FEBS openbio

Volume 13 Supplement 2 July 2023

POSTERS

Table of Contents

POSTERS – RESEARCH

POSTERS – EDUCATION

Abstracts submitted to the 47th FEBS Congress from 8th to 12th July 2023 and accepted by the Congress Management Board are published in this Supplement of *FEBS Open Bio*. Late-breaking abstracts are not included in this supplement. The abstracts are available as two PDF files: Talks (Plenary Lectures, Symposia and Speed Talks) and Posters.

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Indexing

Abstracts published in *FEBS Open Bio* Supplement for 47th FEBS Congress will be included individually in the Conference Proceedings Citation Index published by Web of Science.

How to cite these abstracts

AuthorOne, A., AuthorTwo, B. (2023). Abstract title. FEBS Open Bio, 13: Abstract number*. doi:10.1002/2211-5463.13646

* Each poster has been given a unique number beginning with the letter P; the next part relates to the session in which the poster will be presented (see p.62 for key).

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P-01.1 Cancer and ageing
P-01.2 Immunometabolism in cancer development and therapy
P-01.3 The exposome and cancer
P-02.1 Autophagy
P-02.2 Cell death, and inflammation
P-02.3 Cell metabolism and stress
P-03.1 Biotech solutions to current problems
P-03.2 Chemical biology
P-03.4 Emerging technologies for the future
P-04.1 Gene expression/epigenetics
P-04.2 RNA Biology
P-05.1 Host–Microbial Interactions
P-05.3 Mitochondria in health and disease
P-06.1 Protein life cycle I: localisation, dynamics, functioning
P-06.3 Protein life cycle III: ribosomes, folding, chaperones
P-07.1 Supramolecular assemblies I: signal transduction
P-07.2 Supramolecular assemblies II: RNA–protein complexes, molecular machines
P-07.3 Supramolecular assemblies III: metabolons, multienzyme complexes
P-08.1 Neurobiochemistry (including neurodegenerative diseases)
P-08.2 Medicinal biochemistry
P-08.3 Food and nutrition in biochemistry
P-08.4 Cardiovascular diseases
P-08.5 Molecular basis of disease (excluding cancer)
P-E-09.1 Undergraduate teaching/learning
P-E-09.2 Postgraduate teaching/learning

the flavin transference have been obtained by using docking and molecular dynamics computational approaches.

P-07.3-03
Molecular details of unusual oxime-forming chemistry during bacterial polyketide biosynthesis

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Trans-acyltransferase polyketide synthases (*trans*-AT PKSs) are enzymatic assembly lines responsible for the biosynthesis of complex bioactive natural products. They act as a series of modules elongating carrier protein-bound intermediates. A unique feature of *trans*-AT PKSs are ketosynthase domains that phylogenetically clade according to the incoming substrate. This property allows the prediction of enzymology occurring upstream of the domain analyzed and thus, enables to uncover unusual biochemistry by analyzing unassigned KS clades. This approach revealed a new enzymatic activity in the lobatamide *trans*-AT PKS that *in vitro* and *in vivo* experiments carried out by Pr. Jörn Piel's group (ETH, Zürich) proved to be an oxime-forming reaction. In order to gain details into this newly-discovered enzymology, the flavin-dependent monooxygenase (FMO) domain and the downstream carrier protein, were expressed, crystallized, and the di-domain structure was solved by molecular replacement. This first PKS oxime-forming domain structure allowed to identify the residues involved in cofactors binding and potentially involved in substrate binding and catalysis. Point mutations, enzymatic assays and LC-MS characterization of the reaction products validated the role of these particular amino acids. Moreover, *in silico* docking experiments carried out with the FMO structure, the enzyme's substrate and the carrier protein structure which natively exhibits the substrate provided an interaction model and gave evidence that the FMO domain more likely interacts with the upstream substrate-bound carrier protein rather than the downstream crystallized one. Taken together, these data give the first insights into the molecular, protein-protein and protein-substrate mechanisms responsible for oxime formation in growing polyketide chains and could pave the way to the rational oxime insertion into other polyketide pathways through genetic engineering.

P-07.3-04
Enzymatic and structural approach for the synthesis of macrolactams

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The enrichment of the 'biocatalytic toolbox', from the bench-to-demonstration pilot, is a driving force for the discovery of new enzymes expanding the reaction repertoire for their integration in bioresourced industrial processes. Of particular economic interest, the lactam function is widespread in natural and synthetic compounds. Access to an increased diversity of variable size and/or functionalized lactams by enzymatic synthesis is highly desirable. The thesis project aims to obtain the fundamental knowledge necessary to identify the high catalytic efficiency, and the tolerance to various substrates of macrocycling domains of mega-enzymes such as polyketide synthases and hybrids with nonribosomal peptide synthetases, catalyzing the biosynthesis of compounds of high medicinal value in bacteria and fungi, from simple acyl-CoA. In native systems, macrocyclization is catalyzed in high cis-yield by a C-terminal thioesterase (TE) domain of the multienzyme, the subject of the study. These thioesterase domains will be characterized by an enzymatic and structural approach using in particular X-ray crystallography. This work is supported by the ANR SMALA: From small to macrolactams: an enzymatic approach.

P-07.3-05
Understanding docking in the unusual toblerol trans-AT polyketide synthase

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Polyketides are bacterial specialized metabolites which exhibit a range of valuable therapeutic properties. They are synthesized by gigantic multienzymes called modular polyketide synthases (PKSs) by successive condensation of acyl-CoA units. In these systems, the correct arrangement of the many subunits is enforced by short C- and N-terminal protein–protein interaction regions called docking domains (DDs). DDs have been demonstrated to be portable and therefore of interest in engineering PKSs and other metabolic pathways, but the high specificity of their interactions can also be used to interrogate multienzyme ordering within the assembly lines. In this context, we have studied docking domains present within the architecturally atypical *trans*-AT PKS responsible for toblerol biosynthesis in the methylotroph *Methylobacterium extorquens*. Biophysical characterization of the DDs of subunits TobC and TobE demonstrated that they interact, confirming the proposed ordering of subunits in the system. Elucidation of the structure of a non-covalent complex between the two domains revealed that the interaction is novel among known types of DDs. The roles of amino acids at the interdomain interface were further explored using site-directed mutagenesis coupled with isothermal titration calorimetry (ITC). Overall, our data deepen our understanding of sequence-structure relationships among DDs and expand the DD toolbox available for PKS synthetic biology.

P-07.3-06
Functional interaction between mitochondrial citrate transporters Ctp1p-Yhm2p and Complex III in *Saccharomyces cerevisiae*

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The cytochrome bc_1 complex, or complex III, is a component of the mitochondrial respiratory chain. In the yeast *S. cerevisiae*, this respiratory complex is inserted into the inner mitochondrial membrane as a homodimer, with each monomer containing ten

distinct protein subunits. Three of them, cytochrome *b*, cytochrome c_1 and the Rieske iron–sulfur protein, have a catalytic role whereas the remaining seven non-redox subunits (core proteins 1 and 2, Qcr6p, Qcr7p, Qcr8p, Qcr9p, Qcr10p) have no apparent role in complex activity[1]. Complex III catalyzes the transfer of reducing equivalents from quinol to cytochrome *c* and, at the same time, is responsible for proton pumping across the inner mitochondrial membrane towards the intermembrane space. The inner mitochondrial membrane, besides the respiratory complexes, also contains some hydrophobic proteins, known as mitochondrial carriers, which transport charged or polar metabolites across the lipid bilayer. Among these proteins, Ctp1p and Yhm2p, in *S. cerevisiae* mitochondria[2,3], are responsible for the transport of citrate, an important intermediate involved in several metabolic pathways. In this study, we have investigated a possible functional link between Ctp1p-Yhm2p, on the one hand, and the complex III, on the other hand. This on the basis of the assumption that the transported molecule of citrate is somehow connected, directly or indirectly, to the supply of reducing equivalents to the mitochondrial respiratory chain. Preliminary experiments, carried out in yeast mutant cells in which the gene encoding either mitochondrial citrate carrier has been deleted, showed a modulation of respiratory activity when the transport of citrate was impaired. A structural and functional analysis of the mitochondrial complex III was then performed under these experimental conditions. 1. Zara V et al. (2022) Int J Mol Sci 23, 10537. 2. Kaplan RS et al. (1995) J Biol Chem 270, 4108–4114. 3. Castegna et al. (2010) J Biol Chem 285, 17359–17370.

P-07.3-07
Investigation of the biological and mechanical properties of platinum nanoparticle incorporated dental zinc oxide eugenol cement material

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This study is aimed to develop platinum nanoparticle (Pt) incorporated zirconia-zinc oxide eugenol (ZZrOE) dental restorative material for helping biological and mechanical properties. After the setting time and mechanical properties of ZZrOE incorporating varying amounts of Pt (0, 0.5, 1, and 2 wt% in powder) were characterized, the surface morphology and composition of the resulting Pt-ZZrOE materials were investigated. To elucidate the surface properties, scanning electron microscopy, and energy-dispersive spectroscopy were used and setting time, solubility, sorption, micro vickers hardness and were compressive strength analyzed to evaluate the physical properties. Chemical properties were investigated by pH change and ion release measurements. The antibacterial effects of the bioactive set Pt-ZZrOE were tested with *Enterococcus faecalis* and the viability of human exfoliated deciduous teeth stem cells (SHED) with this biomaterial was examined. There was no significant difference of 0.5, 1, 2, and 3% Pt-ZrOE in compressive strength, but the higher the pt content in Micro Vickers hardness. A SHED cell viability of less than 70% was observed with 25% diluted extract in Pt-ZZrOE. The content of platinum nanoparticles has increased and antibacterial effects have increased All Pt-ZZrOE showed moderate-to-severe cytotoxic response. When platinum nanoparticles are mixed, the compressive strength is maintained, and the hardness is increased. Pt were found to reduce *E. faecalis* growth and inhibit biofilm formation remarkably. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT, No. 2021R1C1C1010005), by the Basic Science Research Program funded by the Ministry of Education (NRF-2022R1I1A1A01069606), and by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT, No. 2022R1F1A107489212). *The authors marked with an asterisk equally contributed to the work.

Neurobiochemistry (including neurodegenerative diseases)

P-08.1-01
Chaperone regulation of tau liquid–liquid phase separation

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Liquid-liquid phase separation (LLPS) of tau is increasingly recognized as a process implicated in the initiation of tau aggregation and formation of pathogenic conformers in Alzheimer's disease (AD) (Kanaan NM et al. 2020 Nat Commun). Tau pathology is accompanied by neuroinflammation, and while alarmin released by astrocytes in late AD stages is aggravating, early inflammatory responses encompass protective functions. This is the case of the Ca^{2+}-binding protein S100B, which we recently implicated as a proteostasis regulator that inhibits amyloid β (Cristovão JS et al. 2018 Sci Adv) and tau aggregation and seeding (Moreira GG et al. 2021 Nat Commun) suggesting its widespread action as a holdase-type chaperone in the prevention of misfit protein conformations. Here we report that S100B is also a Ca^{2+}-dependent inhibitor of tau LLPS. Phase diagrams of PEG-induced tau LLPS denote a significant suppressor effect by Ca^{2+}-S100B over tau droplet formation, without jeopardizing the droplets' liquid properties as assessed by fluorescence recovery after photobleaching (FRAP) and fusion events. The addition of Ca^{2+} to PEG-induced LLPS containing apo-S100B leads to an immediate decrease in the levels of tau droplets, revealing the ability of Ca^{2+}-S100B to interfere with these structures demonstrating how this process is both calcium-triggered and highly dynamic. Likewise, S100B can completely halt PEG-free Zn^{2+}-promoted tau LLPS, in virtue of its combined Zn^{2+}-buffering and tau-interaction abilities. Altogether, these data imply the S100B chaperone as a regulator of the formation of multiple pathological conformers and phase-separated systems, reinforcing its central role as a relevant proteostasis regulator in early neurodegeneration. FCT/MCTES (Portugal) is acknowledged for funding UIDB/04046/2020 and UID/MULTI/04046/2020 (to BioISI) and for PhD grant 2020.06443.BD (to GGM). Agilebio is acknowledged for grant LabCollector Scientific Award 2021 (to CMG).