Homology modeling and domain analysis studies on (CHRNA5) lung cancer protein using bioinformatics methods

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Abstract
Globally, lung cancer is the most common cancer among men in terms of both incidence and mortality and among women has the third highest incidence, and is second after breast cancer in mortality. The aim of the research work is to find out the potential mutation gene involved in human lung cancer. Based on literature studies, we identified the potential gene candidate for drug docking studies. Our protein modeling results show the molecular structural regions present in CHRNA5 protein. We also identified the potential domain regions of the protein sequences of the CHRNA5 protein. The results clearly elucidate that the modeled protein candidate acts as a very good candidate for introducing the various novel chemical molecules.

Keywords: Lung, CHRNA5 protein and Drug Docking studies

INTRODUCTION
Worldwide, lung cancer is the most common cancer among men in terms of both incidence and mortality, and among women has the third highest incidence, and is second after breast cancer in mortality. In 2012, there were 1.82 million new cases globally, and 1.56 million deaths due to lung cancer, representing 19.4% of all deaths from cancer. The highest rates are in North America, Europe and East Asia, with over a third of new cases in 2012 in China. Rates in Africa and South Asia are much lower [1]. The population segment most likely to develop lung cancer is people aged over 50 who have a history of smoking. In contrast to the mortality rate in men, which began declining more than 20 years ago, women's lung cancer mortality rates have been rising over the last decades, and are just recently beginning to stabilize [2]. In the USA, the lifetime risk of developing lung cancer is 8% in men and 6% in women [3].

Methodology
In this present research investigation, we focus on protein modeling and domain prediction of human lung cancer protein. Based on the literature studies (OMIM and PMC), the target CHRNA5 was identified and the sequence was retrieved from UNIPORT database. The selected protein sequence was modeled using CPH 3.0 model server [4] in order to convert the sequence to 3D form and validation of the modeled protein was done using Rapper server. Finally we used DLV-SVM [5] server for Domain prediction studies of CHRNA5 protein.

RESULTS AND DISCUSSION

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Fig 2. Domain prediction (DLM-SVM server)

![Result of domain linker prediction by DLM-SVM server](image)

<table>
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<th>Candidate Regions</th>
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Domain regions of CHRNA5 protein

Fig 3. Domain prediction (DLM-SVM server)

![Plot](image)

Domain regions of CHRNA5 protein

Fig 4. Protein modeling - CHRNA5 (Discovery studio software)

![Secondary structure view of CHRNA5](image)

Secondary structure view of CHRNA5
Nicotinic acetylcholine receptors (nAChRs), such as CHRNA5, are members of a superfamily of ligand-gated ion channels that mediate fast signal transmission at synapses. The nAChRs are thought to be (hetero)pentamers composed of homologous subunits. The length of the selected protein target (CHRNA5) is 460 aa which is retrieved from uniport database and which is located at the 15th chromosome [6].

In separate large genomewide association studies to find variants associated with risk of lung cancer identified strong association with variation in the nicotinic acetylcholine receptor gene cluster on chromosome 15q24. These studies identified 2 single-nucleotide polymorphisms (SNPs) in strong linkage disequilibrium, one in the CHRNA5 gene (D398N; 118505.0001) and the other in the CHRNA3 gene (118503.0001), as representing the strongest associations. In Fig (2 and 3) shows the Domain regions of the CHRNA5 protein [7]. In Fig (4 and 5) represents that 3D structure of the CHRNA5 protein in discovery studio software.

**CONCLUSION**

In this research investigation, we modeled the target protein (CHRNA5) and then identified the domain regions of the target protein. Thus we conclude that the modeled protein and the identified domain regions are potential candidates for drug designing and docking studies. This insilico research investigation can be extended in future in pharmacological studies.
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ACKNOWLEDGEMENT
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CONFLICT OF INTEREST
No conflict of interest.

REFERENCES