



## Blood Cell Signals and Heart Attacks

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Miscommunication between two human blood cells can result in a series of molecular events ultimately leading to heart attack, stroke, atherosclerosis, and other inflammatory diseases, a new study has found. The two blood cells are actually responsible for fighting blood loss, infection and inflammation. However they can also cause overproduction of Cox-2, an enzyme involved in all of the above diseases.

This path breaking study by researchers from the University of Utah and the University of South Carolina has the potential to provide scientists the means to develop medications to prevent or reduce the severity of diseases like atherosclerosis and heart attack. According to Dr. Guy A. Zimmerman, Professor of Internal Medicine at the University of Utah School of Medicine and senior author of the study, Discovery of the signaling mechanism will be invaluable in sorting out the roles Cox-2 plays in those diseases.

This discovery has immediate clinical relevance, said Dr. Zimmerman, Director of the medical school's Program in Human Molecular Biology and Genetics. This opens the potential of developing medications for both the prevention of long-term atherosclerosis (clogged arteries) and the acute events of heart attack.

A biochemical pathway between human blood platelets (cells required for blood clotting) and monocytes (white blood cells responsible for the body's fight against inflammation and infection) was identified by the researchers during their research. They found production of Cox-2 was triggered by a double signal to the monocytes from the blood platelets.

While Cox-2 is necessary to regulate inflammation, its over-abundance can result in cardiovascular diseases and prove fatal. When the signals from blood platelets and monocytes get mixed up, Cox-2 production runs into overtime. In other words, the

biological systems involved in blood clotting and inflammation can also cause a number of other diseases.

The researchers discovered when blood platelets send the first signal to the monocytes, the latter turn on the gene providing instructions necessary to produce Cox-2. The instructions are delivered via small molecules called messenger RNA. A process called transcription is utilized by the monocytes to decipher the instructions from the Cox-2 gene which gives rise to messenger RNA that specifically codes for Cox-2.

The next step of the process involves further decoding of the genetic information and is called translation. In this, a second message passes between the blood platelets and the monocytes after the messenger RNA is transcribed. This message regulates the stability of the Cox-2 messenger RNA and also results in production of the Cox-2 protein, its quantity and exact moment of production.

Describing the signaling between blood platelets and monocytes as a pair of molecular switches that turns Cox-2 production on and off, Dr. Zimmerman said, Its a mechanism for precise control of Cox-2 production. But if one of the switches is turned on too high or low, it can lead to inappropriate production of Cox-2 and result in disease.

Non-steroidal anti-inflammatory agents or NSAIDs are widely used medications for treatment and relief from arthritis and other inflammatory diseases because they inhibit production of Cox-2 to reduce inflammation. However some such inhibitor drugs like Vioxx have also been found to increase the chances of heart attack.

Armed with this new knowledge of the signaling mechanism between blood platelets and monocytes, scientists can get down to developing new drugs to modify Cox-2 production. Knowing these steps gives you an initial blueprint about how to modify Cox-2, Dr. Zimmerman said. Understanding this mech-

anism may enable researchers to develop drugs that help people during a heart attack, or prevent heart attack, stroke or other inflammatory diseases.