Scaffolding protein

Scaffolding proteins represent an evolutionary solution to controlling the specificity of information transfer in intracellular networks. They are highly concentrated in complexes located in specific subcellular locations. One of these complexes is the postsynaptic density of the excitatory synapses. There, scaffolding proteins regulate various processes related to synaptic plasticity, such as glutamate receptor trafficking and signalling, and dendritic structure and function. Most scaffolding proteins can be grouped into 4 main families: discs large (DLG), discs-large-associated protein (DLGAP), Shank and Homer. Owing to the importance of scaffolding proteins in postsynaptic density architecture, it is not surprising that variants in the genes that code for these proteins have been associated with neuropsychiatric diagnoses, including schizophrenia and autism-spectrum disorders. Such evidence, together with the clinical, neurobiological and genetic overlap described between schizophrenia and autism-spectrum disorders, suggest that alteration of scaffolding protein dynamics could be part of the pathophysiology of both. However, despite the potential importance of scaffolding proteins in these psychiatric conditions, no systematic review has integrated the genetic and molecular data from studies conducted in the last decade. This review has the following goals: i) to systematically analyze the literature in which common and/or rare genetic variants (single nucleotide polymorphisms, single nucleotide variants and copy number variants) in the scaffolding family genes are associated with the risk for either schizophrenia or autism-spectrum disorders; ii) to explore the implications of the reported genetic variants for gene expression and/or protein function; and iii) to discuss the relationship of these genetic variants to the shared genetic, clinical and cognitive traits of schizophrenia and autism-spectrum disorders [1)].

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Soler J, Fañanás L, Parellada M, Krebs MO, Rouleau GA, Fatjó-Vilas M. Genetic variability in scaffolding proteins and risk for schizophrenia and autism-spectrum disorders: a systematic review. J Psychiatry Neurosci. 2018 May 28;43(4):170066. doi: 10.1503/jpn.170066. [Epub ahead of print] PubMed PMID: 29808791.