## MS07-P03

### The influence of nucleotide sequence of RNA 5' end on the electrostatic interaction energy of IFIT5 proteins with RNA

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The aim of my current project is to characterize electrostatic interactions in selected complexes of IFITs proteins with RNA with the use of the University at Buffalo Pseudoatom DataBank (UBDB). IFIT proteins (Interferon-induced proteins with tetratricopeptide repeats) are effectors of innate immune system, which are getting expressed in cell infected by viruses. By binding foreign RNA they prevent synthesis of viral proteins in human host cell. It has been shown, that IFIT1, IFIT2 and IFIT5 bind different forms of RNA (with triphosphate group or cap at 5' end of RNA), however literature data are not consistent about selectivity of IFITs protein and their preferred RNA forms. We want to verify the hypothesis of the lack of influence of RNA sequence on interaction energy in IFIT-RNA complexes investigating the structures of IFIT5-pppRNA complexes.

Electrostatic energy usually has the most significant contribution to interaction energy (especially in the biological systems) and at the same time it can be calculated for large complexes, thus it is a perfect tool for estimating interaction energy in biomacromolecules. One of the more advanced methods to calculate electrostatic interaction energy is UBDB used together with Exact Potential Multipole Method (EPMM). UBDB enables reconstruction of charge density for macromolecules in quantitative manner. By UBDB+EPMM approach, which takes also charge penetration effects into account, it is possible to compute electrostatic energies with similar accuracy as with quantum chemistry methods, for wide range of types of interactions (hydrogen bonds, π-π stacking) and distances (not only at equilibrium geometry but also below or above). Calculations of energy are based on the structures of IFIT5 proteins deposited in Protein Data Bank (PDB) as 4HOR, 4HOS and 4HOT. After proper structure preparation, UBDB is transferred using LSDB program to reconstruct electron density distribution. Afterward, electrostatic interaction energy of protein-ligand complexes is calculated with EPMM method. Describing the nature of IFIT proteins interaction can help to expand our knowledge about mechanism of selective binding RNA and how human immune system recognizes and destroys viruses.

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## MS07-P04

### HpDprA domains involved in interaction with DNA

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Natural transformation in bacteria is a horizontal gene transfer mechanism that allows exogenous DNA internalization and integration into the bacterial genome. The uptake of double-stranded DNA (dsDNA) from the outer environment is followed by the conversion of dsDNA to single-stranded DNA (ssDNA) and its transport into the cytoplasm (Mortier-Barrière *et al.*, 2007). The transforming ssDNA is proposed to be bound and protected from the cytoplasmic nucleases by DprA (for DNA processing protein A) (Dwivedi *et al.*, 2013). DprA is a ubiquitous protein in bacteria that has a key role in natural transformation process (Ando *et al.*, 1999). In most bacteria, DprA is divided into three domains: a N-terminal domain, a conserved central domain and a C-terminal domain. In *Helicobacter pylori*, DprA (*Hp*DprA) possesses only the central and the C-terminal domains (Ando *et al.*, 1999). Functional analysis of *Hp*DprA highlights the essential role of C-terminal domain in *H. pylori* natural transformation process.

In order to find the function of C-terminal domain in natural transformation process, an analysis of *Hp*DprA's 3D structure was performed. This structure result of the data compilation arising from the X-ray structure of the central domain dimer, the NMR structure of the C-terminal domain, and the structure of the full-length DprA dimer obtained in solution by SAXS. Putative interaction sites between *Hp*DprA and DNA were identified. Using a site directed mutagenesis approach, several mutants of *Hp*DprA were generated. Electrophoretic Mobility Shift Assay shows that the isolated C-terminal domain is not able to interact neither with ssDNA nor dsDNA, although its structural homology to winged helix DNA binding motifs. In contrast, the key residues of the central domain are crucial for both interactions. The cellular function of the C-terminal of *Hp*DprA stays to be elucidated.

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