Treatment for Inflammatory Joint Flares

A novel approach to treat inflammatory joint flare caused by rheumatoid arthritis, joint trauma, and osteoarthritis.

Problem Solved by This Technology
The incidence of Rheumatoid Arthritis (RA), a chronic inflammatory disorder of the joints with episodes of flares, has steadily been increasing around the world. Several clinical observations implicate the lymphatic system in RA pathogenesis. In particular, loss of the lymphatic pulse and popliteal lymph nodes (PLN) causes the typical aggressive episodes of arthritic flares often experienced by RA patients. Pharmaceutical strategies to tackle RA involve developing therapies that treat inflammatory joint flares, promote lymphatic function, and prevent tissue damage in joints. Routine RA treatments to improve lymphatic functions include anti-TNF therapies (DMARD drugs) and about 30% of patients are reported to be refractory to these drugs. Therefore, there is an urgent need for alternate therapeutic strategies.

Soluble Guanylyl Cyclase (sGC), a key regulator in Nitric Oxide signaling pathways, plays a major role in smooth muscle proliferation and lymphatic vessel contractility. sGC is increasingly being recognized as a major therapeutic target in treating cardiopulmonary disease, neurological disorders, and several sGC agonists are currently in clinical development. Until now, sGC agonists have not been tested for the treatment of RA.

Applications of This Technology
The novel approach developed by Schwarz and Colleagues at the University of Rochester entails the use the sGC inhibitor to effectively treat joint inflammation due to RA, joint trauma, and osteoarthritis. Using RA mice models (TNF-Tg) and advanced imaging techniques, the inventors showed that sGC was present in the lymphatic vessels of TNF-Tg mice. Additionally, they demonstrated that sGC inhibitor NS-2028 can resume lymphatic pulse, reduces joint flares, and overall improves lymphatic functions in TNF-Tg mice. More importantly, the inventors depicted that NS-2028 is safe and does not induce any adverse systemic effects in TNF-Tg mice. Currently, Schwarz and Colleagues are working to improve the novel sGC inhibitor therapeutic system by incorporating additional anti-inflammatory agents.