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High disease burden in human synaptic protein complexes identified by proteomics and bioinformatics

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Synapses are fundamental components of brain circuits as they mediate neuronal communication. Synapses are classified according to the neurotransmitter they use. Of all synapse types those using glutamate have been the most extensively studied at the proteomic level. The post synaptic proteome of these synapses is organized into very large multi protein complexes of which the most outstanding is the post synaptic density (PSD) containing hundreds of different proteins. We have proteomically characterized for the first time the human PSD and the protein complex associated to MAGUKs, a family of adaptor proteins that are major organizers of the glutamatergic post synaptic proteome. We have developed methods to estimated protein complex stability in human postmortem tissue. Using these approaches we have shown that these structures can be efficiently isolated form biopsy but also from post-mortem cortex. Directly characterizing human synapses and their multi protein complexes from post-mortem tissue will be essential to understanding disease mechanisms. Overall we have identified around 1500 proteins from the human PSD and 300 from the human complex of MAGUK proteins. Using bioinformatics and data mining tools we have established that this supra-molecular structures carry a very high disease burden, as many of its components are involved in disease. PSD proteins are disrupted in over 100 neurological and psychiatric diseases. Furthermore, polygenic mutations converge on post synaptic complexes in schizophrenia, autism spectrum disorders and intellectual disability.

Biography

Alex Bayes has received his PhD on Biochemistry in 2005 by the Universitat Autònoma de Barcelona, Spain then he performed a Post-doctoral stay between 2006 and 2012 at The Sanger Institute (Cambridge, UK) and briefly at Edinburgh University (UK) with Professor Seth GN Grant. Since May 2012, he is independently running his own research laboratory at the Biomedical Research Institute Sant Pau in Barcelona. His lab main challenge is to understand the dynamics of the synaptic proteome in relation to synaptic function. He is also interested in studying how dysfunction of synaptic molecular machines can cause cognitive disorders especially intellectual disability.

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