

# Scientists discover how gold eases pain of arthritis

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Scientists at Duke University Medical Center may have solved the mystery surrounding the healing properties of gold – a discovery they say may renew interest in gold salts as a treatment for rheumatoid arthritis and other inflammatory diseases.

Physicians first used injections of gold salts in the early 1900s to ease the pain and swelling associated with arthritis. But treatment came at a high cost: The shots took months to take effect and side effects included rashes, mouth sores, kidney damage and occasionally, problems with the bone marrow's ability to make new blood cells. Recently, new treatments like methotrexate and biologically engineered drugs have replaced gold as a preferred treatment, and gold salts, while remaining effective, are usually administered as a last resort.

But Dr. David Pisetsky, chief of the division of rheumatology and immunology in the department of medicine at Duke, says “we shouldn't dismiss gold salts so quickly. We scientists have really never understood why gold works. Now that we have a better handle on its action, we may be able to use that mechanism to create new and better gold-like drugs to treat arthritis.”

Pisetsky had long been interested in a particular molecule, HMBG1, which provokes inflammation, the key process underlying the development of rheumatoid arthritis. HMBG1 is a dual-function molecule, which means that it behaves one way when it's inside the nucleus of a cell, and quite another way when it's released from the cell.

Pisetsky says that inside the nucleus, HMGB1 is a key player in transcription, the process that converts genetic information in DNA to its RNA equivalent. But when HMGB1 is released from the cell – either through normal processes or cell death – it becomes a stimulus to the immune system and enhances inflammation.

“Interestingly, HMGB1 is not produced evenly throughout the body,” says Pisetsky.

“There is an unusually high amount of it in the synovial tissue and fluid around the joints – where arthritis occurs.”

Pisetsky, working with colleagues at the University of Pittsburgh and the Karolinska Institute in Sweden, stimulated mouse and human immune system cells to secrete HMGB1, then treated them with gold salts. They found that the gold blocked the release of HMGB1 from the nucleus. That, in turn, should lessen the amount available to provoke the body’s immune system, weakening the inflammatory response.

“Basically, keeping HMGB1 corralled inside the nucleus is a good thing, when it comes to arthritis,” says Pisetsky.

Pisetsky says gold inhibits the release of HMGB1 by interfering with the activity of two helper molecules that ease HMGB1’s release from the cell, interferon beta and nitric oxide.

The study will appear in the January, 2008 issue of the *Journal of Leukocyte Biology*, but a preprint is already online at the journal’s website at: <http://tinyurl.com/3cd957>.

“Now that we have identified at least one of the ways gold can help arthritis sufferers, perhaps we can use that knowledge to build new and safer-acting, gold-based treatments,” says Pisetsky, a senior author of the

study.

Pisetsky is encouraged by the results but says additional studies need to be done to find out if the same mechanism is active in animals and people and not just in laboratory studies.

Source: Duke University

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