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Application of modular chemoenzymatic conjugation strategies for the semi-rational engineering of biologicals

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Binder drug conjugates such as antibody drug conjugates have led to major improvements of personalized therapy of diseases such as cancer, autoimmunity and pathogenic virulence. The underlying methods which enable the position specific functionalization or semi-rational mutagenesis of bioactive proteins have been the key innovations. While academic research groups are already managing to computationally design small bioactive peptides, the majority of protein engineering projects are still relying on semi-rational directed evolution to identify protein with desirable properties. Here a main leap forward has been the site-directed post-translational mutagenesis of proteins by means of state-of-the art bioconjugation methods including enzymatic sortase A transpeptidation and chemical indium catalyzed mild radical addition of diverse iodoalkanes to sp2-hybridized amino acids. Above all, a multitude of chemoenzymatic functionalization methods are continuously being improved and are fully compatible with directed evolution via cell surface display library screenings

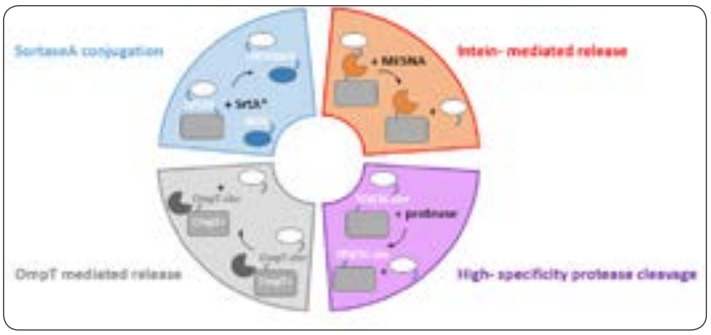

Figure 1: Different ways to functionalize E.coli display proteins while simultaneously releasing them from the cell surface. Blue: transpeptidation of peptides to the cell surface proteins via Staphylococcal sortase A. Orange: Surface release and functionalization of surface displayed proteins by means of expressed protein ligation. Violett: Surface cleavage of surface display proteins by high-specificity proteases. Grey: Surface release of E.coli display proteins be genetically encoded outer membrane proteases

Biography

Christoph Hiemenz has completed his MSc from Ruprecht-Karls University Heidelberg. He work as a bioinformatician at PEPperPRINT GmbH and is the scientific instructor of the iGEM Team Heidelberg 2019. He has worked on diverse research projects: -DKFZ Heidelberg, Prof. Jörg Hoheisel- Kinase activity profiling with peptide arrays -BioQuant Heidelberg, Prof. Roland Eils/Prof. Barbara Di Ventura- Optogenetic nuclear protein shutteling and ODE modeling -KTH Stockholm, Prof. Stefan Ståhl – Surface functionalization of E.coli cells via sortases and inteins - EMBL Heidelberg, Dr. Carsten Schultz- Bioactivity of trifunctional Sphingolipids -IPMB Heidelberg, Prof. Andres Jäschke- Multivalent fluorescent turn-on probes for RNA imaging.

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