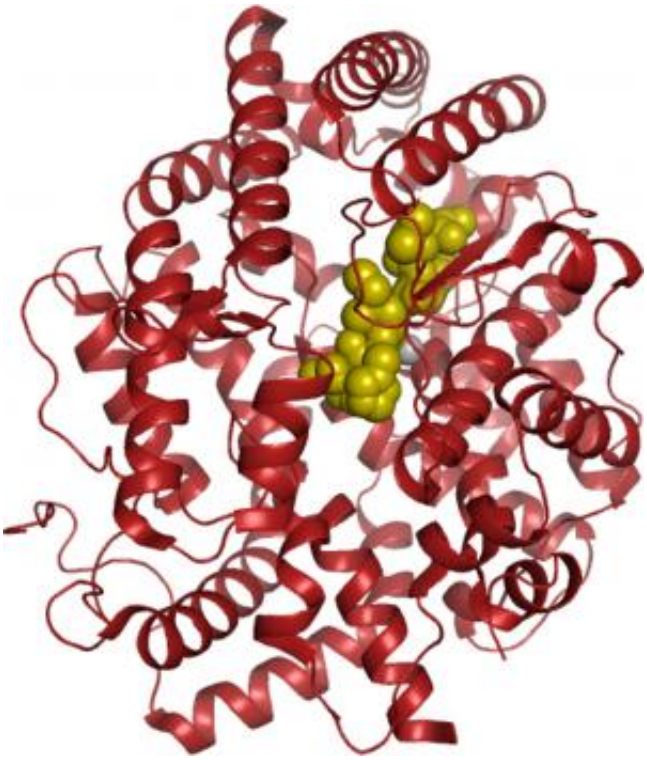
Snake venom could be used to design new heart disease drugs

October 10 2012



(Phys.org)—Research led by the University of Bath has identified two possible new routes for developing novel drugs for high blood pressure and heart disease.

The research, published in the prestigious *Nature* journal *Scientific*

Reports, was led by Professor K. Ravi Acharya in collaboration with the Universities of Leeds and Cape Town, South Africa.

The scientists created images of the 3D molecular structures of two peptides, including one from snake venom, that inhibit angiotensin-I converting enzyme (ACE), a key protein that regulates blood pressure.

ACE inhibitors, such as the drug Captopril, are taken by millions of people in the UK to treat high blood pressure (hypertension) and heart disease. However the drugs cause side effects such as a persistent cough and angioedema (swelling of the face and throat).

In this Medical Research Council funded study, the team produced images of a snake venom peptide BPPb binding to ACE. Although this peptide has been identified previously as a possible template for drug design, it is the first time scientists have been able to see at the molecular level how the peptide binds to ACE and blocks its action.

Professor Ravi Acharya, from the Department of Biology & Biochemistry at Bath, said: "We found that the BPPb peptide binds to a major portion of the active site of the ACE molecule pushing out a zinc atom which is essential for its correct functioning.

"This is the first time we've observed zinc-independent inhibition of ACE, and so these findings highlight a very exciting opportunity to design new antihypertensive drugs based on this peptide."

In addition, the researchers looked at the structure of angiotensin-II (Ang-II) bound to ACE. Ang-II is a hormone produced by ACE that also inhibits it, creating a feedback loop that stops levels of Ang-II getting too high.

Professor Acharya commented: "We already knew that Ang-II blocks

ACE, but not how it does this at the molecular level. This study has shown for the first time how ACE self-regulates by producing a molecule that obstructs its active site when the concentration reaches a certain level."

The next step is to use this structural knowledge as a basis for accelerating the on-going work carried out by Professor Acharya and his collaborators on the development of next generation ACE inhibitors that have improved efficacy and fewer side effects.

The scientists will first use computers to predict the action of different drug designs, then take the best drug candidates and test them in vitro, followed by tests in animal models for hypertension.

More information: www.nature.com/srep/2012/12100 … /full/srep00717.html

Provided by University of Bath