LEO Pharma Open Innovation Chemistry course module

Together with DTU Chemistry and SkyLab

Using Pharma Open Innovation as a tool for Medicinal Chemistry education

Background

LEO Pharma Open Innovation will provide an open innovation platform for students at DTU Medicinal Chemistry in 2018. As a scheduled part of the module in the course 26426 - *Introduction to Medicinal Chemistry*, pharmaceutical drug research will be explained from an open source and open science perspective providing students with real and relevant industry insights as well as concrete tool to engage hands on. Teaming up with DTU's makerspace Skylab students will be given the opportunity to design and synthesis new molecules that will be tested in disease-relevant biological assays provided by LEO Pharma Open Innovation.

What LEO Pharma Open Innovation offers

The Open Innovation platform is disclosing a target class, known molecules and scientific know-how of the disease biology, as well as offering free and unconditional access to testing new molecules in the pharmaceutical research platform.

Set-up and idea

The main intention with the open innovation module is to provide a more concrete, hands on and relevant relationship between industrial pharmaceutical R&D and Academic education. Furthermore there is a growing need to solve research questions differently than what we've done in the past, hence we are turning to open innovation as a way to improve our joint efforts to translate science into new treatments for patients.
The entire open innovation module is open source which means that we aim to disclose and publish everything we accomplish, including the structure of the novel educational molecules.
We introduce the concept of open innovation, provide insight on how drug research is conducted in the pharmaceutical industry and in a completely new manner disclose some of our R&D models and provide access to testing new molecules. Jointly with **DTU Chemistry**, **Skylab** and **LEO Pharma Open Innovation** we will provide the means for students to learn about and explore medical chemistry including the option of designing, synthesizing and testing of their own molecules.

The science

JAK-kinases (JAK), or Janus kinases, is a family of enzymes acting as transducers of cytokine-mediated signals, often related to inflammation (wiki). JAK is involved in the disease progression of eczema and is currently a hot target for drug discovery. Several projects are ongoing with clinical trial, but also in earlier stages to identify novel JAK inhibitors with unique properties.

An example of a well-known and characterized JAK inhibitor is Tofacitinib and PF-04965842 (CAS no: 1622902-68-4) that can be used a starting point for both theoretical discussions and as practical starting point for new design and synthesis. More on JAK inhibitors.
JAK inhibitors are biologically active in the advanced **eczema-relevant bioassays** (link).

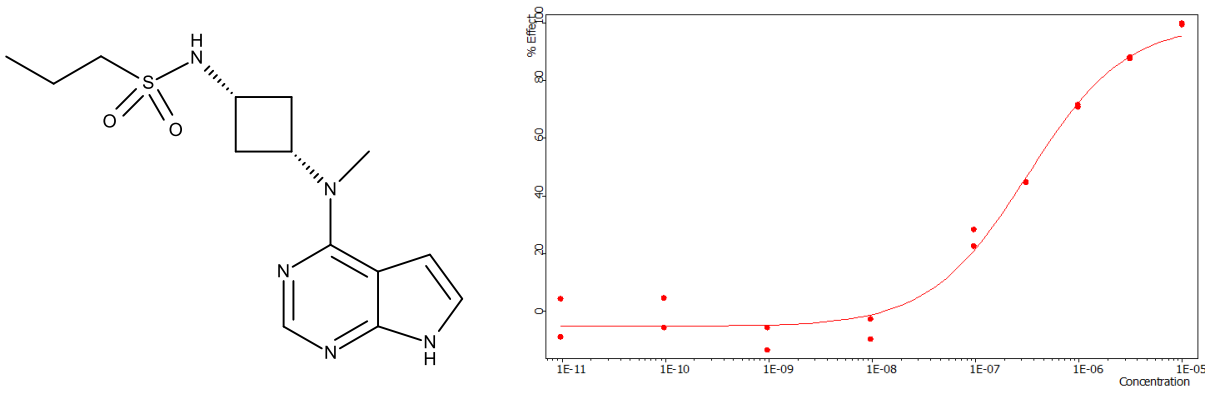
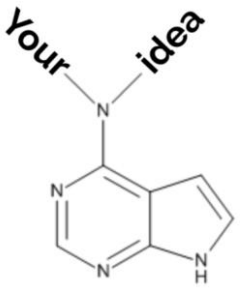


Figure. PF-04965842 currently in clinical testing and example of biological activity. Increased effect (up on the Y-axis) indicate an inhibitory effect, i.e. reduction of CCL2 release. The potency of the molecule is about 350 nM and the efficacy is approximately 100%.

The student's opportunity and challenge



Participate in relevant open drug discovery by designing, creating and testing your own molecules for possible eczema treatment. Using Tofacitinib and PF-04965842 and the deazapurine as base structure, explore and create a new molecule and have it tested for JAK inhibition by reducing inflammation in LEO Pharma Open Innovation's eczema-relevant biological assay.

The challenge is to 1. synthesis a molecule, 2. keep biological effect, 3. maintain water solubility and 4. search databases to determine structural novelty, if possible.

Some resources

Two very relevant Medicinal Chemistry articles with JAK kinase inhibitors;
https://pubs.acs.org/doi/abs/10.1021/acs.jmedchem.7b01598,
http://pubs.rsc.org/en/content/articlelanding/2018/md/c7md00568g/unauth#!divAbstract