Zn^{2+} and Cu^{2+} Interaction with the Recognition Interface of ACE2 for SARS-CoV-2 Spike Protein

Autorzy

Alessio Pelucelli

Massimiliano Peana

Bartosz Orzeł

Karolina Piasta

Elżbieta Gumienna-Kontecka

Serenella Medici

Maria Antonietta Zoroddu

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Streszczenie

The spike protein (S) of SARS-CoV-2 is able to bind to the human angiotensin-converting enzyme 2 (ACE2) receptor with a much higher affinity compared to other coronaviruses. The binding interface between the ACE2 receptor and the spike protein plays a critical role in the entry mechanismof the SARS-CoV-2 virus. There are specific amino acids involved in the interaction between the S protein and the ACE2 receptor. This specificity is critical for the virus to establish a systemic infection and cause COVID-19 disease. In the ACE2 receptor, the largest number of amino acids playing a crucial role in the mechanism of interaction and recognition with the S protein is located in the C-terminal part, which represents the main binding region between ACE2 and S. This fragment is abundant in coordination residues such as aspartates, glutamates, and histidine that could be targeted by metal ions. Zn2+ ions bind to the ACE2 receptor in its catalytic site and modulate its activity, but it could also contribute to the structural stability of the entire protein. The ability of the human ACE2 receptor to coordinate metal ions, such as Zn2+, in the same region where it binds to the S protein could have a crucial impact on the mechanism of recognition and interaction of ACE2–S, with consequences on their binding affinity that deserve to be investigated. To test this possibility, this study aims to characterize the coordination ability of Zn2+, and also Cu2+ for comparison, with selected peptide models of the ACE2 binding interface using spectroscopic and potentiometric techniques.

Słowa kluczowe

ACE2, peptides, zinc complexes, copper complexes, metal interaction, potentiometry, spectroscopy, NMR

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