Application of Cryogenic Electron Microscopy (cryoEM) for Structural Biology on the Example of NavPaS Channel

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Human voltage-gated sodium (Nav) channels are essential for the proper function of the nervous and muscular systems and represent a key target for pharmaceutical drug development. Insect Nav channels serve as primary targets for novel insecticides. Structurally, Nav channels are composed of a central α-subunit—a single-polypeptide chain protein that forms four homologous pseudosubunits arranged around a central ion-conducting pore—along with an auxiliary regulatory β-subunit. Despite their great relevance to medical and agricultural applications, understanding of the structure and regulatory mechanisms of Nav channels remains limited.

Here, we presented structure of NavPas channel from American cockroach, which were studied by cryo-EM in lipid-protein nanodiscs. Application of cryo-EM allowed to obtain protein structure with resolution in order of angstroms, therefore in this work we reached a resolution of 2.9 Å for monomeric form of NavPaS structure. This resolution is enough for detailed characterisation of protein structure as well as for comparison with previous knowing structures of NavPaS. Another important achievement of current study is obtaining the first structure of dimeric form of NavPaS with overall resolution 7.1 Å. On this basis, an analysis of the NavPaS dimerization interface is carried out.

Usage of classical processing methods along with additional cryo-EM image processing technics has made it possible to characterize NavPaS channel in lipid-protein nanodiscs and reveal dimerization of NavPaS channel. The talk contains short description of the methods, which have been used in the study.

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