Fluorine in peptide, protein and bacterial cell engineering

B. Koksch

Freie Universität Berlin, Institute of Chemistry and Biochemistry, Arnimallee 20, 14195 Berlin, Germany
email: beate.koksch@fu-berlin.de

In a league of its own, fluorine enables us to engineer biopolymers with highly desirable properties. [1] The particular challenge in using it as a tool lies in our ability to juggle the interplay between the specific properties of the fluorinated building block such as hydrophobicity and structural properties [2] and its responsiveness to the environment it is exposed to. [3-6]

One of our current projects studies the way in which not just biomolecules in the laboratory, but whole living organisms accommodate fluorine. Fluorine incorporation into single proteins via related amino acid analogues has become common practice. However, an essential question remains: Can fluorinated amino acids generally be used to build up biomass or does the presence of large amounts of fluorine in cells render them nonviable?

To gain information about the effect of long-term exposure of living cells to fluorine, we constructed an experiment based on bacterial adaptation in artificial fluorinated habitats. We propagated *Escherichia coli* (*E. coli*) in the presence of different fluoroindoles as essential precursors for the *in situ* synthesis of tryptophan analogues and could show the proteome-wide incorporation of fluorotryptophanes via translation in *E. coli*. Genomic, proteomic and metabolomics analyses reveal that full adaptation requires astonishingly few genetic mutations but is accompanied by large rearrangements in regulatory networks, membrane integrity and quality control of protein folding. [7]

This talk will introduce some of our recent results.

[1] A.A. Berger, J.-S. Völler, N. Budisa, B. Koksch. *Acc. Chem. Res.* **2017**, 50 (9), 2093

[2] U.I.M. Gerling, M. Salwiczek, C.D. Cadicamo, H. Erdbrink, S. Grage, P. Wadhwani, A. Ulrich, M. Behrens, G. Haufe, C. Czekelius, B. Koksch. *Chem. Sci.* **2014***, 5 (2),* 819

[3] S. Chowdhary, J. Moschner, D. J. Mikolajczak, K. Folmert, A.-K. Stegemann, A. Thünemann, B. Koksch. *ChemBioChem* **2020**, https://doi.org/10.1002/cbic.202000373 (VIP paper, Cover)

[4] S. Huhmann, B. Koksch. *Eur. J. Org. Chem.* **2018**, 3667 (VIP)

[5] J. Völler, M. Dulic, U. Gerling-Driessen, H. Biava, T. Baumann, N. Budisa, I. Gruic-Sovuli, B. Koksch. *ACS Central Science***, 2017,** *3* (1), 73

[6] S. Ye, B. Loll, A.A. Berger, U. Mülow, C. Alings, M. Wahl, B. Koksch. *Chem.Sci.* **2015**, *6*, 5246

[7] F. Agostini, L. Sinn, D. Petras, P.C. Dorrestein, J. Rappsilber, N. Budisa, B. Koksch. *ACS Central Science* **2020***, published online*