POSTER ABSTRACT PRESENTATIONS

SESSION TITLE: STRUCTURE OF MEMBRANE PROTEINS

DOI: 10.21103/IJBM.11.Suppl_1.P13

Abstract P-13: Structural Studies of Insulin Receptor-Related Receptor Ectodomain

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Background: The insulin receptor-related receptor (IRR) was originally discovered due to its high homology to the other family members (insulin receptor and insulin-like growth factor 1 receptor). We determined that IRR can be activated by mildly alkaline extracellular media and has typical features of the ligand-receptor interaction, including its specificity and dose-dependence. Since pH-sensitive properties of IRR are determined by its ectodomain; therefore, we chose as an option to study the soluble extracellular domain IRR.

Methods: The investigation carried out in Titan Krios 60-300 TEM/STEM (FEI, USA) CryoEM, equipped with direct electron detector Falcon II (FEI, USA) and Cs image corrector (CEOS, Germany), at an accelerating voltage of 300 kV. Data processing and 3D reconstruction were carried out using computing resources of the Federal Collective Usage Center Complex for Simulation and Data Processing for Mega-Science Facilities at NRC "Kurchatov Institute."

Results: The obtained 2D classifications of particles of the ectodomain IRR at a neutral pH form several 3D models. This indicates that the ectodomain has several possible conformations, which is consistent with our previously obtained data using SEC-SAXS and AFM. In the future, additional careful data processing is required, as well as studies of the IRR ectodomain in mildly alkaline pH.

Conclusion: In this study, we presented the structural characteristics of the IRR ectodomain obtained by CryoEM. These results are an important step towards understanding the mechanism of functioning of the IRR.

Key Words: receptor tyrosine kinases • insulin receptor-related receptor • CryoEM

This work was supported by the Russian Foundation for Basic Research (Grant No. 20-04-00959)

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International Journal of Biomedicine. 2021;11 Suppl 1: S16-17.

doi: 10.21103/IJBM.11.Suppl_1.P13

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