MS11-03 **Human DOPA decarboxylase: structural snapshots of PLP binding**. Francesca Cutruzzola,[ab] Giorgio Giardina,[ab] Riccardo Montioli,[c] Stefano Gianni,[d] Barbara Cellini,[c] Alessandro Paiardini, [a] Carla Borri-Voltattorni [c]
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DOPA decarboxylase, the dimeric enzyme responsible for the synthesis of neurotransmitters dopamine and serotonin, is involved in severe neurological diseases such as Parkinson disease, schizophrenia, and depression. Binding of the pyridoxal-5**'**-phosphate (PLP) cofactor to the apoenzyme is thought to represent a central mechanism for the regulation of its activity. We solved the structure of the human apoenzyme [1] and found it exists in an unexpected open conformation: compared to the pig kidney holoenzyme [2], the dimer subunits move 20 Å apart and the two active sites become solvent exposed. Moreover, by tuning the PLP concentration in the crystals, we obtained two more structures with different conformations of the active site. Analysis of three-dimensional data coupled to a kinetic study allows to identify the structural determinants of the open/close conformational change occurring upon PLP binding and thereby propose a model for the preferential degradation of the apoenzymes of Group II decarboxylases [3].

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MS11-04 **Reaction Mechanism of Chorismate Mutase, a Model Enzyme for Pericyclic Reactions, Finally Resolved**
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Chorismate mutases (CMs) are the only well-characterized enzymes that catalyze a pericyclic reaction, and are therefore of significant interest to bioorganic chemists. So far, however, the exact nature of the catalytic mechanism and the high rate acceleration are still debated, especially the relative contributions of the transition state-stabilizing charges *versus* geometry in the catalytic pocket [1-4]. As an additional point of interest for the study of CM catalysis and inhibition, these enzymes are confined to bacteria, fungi and plants, and therefore they represent potential targets for antibiotics, fungicides or herbicides without adverse effects for animals and humans.

In this work, we have elucidated the enzyme mechanism by structurally and biochemically analyzing a variant of the CM of *Bacillus subtilis* (BsCM), where the non-natural amino acid citrulline was used to replace an important arginine residue in the catalytic center, decreasing the activity more than 10^4-fold [5]. Citrulline, in which the guanidinium group of the arginine side chain is substituted with a urea group, retains the overall shape, size and hydrogen bonding capabilities of arginine, but is not charged. Therefore, with the rest of the active site being equal, the importance of the positive charge can be assessed. Here, we present the crystal structures of the non-native CM variant in complex with substrate, transition state analog and product, as well as the apo structure, finally resolving the debate on the mechanism of this unusual class of enzymes.

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