Poster Abstract Submission

Name	Nesreen Al-Khofash
Position	PhD candidate
Organization	UAEU
Email	201990178@uaeu.ac.ae
Phone Number	00971561296625
Research Title	ACE2 variation and trafficking in the pathogenesis of SARS-CoV-2

Abstract:

Background: COVID-19 pandemic caused by SARS-CoV-2 infection, is initiated by the entry of the virus into cells through angiotensin-converting-enzyme-2 (ACE2) receptor, that is widely distributed in the body. Manipulating cell surface expression of ACE2 might represent a potent therapeutic target of the infection. Objectives: We aim 1) to elucidate the cellular trafficking pathways of WT ACE2 and various selected human missense variants, 2) investigate their degradation pathways and the potency of some molecular modulators and inhibitors to block or slow down ACE2 expression and 3) assess ACE2 response to the dissociation of “ACE2-B0AT Super-complex”. Methods: In-silico prediction tools were used to investigate the effect of the selected missense variants on ACE2 structure. Biochemical and immunofluorescnece assays were used to charachetrize the glycosylation profiles and subcellular trafficking of WT-ACE2 and the studied variants, also analyzing the effect of selected molecular modulators of traansportation. Nimelusde was used to dissociate B0AT-ACE2, where B0AT1 will be later knockedout using Crispr/Cas9. Results: ACE2 missense variants distributed all over the receptor’s domains assessed by in silico prediction tools and biochemical assays display no significant effect on ACE2 expression, intracellular trafficking, and targeting to the plasma membrane. Once treated with several modulators selected for blood pressure regulation, like statins, WT- ACE2 is displaying normal maturation and subcellular localization profiles. Connclusions: Finding that none of the variants display an effect on ACE2 trafficking and expression, our study confirms that ACE2 is intolerant to loss of function and more investigations are required to address its role in COVID-19 progression.