MBG FOCUS TALK

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MBG Focus Talks in Molecular Biology

Monday 18 January 2016 at 10:15-11:00
Aud. D2, Dept. of Mathematics

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Functional and structural innovations in the real-time evolution of TrpF activity in HisA

The isomerase HisA catalyzes the fourth step in the histidine biosynthetic pathway (1). An equivalent isomerization reaction in tryptophan biosynthesis is catalyzed by TrpF. In a study by Näsvall et al.(2) evolution of the hisA gene from Salmonella enterica under selection for both HisA and TrpF activity was followed for 3 000 generations. The evolution followed the duplication-divergence model and generated specialist TrpF mutants, which lost the original activity, as well as generalist enzymes with dual activities.
I will present a genotype to phenotype study where we have clarified how in vivo evolution of an enzyme to a new enzymatic activity acted on the atomic structure, kinetics, thermostability, expression level and bacterial growth rate. Through structures of 13 HisA mutants, some in complex with substrate or product, we find that evolution results in an enzyme that similarly to the long-term evolved equivalent PriA can make a structural swap between the two activities but in a novel manner. We also observe an activity threshold beyond which the enzyme performance does not affect the growth rate.

1. Söderholm A, Guo X, Newton M.S, Evans G.B, Näsvall J, Patrick WM & Selmer M (2015), "Two-step ligand binding in a (βα)8 barrel enzyme – substrate-bound structures shed new light on the catalytic cycle of HisA", J. Biol. Chem. 290(41):24657-68

2. Näsvall J, Sun L, Roth JR, Andersson DI (2012) "Real-time evolution of new genes by innovation, amplification, and divergence." Science 338(6105):384-7

All welcome

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