecules that can inhibit Nogo. They are having preliminary success in their laboratory models.

“As soon as we complete these studies and we publish them then we can try them in humans,” said Michelakis. “A lot of these things we can try have already been used in humans for other conditions.”

Co-authors of this paper from the Faculty of Medicine & Dentistry include graduate students Peter Dromparis and Al Haromy; Prof. Jean Vance and Assistant Prof. Michael McMurtry from the Department of Medicine; and Marek Michalak, the faculty’s vice-dean of research and a professor in the Department of Biochemistry.

This discovery builds on work published last year by Michelakis and Sutendra, in the journal *Science Translational Medicine*, which showed their metabolism is altered in the lung arteries of mice and patients with pulmonary hypertension. The researchers’ latest findings were published in the June 22 edition of *Science Translational Medicine* and show for the first time that Nogo causes suppression of mitochondrial function in cells, and could explain why metabolism is altered in lung arteries. These findings could be important to many other conditions where Nogo is involved, including cancer or diseases of the nervous system.

Michelakis has attracted international attention for other work – he discovered that dichloroacetate, or DCA, a relatively non-toxic,

inexpensive pharmaceutical, could have the potential to treat some types of cancer. This discovery has challenged a dogma that had dominated the field for decades. Michelakis was able to alter the metabolism of tumours (change the way tumours generate energy) by targeting the mitochondria, the energy-producing units in cells. In doing so, he and his team were able to shrink some types of cancer tumours.

Provided by University of Alberta