Phosphate and pyrophosphate binding motifs in proteins – structure and catalytic properties

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Our state of scientific knowledge in the field of protein structures, their functionalities and interactions is still under continuous investigation. Due to the approach of new technologies, such as next-generation sequencing and transcriptome analysis, we are able to find molecules (e.g., RNAs and proteins) yet undiscovered but encoded in genomes. Right now, about thirty eight percent of records in UniProt database, which collects all known sequences of proteins, are named as "uncharacterized protein" [1]. To understand the potential role of a new-known protein we can use amino acid sequence of the molecule and compare it to the proteins with known sequences and structures. As suggested in literature [2,3], vast majority of proteins has a structure, which can be divided into sub-domain "blocks", common in nature, which are responsible for peculiar functionality. My research is focused on phosphate and pyrophosphate binding motifs in proteins, where about forty to fifty percent of them [4] are motifs called P-loop structures (described by Walker A motifs).

To investigate whether amino acid sequences with Walker A motifs are able to bind pyrophosphate molecules on their own, I have synthesized five different peptides, where all of them consist of the aforementioned motif. Moreover, to investigate at which length of the motif the potential functionality begins, peptides differ in length. By using ^{1}H-^{1}H NMR measurements, structures of the peptides were resolved, both with and without phosphate molecules (trisodium trimetaphosphate). Incubation of peptides in a solution with ATP molecules and parallel HPLC analysis were used to check whether peptides are able to facilitate hydrolysis of the ATP molecules.

Peptides with length of twelve amino acids and more can interact with pyrophosphate molecules as it was assessed from ^{1}H-^{1}H NMR spectra. Despite observed potential phosphate-peptide interaction, HPLC analysis reveals that peptides cannot facilitate hydrolysis of the ATP molecules.

[1] - Own statistics; unpublished data

[2] - V. Alva, J. Soding, A. Lupas; *A vocabulary of ancient peptides at the origin of folded proteins*; Elife, Dec 14 (2015);

[3] - J. Soding, A. Lupas; *More than the sum of their parts: On the evolution of proteins from peptides*; BioEssays, 25 (2003)

[4] - Own statistics; unpublished data