

Application of Sequential Palladium Catalysis for the Discovery of Janus Kinase Inhibitors

Novel Janus kinase inhibitors exhibit high selectivity against JAK1, offering reduced side effects for treating autoimmune diseases like rheumatoid arthritis and psoriasis.

An estimated 24 million people in the United States are affected by autoimmune diseases, a group of diseases in which the patient's immune system attacks parts of their own body. One cellular pathway implicated in the pathology of autoimmune disease involves regulation of gene expression mediated by a family of four related molecules known as Janus kinases, JAK1, JAK2, JAK3 and TYK2. Because of their importance in disease, this family of kinases is the target of a number of drug molecules, two of which, tofacitinib and ruxolitinib, have been approved by the FDA. Unfortunately, the approved drugs still suffer from a number of debilitating side effects. One source of these side effects is the lack of these drugs' selectivity among the four Janus kinases. A drug that inhibits only one of the four Janus kinases promises reduced side effects.

Researchers at Purdue University have developed a series of molecules, based on a new JAK inhibitor scaffold, that display selective inhibition for different members of the Janus kinase family. One particular compound, designed for high potency and stability, exhibits very good activity and selectivity against JAK1, with 3.3 nM activity and 10 fold and 30 fold selectivity versus JAK2 and JAK3, respectively. These new inhibitors promise to give relief to sufferers of psoriasis, myelofibrosis, rheumatoid arthritis, and other autoimmune diseases with a reduction in side effects compared to current therapies.

Related Publication:

Mohamed S. A. Elsayed et al., Application of Sequential Palladium Catalysis for the Discovery of Janus Kinase Inhibitors in the Benzo[c]pyrrolo[2,3-h][1,6]naphthyridin-5-one (BPN) Series, J. Med. Chem. 2018

Technology ID

2018-CUSH-68109

Category

Pharmaceuticals/Small Molecule
Therapeutics
Pharmaceuticals/Pharmaceutical
Manufacturing & Methods

Authors

Mark Cushman
Mohamed Elsayed

Further information

Joe Kasper
JKKasper@prf.org

Nathan Smith
nesmith@prf.org

View online



Advantages:

- Reduce side effects
- Allow for more options in treatments

Potential Applications:

- Treatment of autoimmune diseases

TRL: 3

Intellectual Property:

Provisional-Patent, 2017-10-31, United States | Utility Patent, 2018-10-31, United States

Keywords: Janus kinase inhibitor, JAK inhibitor, selective JAK1 inhibitor, autoimmune disease treatment, psoriasis, myelofibrosis, rheumatoid arthritis, new drug scaffold, reduced side effects, gene expression regulation