DEPARTMENT
OF PHARMACEUTICAL SCIENCES

Seminars on Drug Sciences (SDS)

Lecture of

Dr. Gerhard Müller, CSO

SpiroChem AG, Basel, Switzerland

Protein Phosphatases: A widely neglected Target Family

This contribution will highlight the reductionistic, and sometimes misleading approach along which small-molecule drug discovery projects are often pursued. Examples will be given that indicate that occasionally the Medicinal Chemistry community tends to operate “under the lamppost”, i.e., there is hesitation to explore entire new areas of e.g., chemical space, chemical reactions, or target classes.

In that context, the family of protein phosphatases will be used as an example of a therapeutically rich, but completely under-exploited source of validated drug targets modulating signal transduction pathways. Unlike the kinase family, research and development activities have not yet yielded any approved small-molecule drugs against a member of that target class to date.

Approximately 20 years ago, the phosphatase family was classified as undruggable. This was mainly driven by the failure of the industry-wide drug discovery efforts to develop PTP1B inhibitors. These initial inhibitor design strategies focussed on developing substrate analogues, attempting to mimic the phospho-tyrosine pharmacophore, frequently embedded in a peptide-like scaffold. This approach yielded potent, highly polar, often charged compounds that suffered from permeability issues, metabolic liabilities, and lack of selectivity.

Current activities and trends around non-orthosteric modulators of different members of that rich target family will be introduced.

Wednesday, March 27, 2024
17:15 - 18:15

Lecture Hall 1, Pharmacenter, Klingelbergstrasse, 50, Basel
Host: Prof. em. B. Ernst
Molecular Pharmacy

University of Basel

Lecture No. 70469-01 / Spring Semester 2024