

SFB 680

MOLECULAR BASIS OF EVOLUTIONARY INNOVATIONS

Olivier Tenaillon

INSERM

Capturing the mutational landscape of an enzyme: mutation effects on beta-lactamase TEM-1

Adaptation proceeds through the selection of mutations. The distribution of mutant fitness effect and the forces shaping this distribution are therefore keys to predict the evolutionary fate of organisms and their constituents such as enzymes. Here, by producing and sequencing a comprehensive collection of 10,000 mutants, we explore the mutational landscape of one enzyme involved in the spread of antibiotic resistance, the beta-lactamase TEM-1. We measured mutation impact on the enzyme activity through the estimation of amoxicillin Minimum Inhibitory Concentration (MIC) on a subset of 990 mutants carrying a unique missense mutation, representing 64% of possible amino acid changes in that protein reachable by point mutation. We established that mutation type, solvent accessibility of residues and the predicted effect of mutations on protein stability primarily determined alone or in combination changes in MIC of mutants. Moreover, we were able to capture the drastic modification of the mutational landscape induced by a single stabilizing point mutation (M182T) by a simple model of protein stability. Our study thereby provides an integrated framework to predict mutation effects and their epistatic interactions

November 28, 17:00

Institute for Genetics, Zülpicher Str. 47a, Lecture Hall, Ground Floor

Host: Michael Lässig

www.sfb680.uni-koeln.de