SAPIENZA UNIVERSITÀ DI ROMA

Dottorato in Scienze Biochimiche

Dottorato in Scienze della Vita

SEMINAR NOTICE

July 19, 2021 11:00

meet.google.com/ngf-bmpv-rdi

Prof. Dr. Stefan Knapp

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Institute for Pharmaceutical Chemistry - Frankfurt

Modulation of epigenetically controlled gene transcription and cell states by small molecules

Abstract. Epigenetics is a key mechanism regulating context dependent gene expression and chromatin structure. One of the key questions in this area is how the epigenetic code is transferred during cell division leading to bookmarking of transcriptionally active genes and how is the code altered during cell differentiation and the development of diseases. We have been interested in the past 10 years in the reading process of the epigenetic code which is mediated by small protein interaction domains recognizing single or multiple post-translational modifications on histones and other nuclear proteins. One of the major epigenetic reader families are Bromodomains (BRDs), evolutionary conserved protein interaction modules that specifically recognize ε-N-lysine acetylation motifs, a key event in the reading process of epigenetic marks. The human proteome encodes 61 of these highly diverse domains present in 46 mainly nuclear proteins. The recent discovery of potent and highly specific inhibitors for the BET (bromodomain and extra-terminal) family of bromodomains has stimulated intensive research activity in diverse therapeutic areas, particularly in oncology, where BET proteins regulate the expression of key oncogenes and anti-apoptotic proteins. During the recent years we have established a family wide platform of reagents, assays and crystal structures enabling the rational design and comprehensive selectivity screening of bromodomain inhibitors. Using this platform we and our collaborators have developed and comprehensively characterized highly selective chemical tool compounds (chemical probes) for most bromodomain subfamilies. In this talk I will present recent data on the developed tool compounds that cover now most bromodomain subfamilies including their *in vitro* characterization and phenotypic responses observed in cellular model systems as well as their potential for the development of new targeted therapies. I will also show examples how the unencumbered availability of chemical probes leads to rapid validation of new therapeutic strategies in diverse disease areas.

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