MS07-P14 | COMPETITIVE BINDING OF POTENTIAL DRUG MOLECULES AT THE ACTIVE SITE OF AN ACYLPEPTIDE-HYDROLASE

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Acylaminoacyl-peptidases (AAP) are oligopeptidases that cleave short peptides or protein segments, while they function as exopeptidases (processing N-terminal acylated peptides) and endopeptidases too.

For members of its enzyme family two basic ways of substrate selection have been discovered: flexible domain movement between opened and closed form, or multimerization of rigid monomers. The formation of multimers is linked to the shielding of the "sticky edge" of a *β*-sheet - to avoid aggregation. In archeal *Ph*AAP formation of hexamers with a complex channel system is responsible for *β*-edge shielding and for the size selection too, in contrast, *Aeropyrum pernix* AAP (*Ap*AAP) forms dimers capable for a gating mechanism by domain movements providing size selection of the substrates [1]. The mammalian enzyme – present also in the human liver – is a key protein in the upstream regulation of the proteasome [2]. It was also proven to be part of a competitive binding process with a carbapenem type of antibiotics, such as meropenem [3]. The goal of our study is to determine the process of this competition with the help of protein crystallography on the archaeal analogues, since the structure of the mammalian AAP has not yet been determined.

The *Ap*AAP S445A and D524A mutants were crystallized and the obtained crystals were soaked into the meropenem solution for 1, 8 and 20 days to study the effect of time on degradation.

[1] Menyhárd 2013, 2015
[2] Palmieri 2011
[3] Yokogawa 2001