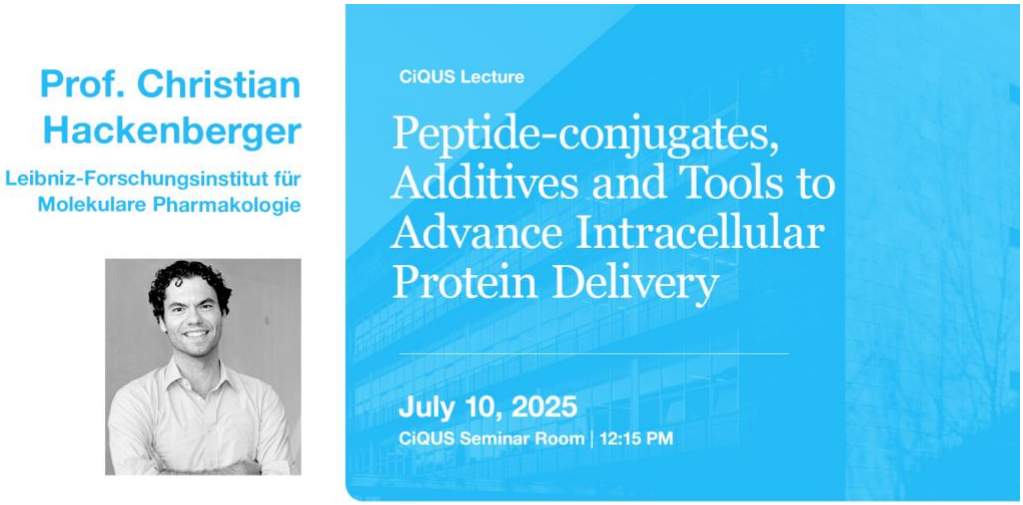

Prof. Christian Heckenberger
Leibniz-Forschungsinstitut für Molekulare Pharmakologie
Department of Chemical Biology
Robert-Rössle Str. 10, 13125 Berlin, Germany
hackenbe@fmp-berlin.de

Abstract

Understanding protein function constitutes a central endeavor in the molecular life sciences. This has been fueled by the development of ingenious chemical methods to synthesize or modify functional proteins, which allowed, for instance, to investigate functional consequences of naturally occurring posttranslational protein modifications (PTMs).[1] Nevertheless, performing such investigations in complex biological environments is severely limited due to the challenges associated with transporting (semi-)synthetic protein materials inside living cells, caused by low delivery efficiency or unwanted intracellular entrapment of protein cargoes.

In this presentation, I will highlight our efforts for the intracellular delivery of protein- and antibody-conjugates. To achieve this, we employ cyclic as well as linear cell-penetrating peptides (CPPs) to enhance the non-endosomal cellular uptake, either as protein conjugates[2] or in form of cell-surface bound CPP-additives.[3] Particular aims include the delivery of cell-permeable nanobodies to allow the visualization of intracellular targets, the identification of interaction partners or the modulation of protein targets inside cells to illustrate their potential as next-generation biopharmaceuticals.[4] Hereby, I will also introduce a recently developed photocatalytic method termed DarT-labeling for the intracellular identification of peptide binders.[5]

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Biosketch

Christian P. R. Hackenberger studied chemistry in Freiburg and Madison/Wisconsin (M.Sc. with Prof. Sam Gellman) and performed his doctoral studies in organic chemistry at the RTWH Aachen with Prof. Carsten Bolm. After a postdoctoral stay at MIT with Prof. Barbara Imperiali, he founded his own research group at the Freie Universität Berlin in 2005 as an Emmy Noether fellow. In 2012, he was appointed as Leibniz-Humboldt Professor and Department Head for Chemical Biology at the Leibniz-Research Institute for Molecular Pharmacology (FMP Berlin) and the Humboldt Universität zu Berlin. In addition, he is an associate editor for Chemical Science, the flagship journal of the RSC and authored over 150 publications.

His group develops highly selective chemical and chemoenzymatic strategies to functionalize proteins and antibodies to generate protein-based therapeutics against cancer, Alzheimer and viral infections. His laboratory invented P5-labeling, a superior bioconjugation platform to generate stable and efficacious antibody-drug-conjugates (ADCs). In addition, he pioneered the development of cell-permeable nanobodies and antibodies for intracellular targeting and the engineering of structurally defined protein-based antiviral compounds.

Christian is a co-founder of the Munich-based company Tubulis, which engineers better tolerable cancer drugs, especially ADCs, using conjugation technologies from his lab, in particular the P5-labeling platform. Recent awards include the Leonidas Zervas Award from the European Peptide Society (2018), the Astra Zeneca Award from the Royal Society of Chemistry (2023) and the Max-Bergmann Medal (2024). In 2020, he was the first recipient of the Falling Walls breakthrough of the year award in the Life Sciences, recognizing his contributions to develop next-generation biopharmaceuticals.