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**15.03.2019, 13.00 Uhr Hörsaal 1 (-1.202), Biologicum**

## Biosynthetic design of nonribosomal peptides

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Nonribosomal peptide synthetases (NRPSs) that protect microorganisms against environmental threats by producing siderophores or antibiotics, for instance, are predisposed for biosynthetic engineering because of their modular molecular structure. We have explored several strategies for the redesign of NRPS specificity [1]. Notable examples are the incorporation of a clickable amino acid through targeted binding pocket mutagenesis [2] or specificity transfer through swapping of small protein fragments [3]. Incorporation of clickable amino acids has further enabled a strategy for high-throughput sorting of mutagenized NRPSs leading to a remarkable switch in substrate specificity from alpha- to beta-phenylalanine [4]. We are currently working on streamlined methods that allow recombination of NRPS building blocks at high throughput. New tools for tailoring non-ribosomal peptides could potentially support the fight against spreading antibiotic resistance.

[1] Kries, H. J. Pept. Sci. 2016, 22 (9), 564.

[2] Kries, H.; Wachtel, R.; Pabst, A.; Wanner, B.; Niquille, D.; Hilvert, D. Angew. Chem. Int. Ed. Engl. 2014, 53 (38), 10105.

[3] Kries, H.; Niquille, D. L.; Hilvert, D. Chem. Biol. 2015, 22 (5), 640.

[4] Niquille, D. L.; Hansen, D. A.; Mori, T.; Fercher, D.; Kries, H.; Hilvert, D. Nat. Chem. 2018, 10 (3), 282.

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