GABAergic synapses on oligodendrocyte precursors: characterization and role of synaptic components in the postnatal cerebellum

E. Boda*[1,2], E. Frola*[1], G. Pregno*[1], R. Barrile[1,2], G. Serra[1], M. Sassoè°[1], A. Buffo°[1,2]

[1]Dept. of Neuroscience, University of Turin, Italy; [2]Neuroscience Institute Cavalieri Ottolenghi (NICO), University of Turin, Italy

Neuronal activity influences the timing of oligodendrocyte precursor (OP) differentiation and myelination during the early postnatal life. Recent work has suggested that such modulation involves synaptic contacts established between neurons and OPs. While the molecular composition and the role of glutamatergic neuron-to-OP synapses have been thoroughly investigated, the source, architecture and function of the GABAergic contacts remain largely obscure. To elucidate these issues, we characterized the repertoire of GABAergic synaptic molecules expressed by OPs in the postnatal (P7 to P40) cerebellum by *in vivo* high-resolution morphological techniques and gene expression analysis on cells acutely isolated from the mouse nervous tissue. This analysis revealed that postnatal OPs express high levels of GABA-A receptor subunits, as well as scaffold proteins and cell-adhesion molecules normally associated to the postsynaptic specialization of inhibitory synapses in neurons. During the first postnatal weeks GABAergic synaptic appositions on OPs were found in both the granule cell layer and the molecular layer of the cerebellar cortex, while the white matter lacked such neuron-to-OP contacts. Moreover, pharmacological blockade of GABA-A receptors in cerebellar organotypic cultures altered the expression levels of myelin-associated genes, indicating that modulation of the GABAergic tone (either directly on OPs, or mediated by changes in global circuit activity) affects OP maturation. To further understand the function of GABAergic synapses in the regulation of OP physiology, we are currently generating a conditional knockout mouse line to selectively delete GABA-A receptors from OPs and evaluate the effect of their ablation *in vivo*. Results of this work clarify the molecular composition of GABAergic contacts in OPs and extend the current knowledge on mechanisms regulating OP maturation. Moreover, they can provide insights into the pathogenesis of developmental disorders and pathological conditions (e.g. schizophrenia, stroke and multiple sclerosis) where alteration of synaptic inhibition is accompanied by myelination/remyelination defects.