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Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares

Conferencia:

The power of chemoselectivity: Functional peptide and protein-conjugates for proteomic and pharmaceutical research

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Aula de Seminarios do CIQUS

12:15 h

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Christian P. R. Hackenberger completed his graduate studies at the universities of Freiburg and UW Madison and his doctoral studies in 2003 at the RWTH Aachen with Carsten Bolm. After a postdoctoral position at MIT with Barbara Imperiali, he started his own group at the Freie Universität Berlin in 2005 funded by the German Science Foundation in the Emmy Noether Program and the Boehringer-Ingelheim Foundation within the Plus 3 award. In 2012, he was appointed Leibniz-Humboldt Professor for Chemical Biology at the Leibniz-Research Institute for Molecular Pharmacology and the Humboldt Universität zu Berlin. His group works on the development of new chemoselective and biorthogonal reactions as well as novel approaches to functional peptide and protein synthesis and delivery, in particular for the analysis of labile posttranslational modifications and the labeling and modification of different antibody formats.
Since 2018, he is co-founder of the planned start-up 'Tubulis Technologies'. This newly established company ventures into developing better tolerable cancer drugs based on antibody-drug conjugates. In March 2018, 'Tubulis Technologies' received the Leibniz Gründerpreis (New Enterprise Foundation Award) of the Leibniz Association.

The power of chemoselectivity: Functional peptide and protein-conjugates for proteomic and pharmaceutical research

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Our lab constantly aims to identify new bioorthogonal reactions for the synthesis and modification of functional peptides and proteins. We apply these highly selective organic reactions[1] to study functional consequences of naturally occurring posttranslational protein modifications (PTMs), in particular phosphorylated Lys- and Cystein-peptides,[2] as well as to generate novel peptide- and protein-conjugates for pharmaceutical and medicinal applications.

In this presentation I will focus on the **chemical modification of functional proteins** as well as their **cellular delivery**. Thereby, we employ cyclic cell penetrating peptides (cCPPs) to transport a functional full length protein to the cytosol of living cells as recently demonstrated by the direct delivery of GFP-conjugates.[3] For protein modification we use a combined approach of intein expression as well as recently developed bioorthogonal reactions and enzymatic ligations, for instance the so-called Tub-tag labeling.[4] This concept is finally applied to generate new **antibody-drug conjugates** as well as **cell-permeable nanobodies**, i.e. small antigen binding proteins that remain active within the reductive milieu inside living cells, to interfere with intracellular targets.[5]

References

1. D. Schumacher, C.P.R. Hackenberger, *Curr. Opin. Chem. Biol.* **2014**, *22*, 62-69.
2. a) J. Bertran-Vicente, R.A. Serwa, M. Schümann, P. Schmieder, E. Krause, C.P.R. Hackenberger, *J. Am Chem. Soc.* **2014**, *136(39)*, 13622-13628; b) J. Bertran-Vicente, M. Penkert, O. Nieto, M. Schümann, P. Schmieder, E. Krause, C.P.R. Hackenberger, *Nature Comm.* **2016**, 7,12703.
3. N. Nischan, H.D. Herce, F. Natale, N. Bohlke, N. Budisa, M.C. Cardoso, C.P.R. Hackenberger, *Angew. Chem. Int. Ed.* **2015**, *54(6)*, 1950-1953.
4. a) D. Schumacher, J. Helma, F.A. Mann, G. Pichler, F. Natale, E. Krause, M.C. Cardoso, C.P.R. Hackenberger, H. Leonhardt, *Angew. Chem. Int. Ed.* **2015**, *54(46)*, 13787-13791, b) D. Schumacher, O. Lemke, J. Helma, L. Gerszonowicz, V. Waller, T. Stoschek, P.M. Durkin, N. Budisa, H. Leonhardt, B.G. Keller, C.P.R. Hackenberger, *Chem. Sci.* **2017**, *8*, 3471-3478
5. H. Herce, D. Schumacher, F.A. Mann, A. Ludwig, A. Schneider, M. Filies, S. Reinke, C. Cardoso, C.P.R. Hackenberger, *Nature Chem.* **2017**, *9*, 762-771.