FAKULTÄT FÜR CHEMIE

universität wien

Einladung zum Vortrag von

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„Chemical degradation of gene regulatory proteins"

Aberrant gene regulation underpins and sustains most if not all aspects of human malignancies. However, therapeutic targeting of oncogenic transcriptional circuits has posed a historic challenge in the field of ligand discovery chemistry owing to the lack of druggable, enzymatically active domains in transcription factors and transcriptional co-activators. To overcome this limitation, and to expand the space of proteins amenable to therapeutic targeting, we recently devised a strategy for ligand-induced target protein degradation using bifunctional small molecules capable of chemically reprogramming the E3 ligase substrate receptor cereblon (CRBN). In detail, these small molecules induce molecular proximity between CRBN and a protein of interest (POI). Induced proximity leads to ubiquitination of the POI and subsequent degradation by the proteasome. Focusing our initial efforts on degraders of the BET family of proteins, we could show that these agents induce pronounced target degradation in vitro as well as in vivo, thus outlining a potential avenue for further therapeutic development. Moreover, we observed that they exhibit superior efficacy than competitive BET bromodomain inhibitors through largely unknown mechanisms. I will discuss our efforts to mechanistically explain this differential molecular pharmacology, as well as our efforts to extend this type of chemistry to new targets.

Mittwoch, 24. Jänner 2018, 16:15 Uhr
Hörsaal 3 der Fakultät für Chemie
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Nuno Maulide
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Bernhard Keppler Dekan	Lothar Brecker Vizedekan	Veronika Somoza Vizedekanin