PhD Thesis Award

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CRYO-EM OF ENVELOPED AND NON-ENVELOPED VIRUSES *IN SITU* AND *IN VITRO*

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Viruses have evolved to infect all domains of life – from bacteria to eukaryotes. The virus must encounter and bind a specific receptor on the cell's surface to start the infection. Then, the virus delivers its genetic material into the host cytoplasm. However, for most viruses, it is still unknown how the genome release mechanism is controlled at a molecular level. In my dissertation thesis I described structures of three viruses – bacteriophage P68 infecting *Staphylococcus aureus*, and rhinovirus 14 and echovirus 18 from genus Enterovirus infecting humans. The structure of bacteriophage P68 was solved by a combination of cryo-electron microscopy and X-ray crystallography. Based on the comparison of structures of phage P68 in different stages of the genome release, I proposed a mechanism of the cell entry. The results may lead to improved phage therapy and a better understanding of the assembly of bacteriophages from the family *Podoviridae* infecting gram-positive bacteria.

The rhinovirus-14-ICAM-1 structure was solved by cryo-EM to the resolution of 2.4 Å. I proved that the receptor ICAM-1 triggers a molecular switch inside the capsid, necessary for the virus to release its genome. Additionally, a structured part of the RNA genome interacting with capsid protein was identified. I proposed orchestrated steps triggered by binding of ICAM-1, which eventually result in uncoating of the viral genome. Along with the structure of the echovirus 18 expelling pentamers to release its genome, the structural analysis of rhinovirus 14-ICAM-1complex provides a seamless mechanism of initial stages of infection of Enteroviruses from the initial receptor binding to final genome release into the host cytoplasm. Our findings uncovered mechanisms of the initial steps of Enterovirus infection that could be targeted by antiviral drugs.

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