Ac_{2-26} modulates glial activation in an *ex vivo* model of Alzheimer's disease

Poster

Neurobiología de enfermedades - Neurobiology of disease

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The accumulation of amyloid-β (Aβ) and hyperphosphorylated Tau (p-Tau) are the main hallmarks of Alzheimer's disease (AD), the leading cause of dementia worldwide. Neuroinflammation, driven by reactive microglia and astrocytes, is also known to contribute to neuronal damage. Annexin A1 (AnxA1), a Ca^{2+}-dependent pro-resolving mediator acting via formyl peptide receptors (FPRs), mainly FPR2, triggers signaling pathways that suppress pro-inflammatory cytokine release and promote resolution.

This study investigated the effects of the AnxA1-derived peptide Ac_{2-26}, which retains most of AnxA1's biological activity, and the FPR2 inhibitor WRW4 in an AD-like model in acute hippocampal slices.

Hippocampal slices were incubated for 4 h with Aβ oligomers ($Aβ_{olig}$, 200 nM) and the p-Tau inducer Okadaic Acid (OKA, 25 nM), in the presence or absence of Ac_{2-26} (3 µM) and WRW4 (10 µM). Protein levels of Iba-1, CD86, CD206, GFAP, C3, S100A10 and IL-1β were evaluated by Western Blot.

Ac_{2-26} prevents the $Aβ_{olig}$/OKA-induced levels of Iba-1, CD86 and IL-1β, while enhancing the expression of GFAP and S100A10. FPR2 inhibition by WRW4 also reduced IL-1β levels but did not affect glial markers, suggesting additional pathways for Ac_{2-26}.

These findings show that the AnxA1-derived peptide Ac_{2-26} modulates glial reactivity in this AD-like *ex vivo* system, reducing pro-inflammatory microglia phenotype, promoting a pro-resolving astrocytic phenotype, and lowering IL-1β levels. These results support the therapeutic potential of AnxA1 mimetics in mitigating AD-related neuroinflammation.

Financiamiento:

Work was funded by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) (grant n° 2022/02327-6). LPSF were supported by the FAPESP scholarships (2021/00270-4 and 2024/05491-7).