## GSI – seminar

Darmstadt, Planckstraße 1 Theory Lecture Hall SB3 3.170a

Monday, April 23, 2018 14:00

Prof. Dr. Felix Hausch TU Darmstadt Department of Chemistry

## "Inhibition of the FK506-binding protein 51 as a novel target for obesity, depression and chronic pain"

The FK506-binding protein 51 (FKBP51) plays a key role in human stress biology and contributes to major depression, obesity and chronic pain. Drug discovery for FKBP51 has been hampered by lack of selectivity against the highly homologous functional counter-player FKBP52. Here, we present the discovery of SAFit2, the first potent and highly selective inhibitor of FKBP51. SAFit2 achieves selectivity for FKBP51 by an unanticipated induced-fit mechanism that is much less favorable for FKBP52. By using this ligand we demonstrate that selective inhibition of FKBP51 enhances neurite elongation in neuronal cultures and improves neuroendocrine feedback and stress-coping behavior in mice. Furthermore, SAFit2 ameliorated inflammatory pain-induced disabilities and diet-induced obesity. Our findings validate and enable FKBP51 inhibition as a novel pharmacological treatment option for depression, obesity and chronic pain.

Hosted by Prof. Dr. Claudia Fournier GSI Helmholtzzentrum für Schwerionenforschung GmbH