DRA lecture
Thursday February 22nd 15:00-16:00

"Structure-based design, synthesis and biological characterization of isoform selective histone deacetylase inhibitors"

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Abstract: Histone deacetylases (HDACs) are important modulators of epigenetic gene regulation and additionally control the activity of non-histone protein substrates. While for HDACs 1-3 and 6 many potent selective inhibitors have been obtained, for other subtypes much less is known on selective inhibitors and the consequences of their inhibition. In the present talk the structure based design of isoform selective HDAC inhibitors will be discussed. Docking studies using available crystal structures have been used for structure-based optimization of several series of compounds. We have investigated the role of HDAC8 and HDAC10 in the proliferation of cancer cells and optimized hits for potency and selectivity, both in vitro and in cell culture. The combination of structure-based design, synthesis, in vitro screening to cellular testing resulted in potent and selective HDAC8 inhibitors that showed anti-neuroblastoma activity in cellular testing. A second project focused on the development of isoform specific inhibitors of parasitic HDACs. Structure based design and crystallization resulted in the development of *Schistosoma mansoni* HDAC8 inhibitors for the treatment of bilharzia.

Organized on behalf of the Drug Research Academy (DRA) and Center for Biopharmaceuticals by Christian A. Olsen (cao@sund.ku.dk). Participation is free of charge and is open for attendance by all interested parties. No registration is required.