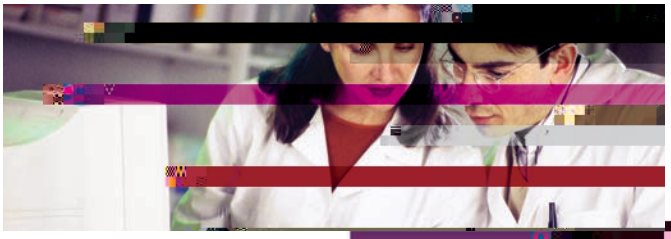
UNDERSTANDING IMMUNE CELL AND INFLAMMATION: TARGETED TREATMENT OF RHEUMATOID ARTHRITIS AND OTHER CONDITIONS

Most of the 1.5 million adults in the United States who have rheumatoid arthritis (RA) take medications to control their pain and slow the damage that is occurring in their joints. RA causes inflammation and pain in the hands, wrists, knees, or other joints and, over time, leads to permanent damage. Like other autoimmune diseases, RA occurs when the immune system attacks a person's body instead of defending it against invading organisms.

Some RA drugs protect joints by blocking interactions between inflammatory molecules and the healthy tissues that they are erroneously targeting. Others destroy the cells that produce the damaging molecules. While these disease-modifying antirheumatic drugs (DMARDs) help many people, some patients do not respond or cannot tolerate the side effects. In 2012, FDA approved another option for people with moderate to severe RA who are not helped by other treatments. This new drug, tofacitinib, fights inflammation from inside immune cells. Because it works differently than many RA drugs, it can be taken as a pill, rather than an injection.

NIH-funded investigators played a large role in discovering and characterizing the molecular interactions that tofacitinib acts on and in predicting the usefulness of this and related pathways as drug targets. Some of that research is described here to illustrate how knowledge about cell behavior at the molecular level can be used to improve health.

IMMUNE CELLS AND INFLAMMATION: THEN AND NOW



THEN

Since the late 1990s, drugs that prevent inflammatory molecules called cytokines from interacting with healthy tissue have helped hundreds of thousands of people who have autoimmune diseases such as rheumatoid arthritis, but these drugs did not work for everyone.

Many of the medications need to be injected instead of swallowed.

NOW

IMPACT OF STUDYING THE JAK-STAT SIGNALING PATHWAY

KNOWLEDGE

Discovery and characterization of the JAK-STAT pathway was one of the earliest demonstrations of how molecules outside a cell control gene expression inside a cell.

Researchers know that signals transmitted through the four JAK family members and seven STAT family members affect tens of thousands of sites in the human genome, regulating the production of thousands of proteins and other molecules.[10]

HEALTH

The finding that alterations in the JAK-STAT pathway are associated with diseases of the immune system and human cancers has led to the development of a new class of drugs, called Jakinibs.

Jakinibs that act on JAK1 or JAK2 are FDA-approved for dogs with allergic dermatitis or for people with certain blood cancers.

People who do not respond to at least one older RA treatment have a new option in the form of tofacitinib, which acts on JAK3. This is the first new oral drug appr