

miR-711 differentially regulates early and sustained A β 42o-induced neuroinflammation in microglia

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miR-711 suppresses early A β 42O-induced neuroinflammation, but prolonged stimulation partially reactivates downstream signaling.

INTRODUCTION

- Alzheimer's disease (AD) is characterized by progressive neurodegeneration associated with chronic microglial activation and sustained neuroinflammation (1). Amyloid- β (A β) oligomers activate the TLR4/NF- κ B/NLRP3 signaling axis, promoting the release of pro-inflammatory cytokines that contribute to disease progression (1,2).
- MicroRNAs are important post-transcriptional regulators of neuroinflammation (3). Although miR-711 has been implicated in inflammatory signaling (4), its time-dependent role during A β -induced microglial activation remains poorly understood.

Objective: To investigate the time-dependent effects of miR-711 modulation on A β 42 oligomer (A β 42o)-induced inflammatory signaling in HMC3 human microglial cells.

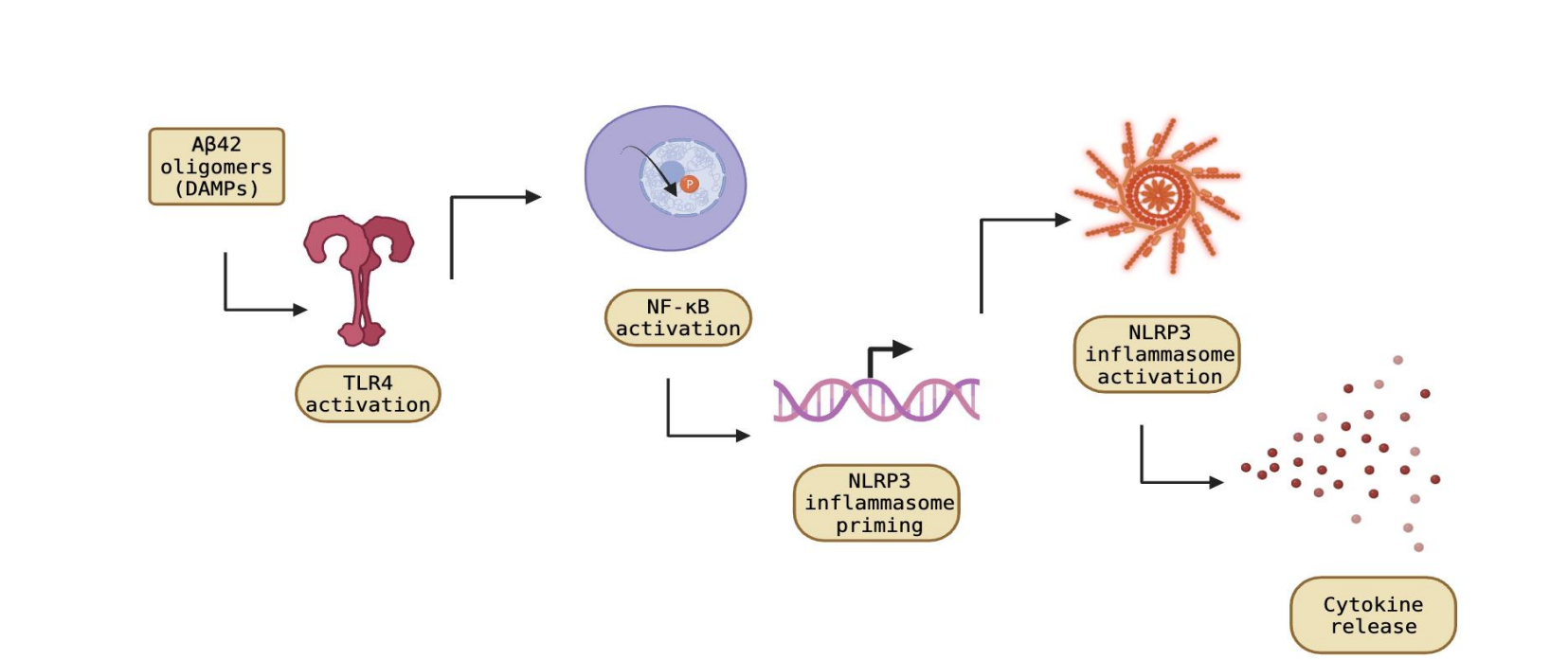


Fig 1. Overview of A β 42O-induced TLR4/NF- κ B/NLRP3 signaling in microglia (Created with BioRender.com).

METHODS

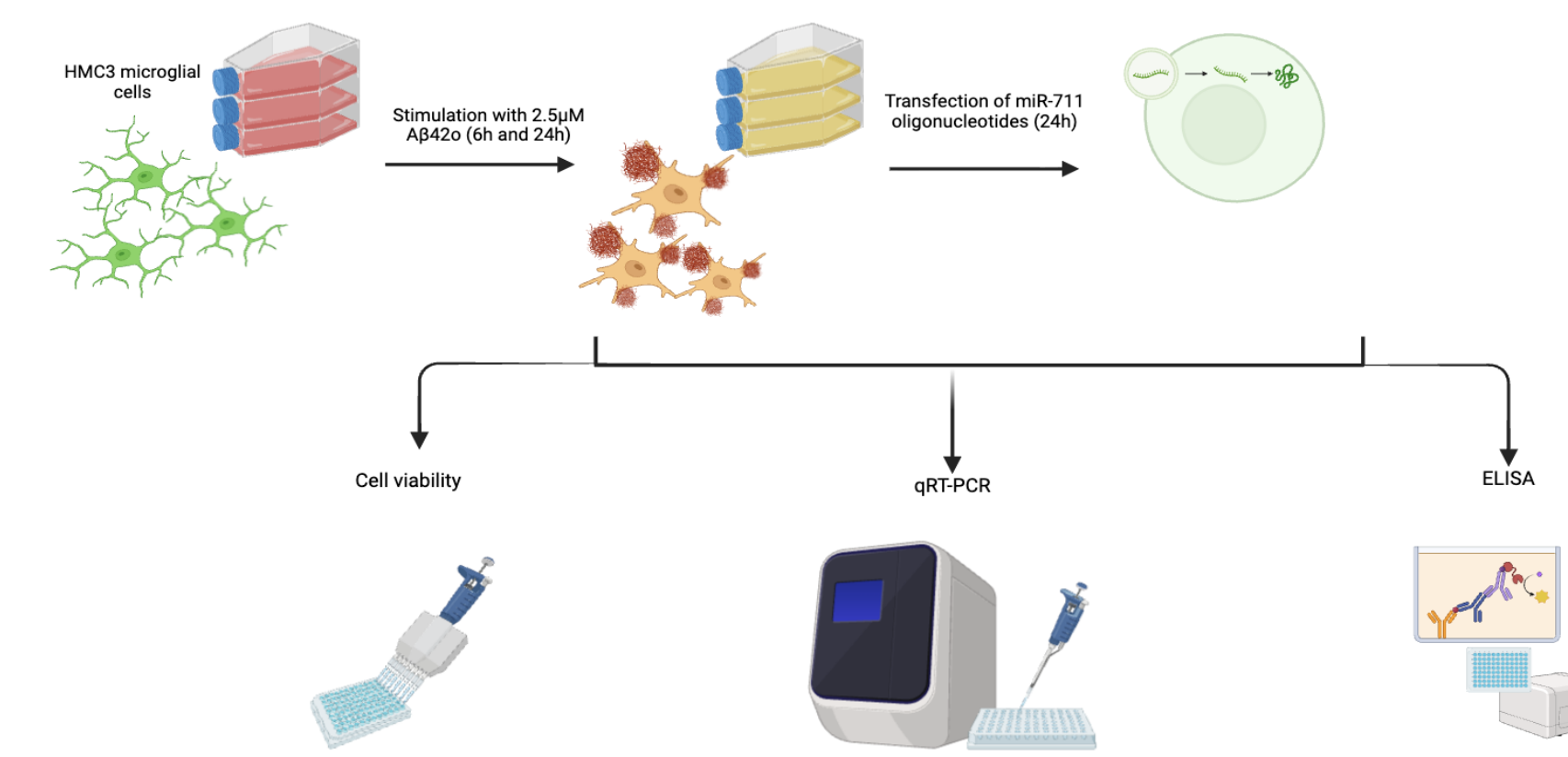


Fig 2. Experimental workflow (Created with BioRender.com).

Experimental workflow is shown in Figure 2.

Statistics

- Data are presented as mean $\pm$ SEM.
- Statistical analyses were performed using GraphPad Prism 10.
- One-way or two-way ANOVA followed by Tukey's multiple comparisons test was used as appropriate.
- $P < 0.05$ was considered statistically significant.

RESULTS

- miR-711 expression was significantly reduced following A β 42O stimulation (6 h: FC = 0.48, $P = 0.0023$; 24 h: FC = 0.62, $P = 0.0249$).
- Based on inflammatory marker induction and viability results, 2.5 μ M A β 42O was selected for subsequent experiments.

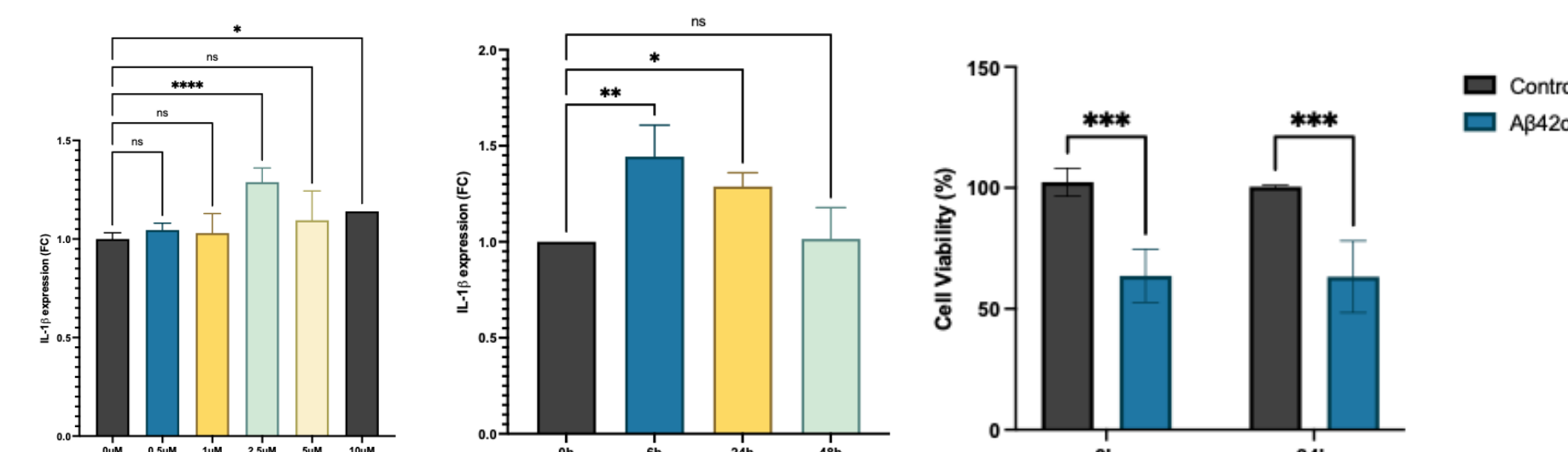


Fig 3. Establishment and validation of the A β 42O inflammatory model. A β 42o-induced inflammatory activation in HMC3 microglia.

- A β 42o significantly increased TLR4, NF- κ B and NLRP3 expression compared with untreated controls at both time points.
- These findings confirmed successful induction of the inflammatory phenotype.
- qRT-PCR confirmed efficient overexpression and inhibition of miR-711 following transfection at both time points.
- These data verified successful modulation before downstream analyses.

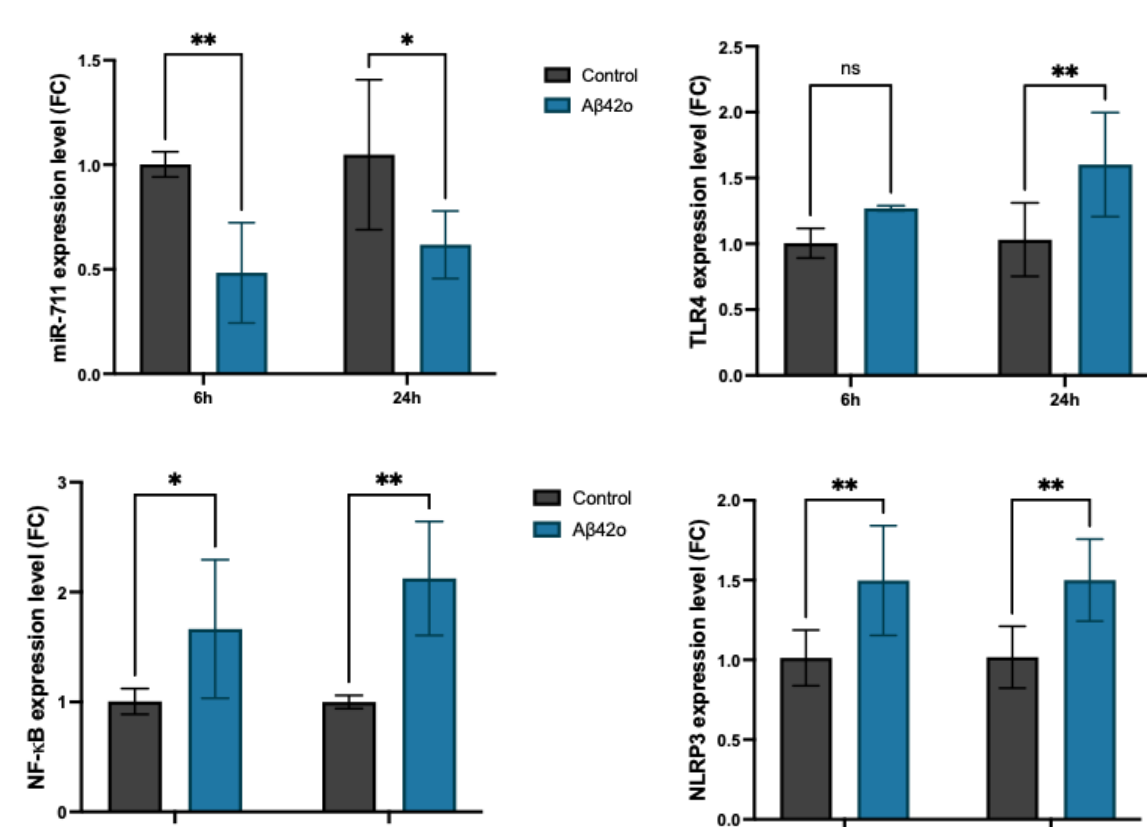


Fig 4. A β 42o activates inflammatory signaling in HMC3 microglia. A β 42o increased the expression of TLR4, NF- κ B and NLRP3 compared with untreated controls.

Fig 5. Validation of miR-711 modulation. qRT-PCR confirmed successful overexpression and inhibition of miR-711 following transfection with miR-711 mimic and inhibitor, respectively.

- miR-711 overexpression suppressed inflammatory signaling at 6 h. After prolonged stimulation (24 h), partial reactivation of downstream inflammatory signaling was observed.

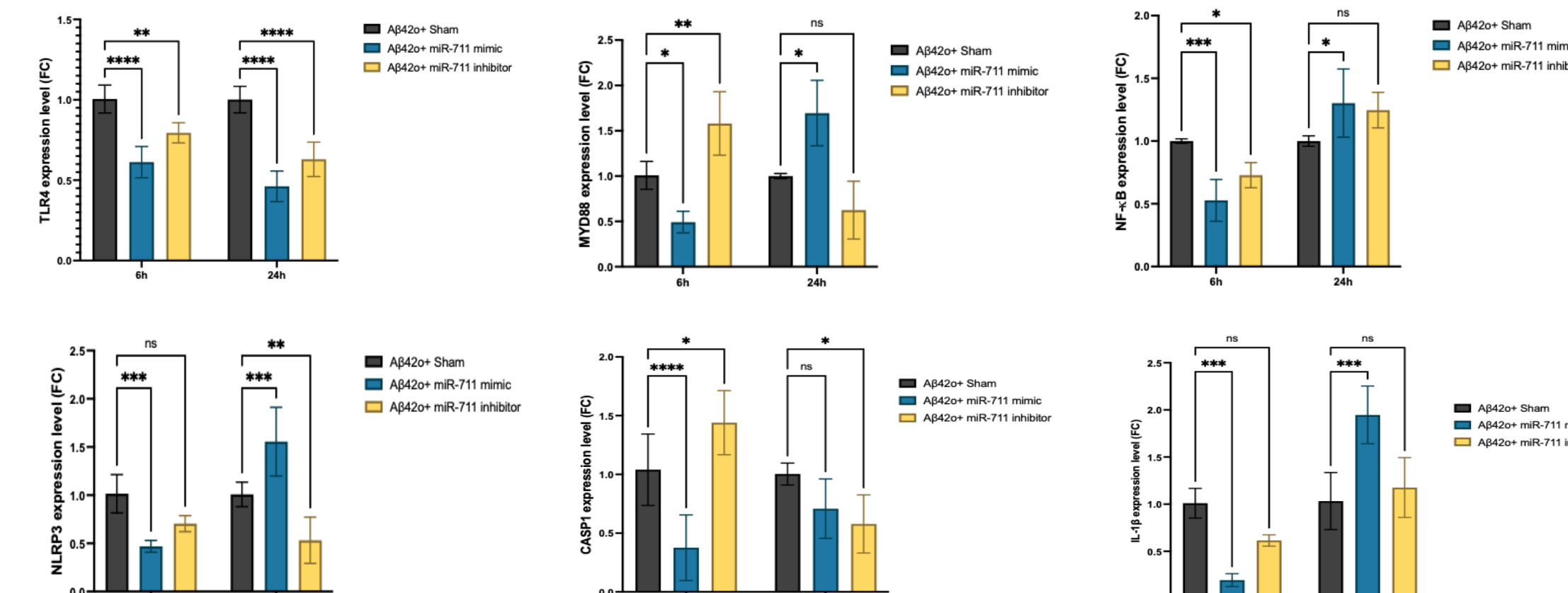


Fig 6. miR-711 modulates inflammatory signaling in a time-dependent manner. miR-711 overexpression attenuated early inflammatory signaling, whereas prolonged A β 42o stimulation was associated with partial reactivation of downstream inflammatory pathways.

- miR-711 modulation altered cytokine secretion without markedly affecting cell viability at 6h.
- These findings support an immunomodulatory rather than cytotoxic effect.

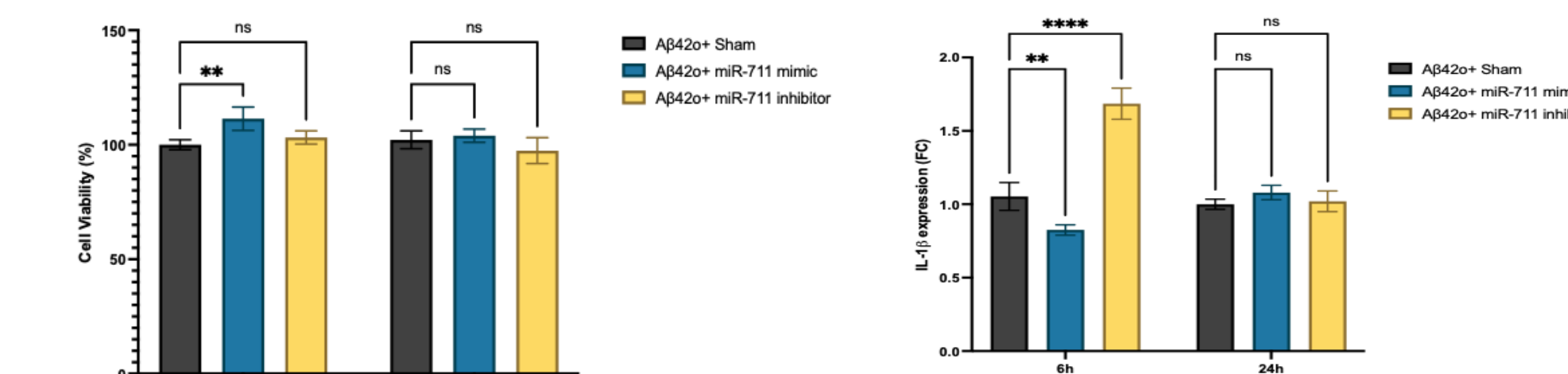


Fig 7. Functional outcomes of miR-711 modulation. miR-711 modulation altered cytokine secretion and influenced cell viability under A β 42o-induced inflammatory conditions.

- A β 42O downregulated miR-711 and activated TLR4/NF- κ B/NLRP3 signaling.
- miR-711 overexpression attenuated early inflammatory responses.
- Prolonged stimulation resulted in partial downstream pathway reactivation.
- miR-711 may represent a potential therapeutic target for modulating AD-associated neuroinflammation in a time-dependent manner.

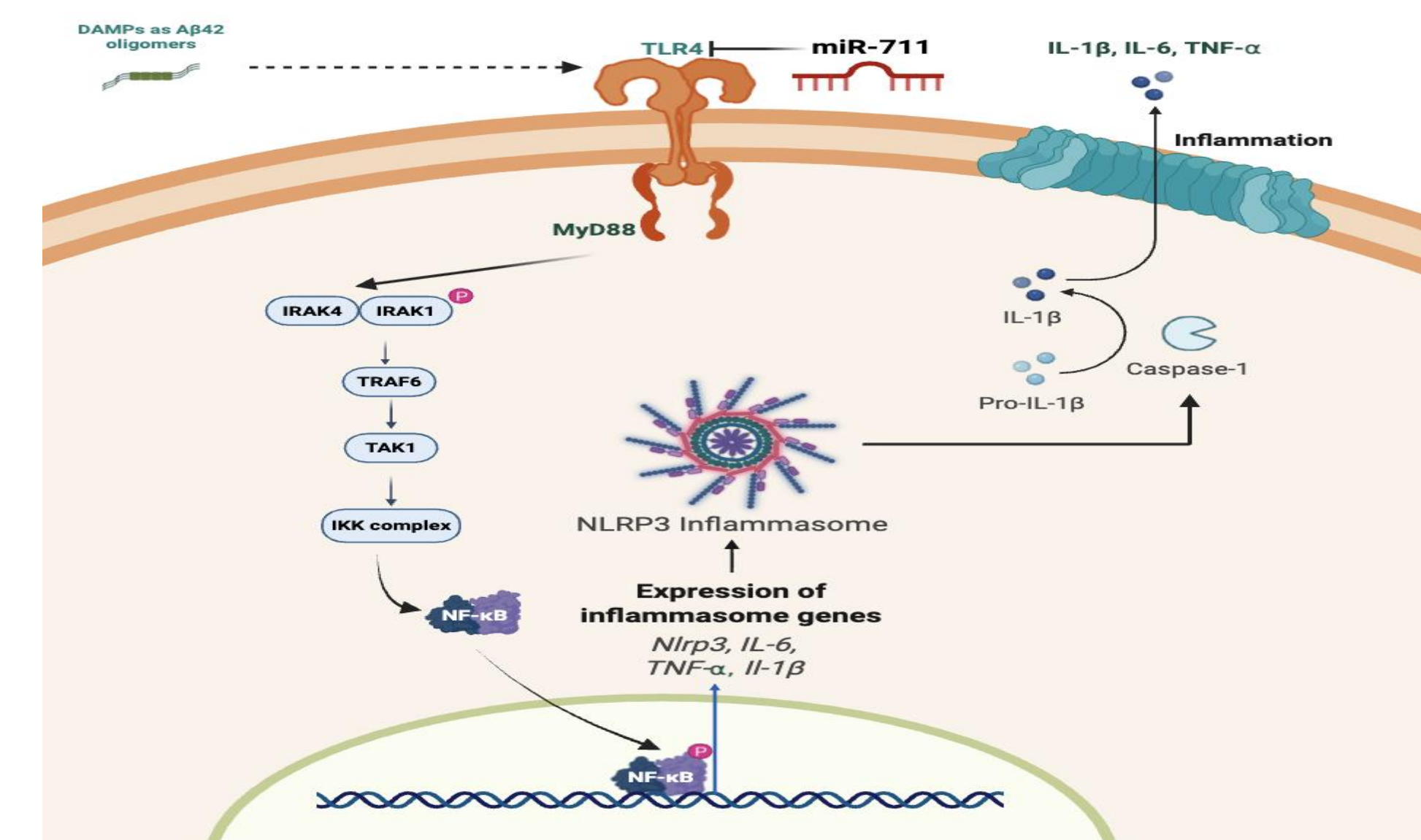


Fig 8. Proposed mechanism based on the present findings. miR-711 suppresses early A β 42O-induced inflammatory signaling, whereas prolonged stimulation results in partial downstream pathway reactivation (Created with BioRender.com).

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CONTACT

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