Exploring lncRNAS in Alzheimer's Disease

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Abstract

Alzheimer's disease (AD) is a progressive and chronic neurodegenerative disorder, recognized as a multifactorial disease, which limits pharmacological options by the multiple pathways involved in the pathogenesis. To date there are no effective therapies for AD, only the symptoms are treated. Recent studies have shown that non-coding RNAs (ncRNAs), including long-non coding RNAs (lncRNAs), are involved in the pathogenesis of AD. It is believed that there is a strong relationship between the structure of lncRNAs and the functions they carry out. However, due to lack of conservation in its primary nucleotide sequence, functional studies of lNcRNAs with the objective of developing new therapeutic methods imply a challenging process. Since the experimental methods for obtaining tertiary structures are not easy to perform, in silico approaches are valuable tools that contribute to this process of understanding the disease and structural bioinformatics can contribute to the prediction of these structures. Therefore, the goal of this project is to predict the tertiary structures of lncRNAs involved in AD. In this first step, we begin by modeling the structure of lncRNA BACE1-AS, which is highly expressed in AD patients. The unit described by Faghihi et al. (2008) (NR_037803.2) was used. Secondary structure prediction was performed using the Mfold software (Zuke, 2000) and the tertiary structure was modeled using the 3dRNA v2.04 software (Wang and Xiao, 2017). The analysis of tertiary structures was performed using MolProbity (Chen et al., 2010) and Pymol (Delano, 2002) softwares. 29 secondary structures were obtained and the selected model presented a value of -240.61 kcal / mol. BACE1-AS primary and secondary structures were used for the tertiary structure modelling. Five models were successfully generated. After analysis by MolProbity and visual analysis, a model was selected for further studies such as normal mode analysis.

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