Proceedings International
Platinum Open Access Journal (ISSN 2668-6384)

Proceedings, Abstract
Volume 3, Issue 5, 2021, 4
https://doi.org/10.33263/Proceedings35.004

Effect of Cysteine Oxidation of Some Protein Structures by Cold Atmospheric Plasma: Insights from Atomistic Simulations †

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† International Conference on Advanced Materials for Next Generation Applications, 29th – 30th September, 2021 (AMNGA-2021)

Received: 10.09.2021; Revised: 20.09.2021; Accepted: 21.09.2021; Published: 29.09.2021

Abstract: One of the important amino acid residues that can play an essential role in the stability of protein structures is cysteine which can easily make disulfide bridges with other thiol groups and H-bonds with other amino acids. Moreover, cysteine is highly reactive and can be easily oxidized to cysteic acid by reactive oxygen species (ROS) generated inside the body or applied by cold atmospheric plasma. In general, intracellular ROS, such as H_2O_2, can oxidize 5% of Cys residues of proteins to cysteic or sulfunic acid, and this effect is enhanced under oxidative stress. Plasma oxidation of amino acids in proteins, especially oxidation of the thiol groups of Cys residues, can disturb the normal function of some antioxidant enzymes. Indeed, ROS-induced protein modifications can alter the protein structure and disrupt their function. In this presentation, we will describe the effect of Cys oxidation to cysteic acid on inhibition of xC- antiporter using molecular dynamics simulations. The xC- antiporter is responsible for translocation of cystine (CYC, i.e., the oxidized dimeric form of Cys) from the extracellular milieu to inside the cell, and for sending out glutamate (Glu) from the intracellular fluid to outside the cell. The inhibition of this antiporter in cancer cells may lead to Cys starvation, suppressing cell growth. Moreover, our new findings reveal that oxidation of Cys residues would be effective in viral infection of the human body by SARS-CoV-2. The binding of SARS-CoV-2 S-glycoprotein to cell receptors is vital for the entry of the virus into cells and subsequent infection. ACE2 is the main cell receptor for SARS-CoV-2, which can attach to the C-terminal receptor-binding domain (RBD) of SARS-CoV-2 S-glycoprotein. GRP78 receptor also plays an anchoring role, which attaches to the RBD and increases the chance of other RBDs to bind to ACE2. Although high levels of reactive oxygen and nitrogen species (RONS) are produced during viral infections, it is not clear how they affect the RBD structure and its binding to ACE2 and GRP78. In this presentation, the effect of oxidation of the highly reactive Cys amino acids of the RBD on its binding to ACE2 and GRP78 is considered. Besides, the Cys oxidation is effective on conformational changes of SARS-CoV-2 S-glycoprotein, which is also considered in this presentation. To engage a host cell receptor, the RBD undergoes hinge-like conformational movements that transiently hide or expose the determinants of receptor binding. Oxidation of some of Cys residues makes the transition from hidden to exposed conformation more difficult, showing the important role of the Cys oxidation on viral infections.

Keywords: SARS-CoV-2; Cysteine Oxidation; plasma

Funding

This research received no external funding.

Acknowledgments

This research has no acknowledgment.

Conflicts of Interest

The authors declare no conflict of interest.