

Mutational Analysis of Interleukin-11 and its Consequences on Cancer and COVID-19 Related Cytokine Storm -An Extensive Molecular Dynamics Study

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Abstract

Interleukin-11 is a pleiotropic cytokine that is known to play an important role in the progression of various forms of cancer by modulating the survival and proliferation of tumour cells. IL11 also demonstrates a structural homology to IL6 - the predominant cytokine involved in COVID-19. This makes IL11 a potential therapeutic target in both diseases. This study aimed to evaluate the impact of two mutations- R135E and R190E on the stability of IL11. Any changes in the interaction of IL11 with its receptor IL11R α , induced by the two mutations were also determined with the help of techniques such as molecular modelling, molecular docking, and molecular dynamics simulations. Our analysis revealed that the two mutations cause a small decrease in the overall stability of IL11, which was evident by the increased atomic fluctuations in the mutated regions. Moreover, mutation R135E led to an increase in the binding affinity of IL11 with IL11R α and the formation of a more stable complex in comparison to the wild-type protein and its receptor. Mutation R190E led to the formation of a less stable complex than the wild-type which suggests a decrease in the binding affinity between IL11 and IL11R α .

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