

Bcl2a1 exacerbates neuroinflammation and memory deficits in a mouse model of Alzheimer's disease

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INTRODUCTION	RESULTS	CONCLUSIONS
Alzheimer's disease (AD) is the most common neurodegenerative disorder. Abnormal activation of microglia triggers excessive inflammatory responses, induces synaptic loss and neuronal cell death, resulting in cognitive decline. However, current research primarily focused on microglia-mediated neuronal apoptosis, with few systematic reports addressing the regulatory mechanisms between microglial apoptosis and neuroinflammation. B-cell lymphoma 2-related protein A1 (Bcl2a1) is one of the anti-apoptotic members of the B-cell lymphoma 2 (Bcl2) protein family, and the role of Bcl2a1 in AD remains unclear.	Knockdown of Bcl2a1 reduces Aβ levels, enhances synaptic plasticity, and improves cognitive function in APP/PS1 mice. Mechanistically, this may be associated with increased apoptosis of inflammatory microglia, thereby increasing the proportion of M2-type microglia and alleviating neuroinflammation. Additionally, MLS-0053105, a selective Bcl2a1 inhibitor, attenuates memory deficits in APP/PS1 mice. DAPI IBA1 TUNEL Merge sh-con sh-bcl2a1 Relative rate of apoptotic cells(%) sh-con sh-bcl2a1 Hippocampal TUNEL immunofluorescence images and apoptotic microglia proportion quantification . sh-con sh-bcl2a1 CD86/CD206 ratio sh-con sh-bcl2a1 Flow cytometry detected CD86/CD206-positive cells, quantified via CD86/CD206 ratio.	AAV mediated Bcl2a1 knockdown, or an inhibitor of Bcl2a1, MLS-0053105, improved cognitive function and alleviated neuroinflammation in APP/PS1 mice, providing a promising therapeutic strategy for AD treatment.

REFERENCES

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