Coronaviruses Vaccines Development Based on Chimeric Proteins

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Session G: Small and Wide Angle X-ray Scattering Applied to Nano- and Biomaterials

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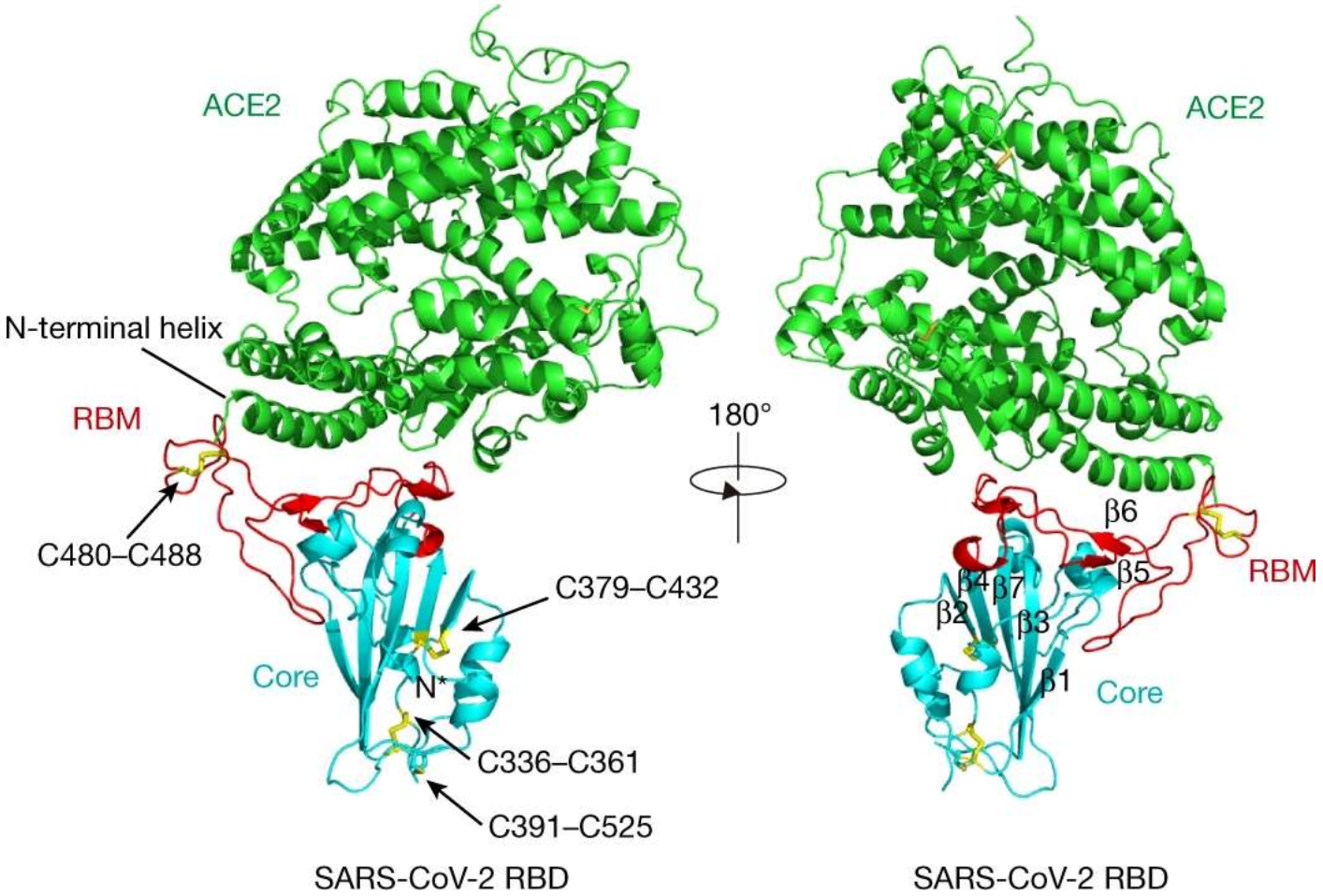
Abstract

The known antiviral vaccines based on ferritin-fused antigens are synthesized in the HEK (Human Embryonic Kidney cells) expression system, making them difficult for large-scale production. In this work, we present the potential vaccine based on Escherichia coli ferritin fused with a receptor-binding domain (RBD) of the spike glycoprotein from SARS-CoV-2 expressed and purified from E. coli cells. This chimeric protein is a potential perspective candidate for creating a platform for rapid development of vaccines against coronaviruses and other pathogens. Expression and purification from E. coli cells together with small-angle X-ray scattering experiments showed multimeric assemblies of these chimeric proteins. Additionally to characterize the nanoparticle we used computer molecular modeling, molecular dynamics simulations and quantum biochemical analysis which provide new information about the interaction driving the complex formation and stabilization as well as the type of interactions that support it. Besides, computational analysis may help in understanding of the best conformations and domains involved in the interactions which may help to engineer the enhanced complex.

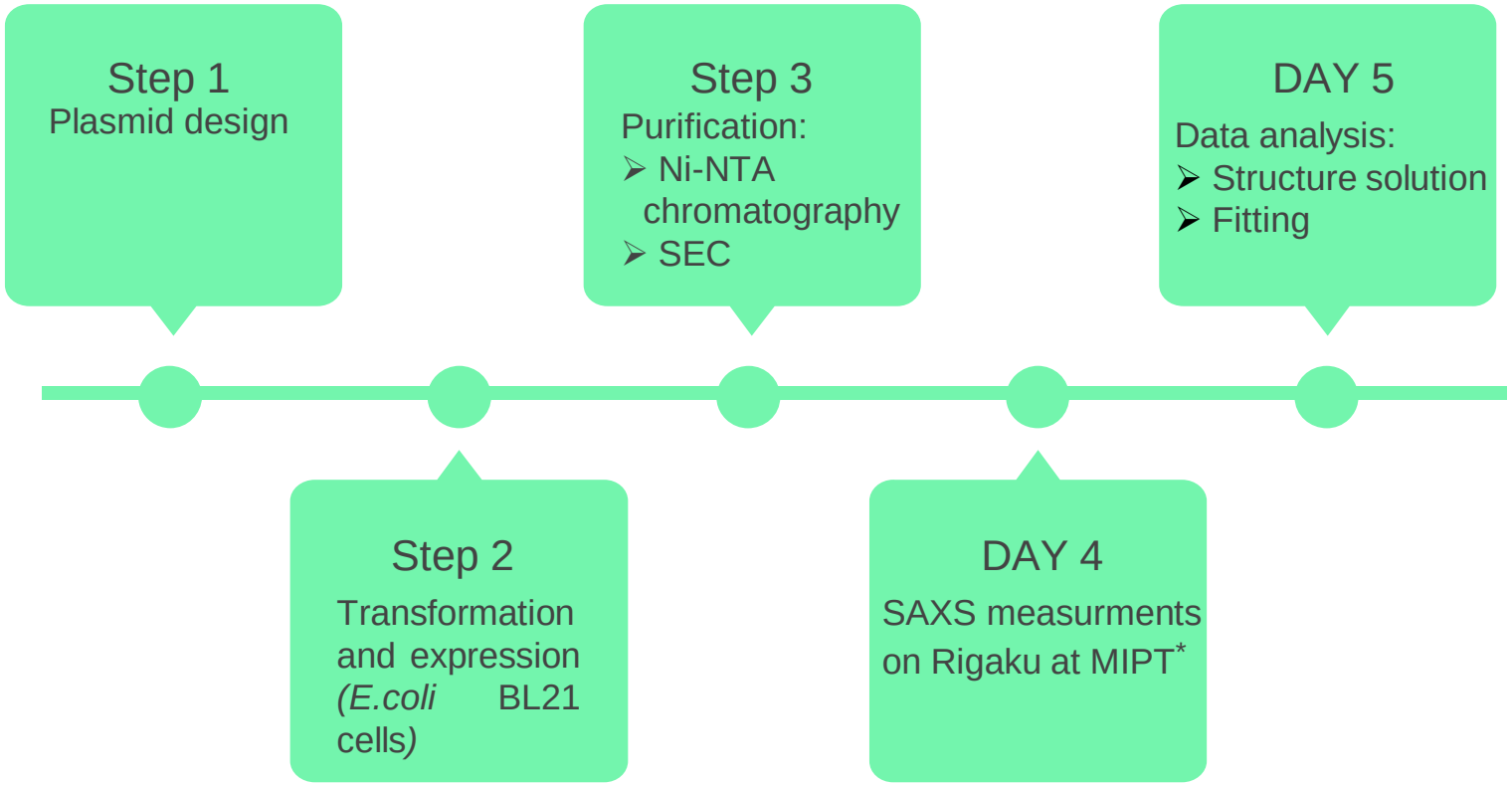
RBD as a target for vaccine



Overall structure of the SARS-CoV-2 RBD bound to ACE2. ACE2 is shown in green. The SARS-CoV-2 RBD core is shown in cyan and RBM in red. Disulfide bonds in the SARS-CoV-2 RBD are shown as sticks and indicated by arrows. The N-terminal helix of ACE2 responsible for binding is labelled.

Lan, Jun, et al. "Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor.“ Nature 581.7807 (2020): 215-220.

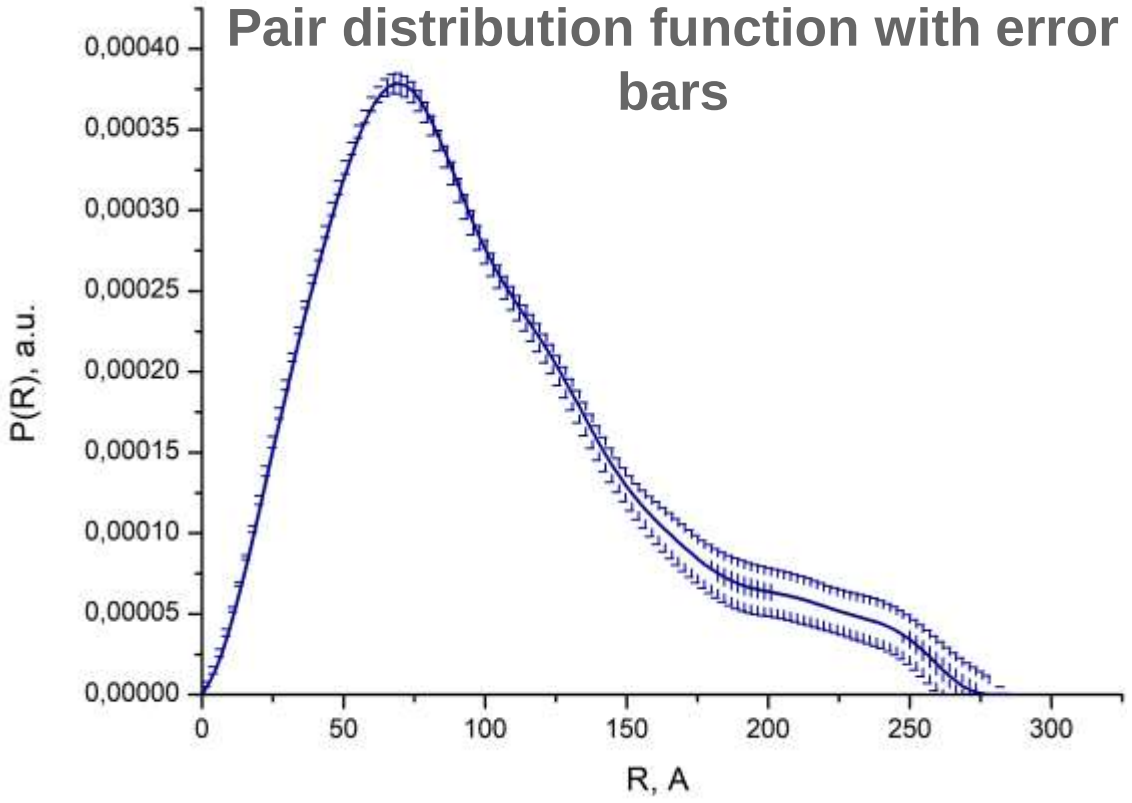
Scheme of the experiment



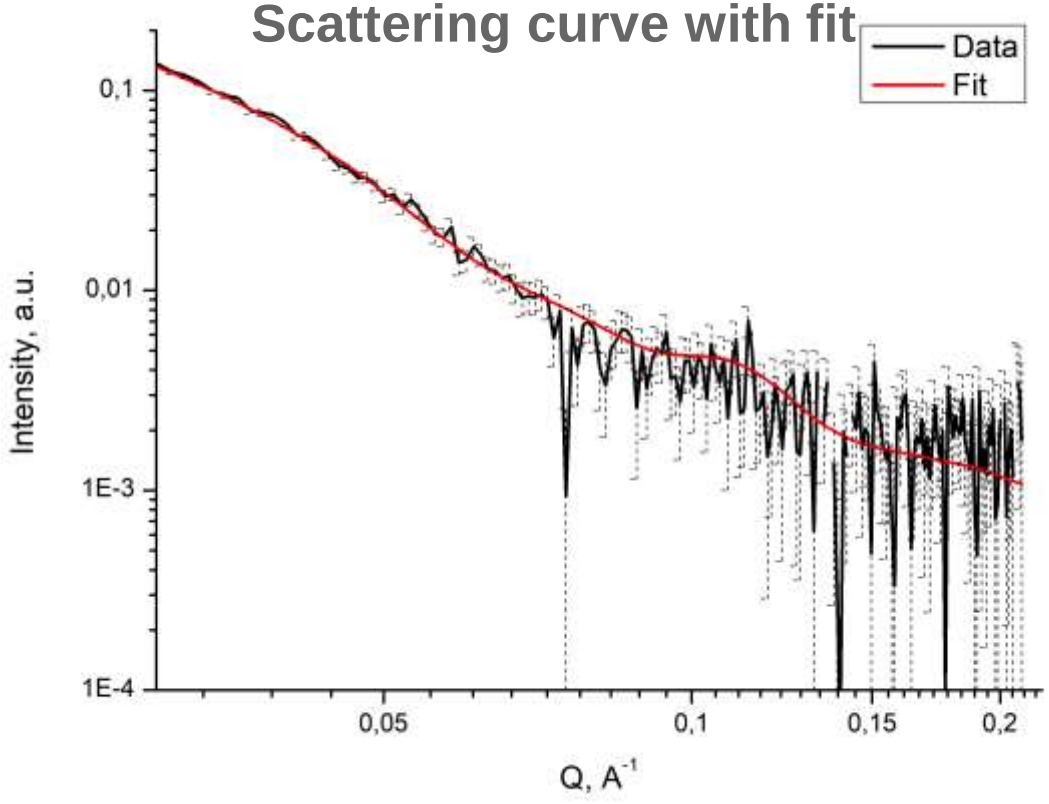
*Murugova, T. N., et al. "Low resolution structural studies of apoferritin via SANS and SAXS: the effect of concentration." J. Optoelectron. Adv. Mater 17.9-10 (2015): 1397-1402.

SAXS data

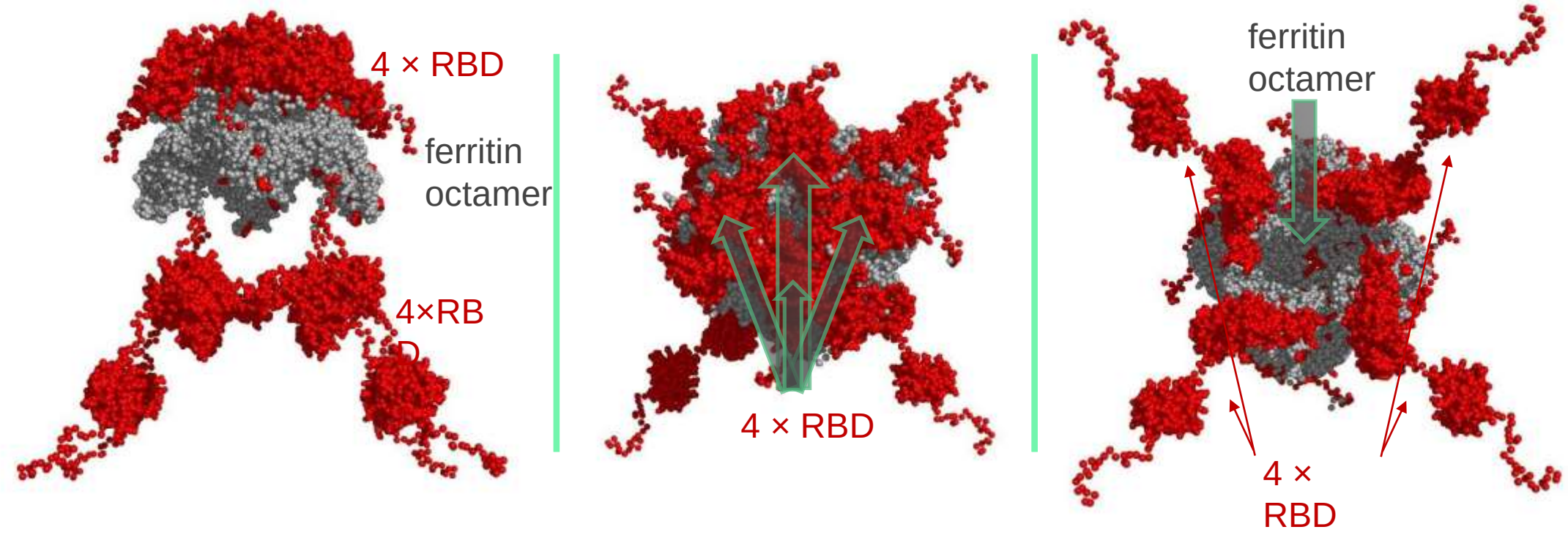
Pair distribution function with error bars



Scattering curve with fit

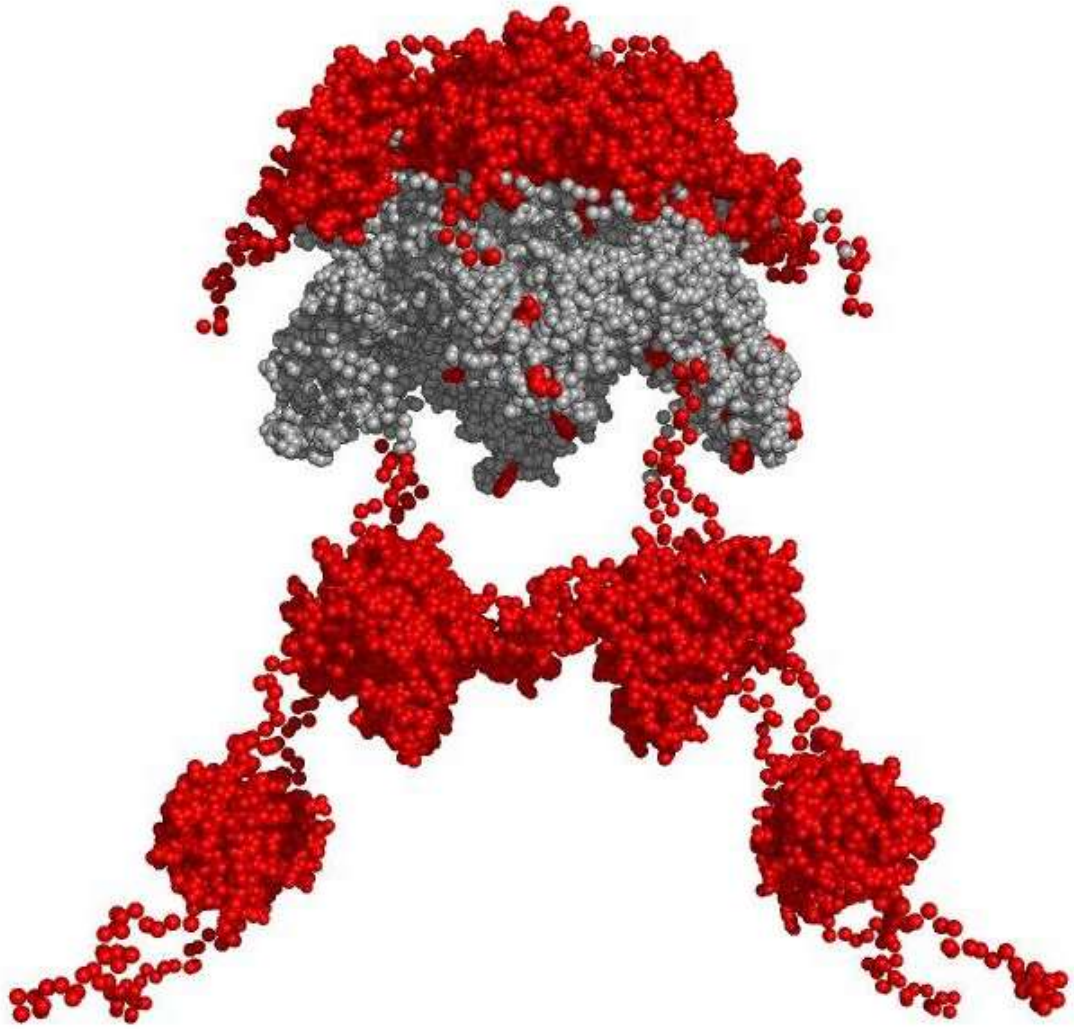


Obtained constructions



Results

- The protocol of expression and purification of recombinant chimeric proteins based on ferritin has been developed
- Low-resolution structure of ferritin-RBD complex has been obtained
- Ferritin subunits (with RBD) form octamer structure
- The model of the ferritin-RBD octamer well fits the experimental SAXS data



Thank you for your attention

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