

## Seminar in Microbiology

Monday, 29<sup>nd</sup> May, 2017

Salle de séminaire, E07.3347.a, CMU

**11:30 – 12:30**

**Marc Creus**

Laboratory of Molecular Evolution  
University of Basel



## Tales of molecular evolution: exploring the origin of new enzymes and of antibiotic resistance

The Creus group focuses on **biomolecular design and evolution**.

- 1) Design of molecular interactions in the context of metalloproteins
- 2) Molecular evolution, including:
  - enzyme mechanisms of resistance to antibiotics
  - enzyme promiscuity
  - biocatalysis
  - functional robustness
  - genetic regulation / epigenetic mechanisms

The **Laboratory of Molecular Evolution** is highly interdisciplinary: by applying techniques of molecular biology (e.g. mutagenesis, in vivo selection and phage display) and a judicious combination of rational design and evolution, the Creus group is investigating the creation of novel activity amongst hundreds of millions of protein variants, a scale currently beyond the reach of traditional "synthetic chemistry".

This 'bottom-up' approach to bioinorganic chemistry may prove fruitful in addressing questions such as: how can we improve homogeneous metallocatalysts, particularly to work efficiently in aqueous environments, a feat that many enzymes have achieved in nature?

The questions addressed in the Creus group are wide-ranging and fundamental in many areas of (bio)chemical understanding: from "how do we create novel biocatalysts" to "how do bacterial enzymes manage to evolve antibiotic resistance?". Many practical applications for this research can be envisaged, including designed metalloproteins as sensors, cellular probes, molecular machines and in drug delivery.

<http://www.chemie.unibas.ch/~creus/>

### **Selected publications:**

Nicolet et al., 2016: Plasmid-mediated colistin resistance in a patient infected with *Klebsiella pneumoniae*. *Lancet Infect Dis.* 16:998-9.

Uda et al., 2014. Zinc-selective inhibition of the promiscuous bacterial amide-hydrolase DapE: implications of metal heterogeneity for evolution and antibiotic drug design. *Metallomics* 6:88-95

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