$P2Y_{12}$ Receptor on the Verge of a Neuroinflammatory Breakdown

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In the CNS, neuroinflammation occurring during pathologies as amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) is the consequence of an intricate interplay orchestrated by various cell phenotypes. Among the molecular cues having a role in this process, extracellular nucleotides are responsible for intercellular communication and propagation of inflammatory stimuli. This occurs by binding to several receptor subtypes, defined P2X/P2Y, which are widespread in different tissues and simultaneously localized on multiple cells. For instance, the metabotropic $P2Y_{12}$ subtype is found in the CNS on microglia, affecting activation and chemotaxis, on oligodendrocytes, possessing a hypothesized role in myelination, and on astrocytes. By comparative analysis, we have established here that $P2Y_{12}$ receptor immunolabelled by antibodies against C-terminus or second intracellular loop, is, respectively, distributed and modulated under neuroinflammatory conditions on ramified microglia or myelinated fibers, in primary organotypic cerebellar cultures, tissue slices from rat striatum and cerebellum, spinal cord sections from symptomatic/end stage SOD1-G93A ALS mice, and finally autoptic cortical tissue from progressive MS donors. We suggest that modulation of $P2Y_{12}$ expression might play a dual role as analytic marker of branched/surveillant microglia and demyelinating lesions, thus potentially acquiring a predictive value under neuroinflammatory conditions as those found in ALS and MS.