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21238 | Regulation of CD47 expression by interferon-gamma under chronic Methamphetamine exposureTitle

Rodrigues, João, Addiction Biology, i3S-Instituto de Investigação e Inovação em Saúde, Universidade do Porto (UP), IBMC - Instituto de Biologia Molecular e Celular, UP, FMUP - Faculdade de Medicina da Universidade do Porto, Portugal

Bravo, Joana, Addiction Biology, i3S-Instituto de Investigação e Inovação em Saúde, Universidade do Porto (UP), IBMC - Instituto de Biologia Molecular e Celular, UP, ICBAS - Instituto de Ciências Biomédicas de Abel Salazar, UP; Escola Superior de Saúde, Politécnico do Porto, Portugal

Andrade, B. Elva, IBMC - Instituto de Biologia Molecular e Celular, UP; ICBAS - Instituto de Ciências Biomédicas de Abel Salazar, UP; Escola Superior de Saúde, Politécnico do Porto, Immunobiology, i3SInstituto de Investigação e Inovação em Saúde, Universidade do Porto (UP), Portugal

Canedo, Teresa; Addiction Biology, i3S-Instituto de Investigação e Inovação em Saúde, Universidade do Porto (UP), IBMC - Instituto de Biologia Molecular e Celular, UP, Portugal

Azevedo, Maria, Advanced Light Microscopy Scientific Platform, i3S-Instituto de Investigação e Inovação em Saúde, Universidade do Porto (UP), Portugal

Summavielle, Teresa, Addiction Biology, i3S-Instituto de Investigação e Inovação em Saúde, Universidade do Porto (UP), IBMC - Instituto de Biologia Molecular e Celular, UP, Escola Superior de Saúde, Politécnico do Porto, Portugal

Abstract

Exposure to methamphetamine (Meth), a highly addictive widely used psychostimulant, is classically associated with damage to neuronal terminals, but its neurotoxicity can also be mediated via activation of the neuroinflammatory response. Microglia, the resident immune cells of the brain, become highly activated and increase the release of proinflammatory mediators upon exposure to Meth. However, their role in Meth-associated neurotoxicity is still not sufficiently understood. Data from our lab shows that, in the hippocampus, chronic Meth administration leads to microglia homeostasis dysregulation, synapse dysregulation, and downregulation of cluster-differentiation 47 protein (CD47). The crosstalk between CD47 and its receptor, signal regulatory protein α (SIRPα), is an important “don’t eat me signal” that inhibits phagocytosis. CD47 has been shown to protect synapses from excessive microglia-mediated pruning during development and neurodegeneration. Of note, in cancer cells CD47 expression is modulated by interferon-gamma (IFN-γ). Consistently, after chronic Meth, we observed a significant decrease of meningeal T cells, and a decrease in the production of IFN-γ by these cells. Here we aim to clarify if IFNγ is regulating CD47 in the brain after chronic Meth administration, and consequently regulating synaptic pruning, using IFNγKO mice and wild-type mice injected with recombinant IFNγ *via* stereotaxic surgery. Preliminary results indicate that IFNγ/CD47 does not modulate microglia morphology and number after chronic Meth in the hippocampus. Currently we are evaluating synapses and phagocytosis, and we further expect to clarify the impact of IFNγ /CD47 in the chronic Meth conditioning and in memory.

Keywords: Methamphetamine, Microglia, Neuron, Neuorinflammation, hippocampus.