Letter to Editor

Disrupted-in-schizophrenia 1 Mutation Prone Positions: A Pathogenesis of Schizophrenia

Sir,

The causes of schizophrenia remain unclear. McClellan *et al*.[1] proposed that schizophrenia was a common disease caused by multiple rare alleles. The role of Disrupted-in-Schizophrenia 1 (DISC1) in major mental disorder as well as schizophrenia was confirmed by Hennah *et al*.[2] The understanding of the role that DISC1 has in neuronal development and cell signaling has been much enhanced by the determination of DISC1 binding partners, an appreciation of DISC1's expression during development and functional studies using ribonucleic acid interference. In modern biomedical science, bioinformatics approach helps prediction of protein nanostructure and function which is necessary for deriving the genomics and proteomics knowledge on disorders. This analysis can be done based on advancement of bioinformatics and the author used this concept to predict specific positions for probable peptide motifs in the DISC1's amino acid sequence. The standard data mining process in bioinformatics was performed using the standard proteomics server of the Swiss Institute of Bioinformatics (SIB), Expert Protein Analysis System (ExPASY). The amino acid sequence of DISC1 was the focused searched sequence. Then a standard bioinformatics technique namely GlobPlot, a web service that allows the user to plot the tendency within the query protein for order/globularity and disorder was used for identification for the weak linkage in derived DISC1. From prediction process, specific positions 1-28, 44-77, 126-143, 179-206, 221-238, 248-262, 287-325, 423-433 and 725-740 are assigned as the motif positions that resistant to mutation within DISC1.

In this work, many positions, some known and the other unknown, were resulted from GlobPlot processing. Some useful information for further possible researches on the diagnosis for DISC1 abnormalities can be derived. The relationship of the location of the identified motifs to the location of binding domains on the DISC1 protein, especially specific sites for proteins like Nudel, Fez, Lis1[3] can be seen. The possible mutation in these areas might alter the natural pathophysiology of schizophrenia. It can be expected that new possible mutations might confer higher risk to schizophrenia. The possible mechanism might be due to neurodevelopmental effects from new possible mutations. Indeed, there are some reports confirming that the new mutations within DISC1 can bring significant neurodevelopmental effects.[4-5] Derived information will be helpful for further work such as developing animal models with assigned new mutate or developing new computational models to test new possible DISC1 mutations.

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