Stability and affinity analysis of commercial anti-TNF-α antibodies: *in-silico* study

M Tabasinezhad[a],H Rahimi[b], H Ghaedi[c], E Omidinia[d]* and F Mahboudi[a]*

[a] Biotechnology Research Center, Pasteur Institute of Iran,Tehran, Iran

[b] Molecular Medicine Department, Pasteur Institute of Iran, Tehran, Iran

[c] *Department of Medical Genetics, Faculty of Medicine, Shahid Beheshti University of Medical Sciences,Tehran, Iran.*

[d] Genetics & Metabolism Research Center, Pasteur Institute of Iran,Tehran, Iran

Correspondence and requests for materials should be addressed to E.O. (email:eomid8@gmail.com) or F.M (email: mahboudif@cinnagen.com)

Abstract: Computational methods are universally established as important tools for the invention of biotherapeutic drugs, helping with tasks such as optimizing affinity for a target, minimizing off-target effects and optimizing pharmacokinetic properties [1].In these contexts, the stepwise *in silico* methods are generally not considered substitutes for empirical testing, but rather a way to generate testable hypotheses, helping to interpret and guide experiments [2]. In the recent study, we aimed to analysis of anti-TNF-α antibodies [3] to find difference in the properties of the antibodies and find out more insight to engineering of them for further *in-silico* and in vitro studies. For achieving the aim, we found 3D structure of adalimumab, infliximab and certulizumab. In addition, structures of golimumab were modeled by Moodeler.9 Package. Following, all structures were docked with TNF-alpha and binding pocket of the complexes were analyzed by ligplot. Stability of the antibodies was assessed by molecular dynamic simulation with Gromacs.5 package. Our data revealed the complex of antibodies and TNF-α have significantly difference in their RMSD and stability during 15 ns. Also, the antibodies revealed different binding pocket to interaction by the antigen result in difference hydrogen bonds, electrostatic and van der waal energy. In addition, the various energies at binding pocket lead to modify binding and affinity of each antibody to TNF-α. The dissimilarity in the properties of the antibodies, play key role to their efficacy of the drugs in clinical studies. In conclusion, computational methods are effective strategies to analysis structures, dynamic and properties of antibodies. Additionally, the prediction methods are potential to determine characterization of antibodies and definite if the features required to further optimization by *in-silico* and experimental studies.

Key word: TNF-α; antibody; in-silico; stability; affinity

References:

[1] D Kuroda, H Shirai, MP Jacobson, H Nakamura. Computer-aided antibody design. J. Protein Engineering, design and selection. Protein Eng Des Sel., 25 (2012) 507-522.

[2] R Barderas, J Desmet, P Timmerman, R Meloen, JI Casal. Affinity maturation of antibodies assisted by in silico modeling. J.Proceedings of the National Academy of Sciences. PNAS., 105 (2008) 9029-9034.

[3] D Shealy,S Visvanathan. Anti-TNF antibodies: lessons from the past, roadmap for the future. J. Handbook of Experimental Pharmacology. Handb Exp Pharmacol., 181 (2008) 101-129