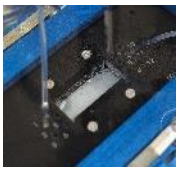
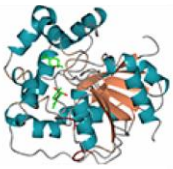
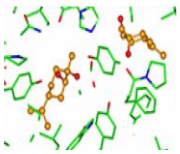
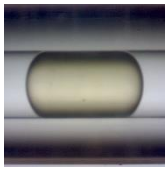

ESAB
European Society of Applied Biocatalysis

ESAB Webinar

AMINE BIOCATALYSIS 4.5

Friday, 26th March 2021 at 10:00 – 12:00 a.m. CET
Welcome Address: Willi Meier, DECHEMA & Roland Wohlgemuth, Lodz University of Technology, Chair ESAB
Chairs: Per Berglund, KTH Royal Institute of Technology, Stockholm, Sweden,
Jennifer Littlechild, University of Exeter, Vice-chair ESAB
Moderator: Willi Meier, DECHEMA, Frankfurt, Germany

PROGRAMME

10.00 Byung-Gee Kim, School of Chemical and Biological Engineering, Institute for Molecular Biology and Genetics and Institute of Bioengineering, Seoul National University, Seoul, Republic of Korea

Amino Acid Decarboxylase (AADC): Protein stability, activity, substrate selectivity, and protein network analysis

Lysine/Ornithine/Arginine decarboxylases (LDC/ODC/ADC) are very useful amino acid decarboxylases (AADCs) following the same reaction mechanism among several AADCs for synthesizing cadaverine, putrescine and agmatine, which are C5, C4 diamines and C4 amino-guanidino compound, respectively. To maximize their productions, improving enzyme activity and stability at alkaline pHs often becomes a common issue. In addition, depending upon the specific AADCs, their target properties to improve for successful process development are different, such as substrate selectivity, structural stability, etc. To overcome such problems, firstly we have undertaken a rational approach to improve both activity and stability of corresponding AADCs. The site-specific mutation sites were guided by mechanistic insights and the knowledge of the enzyme structure obtained from previously reported protein X-ray crystal structure data base. In parallel, protein network analysis was integrated to narrow down possible mutation sites for improving the stability of the AADC. In this talk, to overcome specific problems of AADC, we will discuss various different approaches of protein engineering such as disulfide bond analysis, network analysis, B-factor, Caver, etc., and the results of the production of diamine compounds will be presented.

10.30 Bettina Nestl, Innophore GmbH, Graz, Austria

Structure based semi-rational engineering of imine reductases

Imine reductases (IREDs) have become essential in providing access to chiral amines by catalyzing the asymmetric reductions of imines and stereo-selective reductive aminations. Previously, enzyme engineering of the (*R*)-selective IRED from *Myxococcus stipitatus* ((*R*)-IRED-*Ms*_V8) has led to an NADH-dependent variant with high catalytic efficiency. However, no IRED with NADH specificity and (*S*)-selectivity in asymmetric reductions has not yet been reported. We applied semi-rational enzyme engineering to switch the selectivity of the NADH-dependent (*R*)-IRED-*Ms*_V8. The introduction of five additional mutations resulted in a variant with an inverted stereo-preference reducing the cyclic imine 2-methylpyrroline to the corresponding (*S*)-amine product with >99% conversion and 91% enantiomeric excess.

11.00 Elaine O'Reilly, School of Chemistry, University College Dublin, Dublin, Ireland

Cascading towards new biocatalytic amine shuttling methodology

Catalytically reversible reactions, including alkene metathesis and transfer hydrogenation, have had an enormous impact on the development of synthetic strategies for the synthesis of bioactive compounds and important materials. However, the vast majority of chemically catalysed processes are non-reversible. In contrast, many enzyme-catalysed processes are freely reversible and displacing the reaction equilibrium towards product formation is often achieved (both in Nature and synthetically) by performing cascade reactions, where the product of one biocatalytic step becomes the substrate/reactant for the next transformation. The reversible nature of enzymes means that they can be exploited for mediating reactions in either the forward or reverse direction, and this adds a significant level of flexibility to the development of (chemo)enzymatic routes.

An unexplored aspect of biocatalysis is using enzyme reversibility to 'shuttle' functionality intra- or intermolecularly. Such an approach has the advantage of enabling single product isolation from complex mixtures of reactants, and can act to mask reactive functionality. My group are exploring the area of 'shuttle biocatalysis' using a number of widely used transformations, including the Pictet-Spengler, aza-Michael and Mannich reactions.

11.30 Zhi Li, Department of Chemical & Biomolecular Engineering, National University of Singapore, Singapore

Engineering of enzymes and cascade biotransformations for enantioselective synthesis of amines from racemic alcohols

Green and efficient synthesis of useful and valuable enantiopure amines are highly wanted for pharmaceutical manufacturing. Biocatalysis is a useful tool for enantioselective amine synthesis, and its successful application depends on the development of the appropriate enzymes and efficient reactions. We have been interested in engineering enzymes and cascade biotransformations for enantioselective synthesis of amines from the easily available racemic alcohols. In this presentation, some progresses on this topic will be addressed, including a) the engineering of an amine dehydrogenase (AmDH) for the asymmetric reductive amination of ketones;[1-2] b) the development of cascade biotransformations to convert racemic alcohols into enantiopure amines by using both (R)- and (S)-enantioselective alcohol dehydrogenases (ADHs) with an AmDH;[3] c) the engineering of an ambidextrous ADH to oxidize a racemic alcohol with high conversion;[4] and d) the development of cascade biotransformations to convert racemic alcohols into enantiopure amines by coupling an ambidextrous ADH with a transaminase wherein isopropylamine is used to recycle PMP and NAD+ cofactors via the reversed cascade reactions.[4]

References

[1] Ye, L. J.; Toh, H. H.; Yang, Y.; Adams, J. P.; Snajdrova, R.; Li, Z. ACS Catalysis, 2015, 5, 1119-1122. [2] Liu, J.; Pang, B. Q. W.; Adams, J. P.; Snajdrova, R.; Li, Z. ChemCatChem, 2017, 9, 425-431. [3] Liu, J.; Li, Z. Biotechnol. Bioeng., 2019, 116, 536-542. [4] Tian, K.; Li, Z. Angew. Chem. Int. Ed., 2020, 59: 21745-21751.

ABOUT THE SPEAKERS

Byung-Gee Kim is Professor at the School of Chemical and Biological Engineering, from 1991 up to the present, at Seoul National University, where he has been jointly appointed to the Institute for Molecular Biology and Genetics and the Interdisciplinary program of Biochemical Engineering and Biotechnology, Seoul National University. He obtained his Ph.D. in Food Science and Technology in 1989 at Cornell University, in Ithaca N.Y., U.S.A, after a M.S. in Chemical Technology, College of Engineering, Seoul National University in 1982 and a B.S. in Chemical Technology, College of Engineering, Seoul National University in 1980. Additional tasks include: Commissioner, Bio-MAX/N-Bio Institute, 2019- present Trustee, Suh Kyungbae Foundation (SUHF), 2016- present, President, KSBB (Korean Society of Biotechnology and Bioengineering), 2014, Director, Korea Bio-Hub Center, 2008-2009, Director, Institute of Bioengineering, Seoul National University, 2005-2007.

Bettina M. Nestl is senior scientist and manager at Innophore GmbH, a bioinformatics company based in Graz, Austria. Bettina received her Ph.D. in Chemistry from the University of Graz under the supervision of Prof. Kurt Faber. Following her postdoctoral research with Prof. Nicholas J. Turner at the Manchester Institute of Biotechnology, she moved to the lab of Prof. Bernhard Hauer at the University of Stuttgart to work as a junior research group leader. Bettina has published more than 50 scientific papers, patents and book chapters in the field of biocatalysis. Her research interests lie in the discovery and engineering of new enzymes.

Elaine O'Reilly is Associate Professor of Chemical Biology at University College Dublin and completed her BSc and PhD at University College Dublin (UCD), before moving to the Manchester Institute of Biotechnology to work with Prof. Nicholas Turner and Prof. Sabine Flitsch. She began her independent career in 2014 at Manchester Metropolitan University and from 2015-2019, her research group was based in the School of Chemistry at the University of Nottingham. In 2019, Elaine moved to her current position at the University College Dublin, where her group are interested in the development of enzymes and biocatalytic methodology for synthetic applications.

Zhi Li is Associate Professor at the Department of Chemical and Biomolecular Engineering, National University of Singapore. He obtained his PhD in Organic Chemistry in 1991 at the University of Vienna, after a MEng in Chemical Engineering in 1985 at the Chinese Academy of Forestry in Nanjing, and a BSc in Chemistry in 1982 at Nanjing University. Awards and Honours: IChemE Singapore Award for Sustainable Technology (2013). His research interests focus on advanced biocatalysis for green and sustainable manufacturing of chemicals and pharmaceuticals, production of bio-based fuels and chemicals, and development of functional and smart materials.

NEXT ESAB WEBINARS

ESAB aims to promote the development of Applied Biocatalysis and takes initiatives in areas of growing scientific and industrial interest in the field.

Schedule and Topics of next ESAB webinars:

26 March 2021 Amine Biocatalysis 4.5

29 April 2021 Joint ESAB-SusChem Webinar: Broadening the Scope of Biocatalysis in Sustainable Chemistry

28 May 2021 Biocatalysts from Extremophiles

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