Oligodendrocyte precursor cell dysfunction linked to schizophrenia: from mechanisms towards new therapeutic strategies (OPCphrenia)

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Alterations of inhibitory interneurons and oligodendrocytes, the exclusive cell responsible for myelin production in the brain, have been directly implicated in schizophrenia pathophysiology. However, we do not yet understand to what extent the dysfunctions of these cells are related in the context of schizophrenia.

Our consortium partners have recently discovered a critical form of communication between interneurons and oligodendrocyte precursor cells (OPCs), the obligate progenitor of oligodendrocytes. Moreover, we have also found that OPCs derived from schizophrenia patients carrying a defined familial genetic risk variant have impaired function. Therefore, we propose that schizophrenia is likely to be, at least in part, an OPC disease ("OPCphrenia") arising from aberrant interneuron-OPC signaling. In this proposal, we aim to carefully dissect interneuron-OPC communication and investigate potential therapeutic rescue strategies for aberrant schizophrenia-related OPC dysfunction by re-balancing the levels of interneuron-secreted factors. We will have assembled a strong multi-disciplinary team combining expertise in developmental neurobiology, neurophysiology, myelination and (pre)clinical neurobiology of psychiatric disorders, with considerable preliminary data to support our approach. This project leverages novel methodological advances to improve the understanding of schizophrenia pathophysiology and identify new molecular targets for future therapeutic intervention.