Der Rat für die Verleihung des Otto Naegeli-Preises hat am 24.November 2021 beschlossen, den Otto Naegeli-Preis zur Förderung der medizinischen Forschung 2022

DR NICOLAS H. THOMÄ

zu verleihen.

Dieser Beschluss wurde aufgrund folgender Laudatio gefasst:

DR NICOLAS H. THOMÄ

has made seminal contributions to our understanding of the regulation and mode of action of ubiquitin ligases by determining the structures of large multicomponent complexes with ground-breaking cryo-electron microscopy techniques. He defined the structure of complexes that control the activity of large Cullin-based E3 ligases, and the structure of the ligase itself, which targets proteins within the cell for degradation. He then described how the specificity of the ligase can be reprogramed with the help of small molecules, allowing endogenous cellular machinery to be recruited to destroy proteins that are over-expressed or mutated in disease. Dr. Thomä's work is a prime example how cutting-edge structure biology can have direct and major therapeutic implications on diseases ranging from Alzheimers and infectious disease, to cancer.

The Thomä laboratory has shown on an atomic level how chemical compounds can function as molecular glues, connecting the adaptor domain of the Cul4 E3 ligase complex to a neo-substrate, committing the bound protein to degradation. He showed that previously identified drugs can be repurposed to help treat multiple myeloma and other blood cancers, through the targeted degradation of specific zinc-finger transcription factors. Such studies have profound implications for the modulation of transcriptional regulators that have long been considered undruggable, and yet which lie at the heart of oncogenic transformation. Dr Thomä continues to extend this approach to other classes of proteins, based on fundamental insights into the structure, function and biology of E3 enzymes.

The award of the Otto Naegeli Prize is for work that revealed the structural basis of how ubiquitin ligases, which control more than a third of total protein degradation in mammalian cells, are controlled and can be targeted to trigger the degradation of specific proteins in living cells. He has repeatedly delivered ground-breaking insights through his mastery of cryo-electron microscopy and human biology, to harness the cell's own machinery to regulate genome stability, transcription, and DNA repair. He is a prime example of how cutting-edge structure biology provides not only molecular insights, but drives innovation in biomedical application.

BASEL, 14. Juni 2022

DER PRÄSIDENT DES PREISRATES: