Master switch discovery could provide road map for treatment of arthritis and other inflammatory diseases

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(Medical Xpress)—Scientists trying to create drugs to treat chronic inflammation in diseases like arthritis now have a new culprit known MMP2. New University of British Columbia research shows that this enzyme works as a master switch to activate inflammatory diseases.

The research, published recently in *Science Signaling*, examined the role a group of enzymes known as MMP proteases play in inflammation. Arthritis is caused by excessive inflammation in an overactive immune system trying to repair damaged tissues. In patients with arthritis, the immune system mistakenly attacks healthy tissues, most commonly the joints. This attack leads to inflammation, pain and joint damage.

Chris Overall, a professor in the Faculty of Dentistry and Canada Research Chair in Metalloproteinase Proteomics & Systems Biology, and his team found that the protease MMP2 can remove a block allowing inflammation to become activated. This pathway is often overactive in patients with arthritis and other inflammatory diseases.

"Imagine a cart parked on a hill with a rock behind its wheel to prevent it from rolling down the hill," said Overall. "We found that MMP2 can remove that rock, causing the immune response to activate."

According to Overall, who regularly employs arthritis as a disease model in his research, this is the first study to explain this pathway system.

"We were amazed by these results. This shows us a new way to design drugs to treat many chronic inflammatory diseases like arthritis and even periodontal disease," said Overall.

Findings also provide the basis for a new diagnosis screen such as a blood test to detect the disease before the severe damage to joints occurs.

Arthritis: Impact and treatment

- **First of its kind**: Overall's study of MMP2 role in skin inflammation is the first and only of its kind. The approach is now being used around the world and can be applied to study the components in many diseases including cancer. This means more effective treatments and better quality of life for patients.
- **Arthritis, the disease**: Arthritis is caused by an overactive immune system attacking the body's own tissues, most commonly the joints. This attack leads to inflammation, pain and joint damage. Nature's purpose of inflammation is to find and disarm the intruders, clean up damage and speed healing. In inflammation special components called proteases play key roles.
- **Arthritis on the rise**: Arthritis is a serious and debilitating disease that affects joints, tendons, bones and ligaments. According to the 2000 Canadian Community Health Survey arthritis affects almost four million Canadians and this number is estimated to reach six million in 2026. Arthritis is one of the major causes of pain and physical disability in Canada with an economic burden of around $4.4 billion. This is over 10 per cent of the total economic burden of all illnesses. Currently there is no cure for arthritis.
- **No magic arthritis pill, yet**: Non-steroid anti-inflammatory drugs are commonly used to manage the symptoms of arthritis.

However, these drugs are not specific to arthritis and can also cause serious side effects such as gastrointestinal bleeding. These and other complications further increase the costs to the Canadian health care system.

Provided by University of British Columbia