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Unifying Concepts in Catalysis

UniCat Colloquium

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Lecturer: **Prof. Joelle N. Pelletier**, Associate Professor in the Department of Chemistry and Adjunct Professor in the Department of Biochemistry, University of Montréal, Quebec, Canada

Title: **Chimeric β-Lactamases: Structure, Function and Dynamics of Artificially Evolved Enzymes**

Abstract: Proteins evolve naturally to be well-folded and exhibit specific functions under native conditions. Can proteins be artificially evolved with success? Our model system focuses on β-lactamases, which provide bacterial resistance to widely used antibiotics such as penicillins and cephalosporins. The ever increasing number of clinically isolated variants of β-lactamases highlights the importance of developing a better understanding of the relationship between the structure and function of these proteins. Over the past decades, the TEM-1 and PSE-4 class-A β-lactamases have been well characterized. Recently, artificially-evolved chimeras of TEM-1 and PSE-4 were created and a restricted number were shown to be at least partially functional (Meyer *et al.* PEDS 13:563-570: 2006). We have undertaken the characterization these artificial chimeras at the level of their function, stability and dynamics. Kinetic characterization was performed for selected chimeras to compare their substrate recognition spectrum with that of the 'parental' enzymes, TEM-1 and PSE-4. Thermal denaturation using circular dichoism allowed assessment of the stability of these chimeric enzymes. Structural studies using NMR were undertaken for a selected, heavily-mutated chimera, in order to assess its overall structural and dynamic character. Overall, the artificially evolved chimeras retain much parental character, which is blended to roughly reflect how close each chimera is to either of the parental sequences. This suggests that the effects of mutations are generally additive. Nonetheless, we pay particular attention to two mutations located near the catalytic serine, which cause large variations in stability and function and reflect the unpredictability associated with artificially evolving residues within enzyme active sites.

Date: **Wednesday, 12 May 2010**

Time: **5:15 pm - around 6:45 pm**

Location: **TU Berlin, Institute of Chemistry,**
Straße des 17. Juni 115, 10623 Berlin
Building C, room C 243

Organiser: Dipl.-Biol. Mirja Krause (BIG-NSE PhD Student TUB)

Coffee and tea will be served thirty minutes prior to the lecture start.
Guests are cordially invited to attend!

Prof. Dr. Matthias Driess, Chair of the Cluster of Excellence UniCat