Reunião Anual do INCT-FCx - 2022

De 26 a 29/Outubro de 2022,
Hotel Estância Atibainha, Nazaré Paulista/SP

Binding free energies of the antiviral peptide ATN-161 with integrin $\alpha_5\beta_1$ and target of SARS CoV-2

Rudielson Santos Silva, Lucas Miguel Pereira Souza, Rayla Kelly Magalhães Costa,

Felipe Rodrigues Souza e André Silva Pimentel

Department of Chemistry, Pontifical Catholic University of Rio de Janeiro, Rio de Janeiro, RJ 22453-900 Brazil

Abstract: ATN-161 is a small anti-integrin peptide that has been extensively studied for fighting cancer [1], and has recently demonstrated activity against SARS-CoV-2 in vitro and in vivo [2][3]. Studies indicate that integrins are alternative routes for virus entry into cells[4], but few studies demonstrate how this molecule binds to α5β1 integrin. This work aimed to study the binding affinities and interactions of the ATN-161 pentapeptide with the α5β1 integrin and potential targets against Sars cov-2. We chose the Integrin α5β1 open and closed conformation, SARS-CoV-2 protein S variant omicron linked to hACE2, and SARS-CoV-2 3CL protease (M^{PRO}) as targets. We used molecular docking and molecular dynamics studies to determine the stability of the system and the umbrella sampling method to obtain the binding energy between ATN-161 and each target. Our results showed that ATN-161 can bind α5β1 integrin in both its active and inactive form, weakly binds to hACE2-complexed omicron variant S protein, and shows a high binding affinity for M^{PRO}.

Key-words: coronavirus, integrin, Umbrella sampling method, energy binding.
Support: CAPES, CNPq, FAPERJ, INCT-FCx.

References:

[1] P. Khalili *et al.*, "A non-RGD-based integrin binding peptide (ATN-161) blocks breast cancer growth and metastasis in vivo" (2006), *Mol. Cancer Ther.* Vol. 5. P 2271-2280

[2] B. J. Beddingfield *et al.*, "The Integrin Binding Peptide, ATN-161, as a Novel Therapy for SARS-CoV-2 Infection," (2021), *JACC Basic to Transl. Sci.* vol. 6. p 1-8.

[3] N. Amruta *et al.*, "In Vivo protection from SARS-CoV-2 infection by ATN-161 in k18-hACE2 transgenic mice," (2021), *Life Sci.* vol. *284*

[4] D. Nader et al, "A dual-receptor mechanism between integrins and ACE2 widens SARS-CoV-2 tissue tropism," (2022), *bioRxiv.*