Immune Therapy for Neurological Disorders

Non-confidential – October 2025

Alan Trounson AO
CEO and Executive Chair
Evinco Therapeutics

Acknowledgement of Traditional Owners

In the spirit of reconciliation, Evinco Therapeutics acknowledges the Traditional Custodians of country throughout Australia and their connections to land, sea and community. We pay our respect to their Elders past and present and extend that respect to all Aboriginal and Torres Strait Islander peoples today.

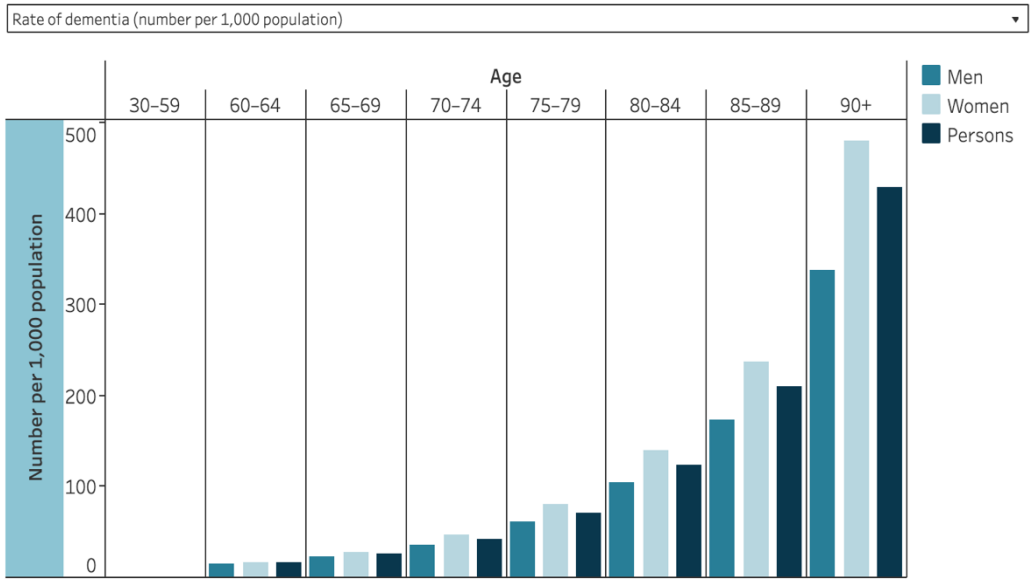
Alzheimer’s Disease: crippling an ageing society

The Problem:

- In 2021, ~57 million people had dementia globally
- ~10 million new cases of dementia worldwide each year
- Alzheimer's disease accounts for 60-80% of dementia
- Projected to more than double by 2050 (*W.H.O)*
- Disease primarily affects older individuals
- In 2025 ~7.2 million Americans aged 65 and older have Alzheimer’s dementia *(Alzheimer’s Association Facts and Figures 2025)*
- In 2024, ~425,000 people in Australia had Alzheimer’s dementia
- 250 Australians are diagnosed with dementia every day *(AIHW Australian Institute of Health and Welfare)*

Mortality:

- In 2024, Australia: Alzheimer's disease is number one cause of death *(Australian Bureau of Statistics)*
- In 2025, USA: Alzheimer’s is 6th leading cause of death
- Globally Alzheimer’s is 3rd leading cause of death, behind cardiac and cancer



Source: The AIHW estimates were derived using prevalence rates from the 2015 World Alzheimer report and Withall et al. 2014, and the ABS 2024 estimated resident population.
http://www.aihw.gov.au

The risk of Alzheimer's disease increases with age. Approximately 1 in 9 people aged 65 and older has Alzheimer’s.

Alzheimer’s Disease: crippling an ageing society

The cost:

Global:

- 2024 The Lancet predicted the global economic burden of Alzheimer’s Dementia Related Diseases could reach $16.9 trillion by 2050.

United States:

- 2025 Projected health and long-term care costs for people with dementia would be $384 billion**.**
- Approximately 11 million Americans provide unpaid care for people with Alzheimer's and other dementias, contributing an estimated $272 billion in unpaid care
- By 2050, the cost for the USA is expected to rise to nearly $1 trillion *(The Alzheimer's Association)*

Australia:

- 2021 estimated annual cost of Alzheimer's to be $26.6 billion
  - direct costs of $9.8 billion (aged care, hospitals)
  - indirect costs of $16.8 billion (informal care, lost productivity) *(University of Canberra Report)*

NK cell therapy as a new treatment approach for AD

Clinical observations from NKGen Biotech's autologous NK cell product [1, 2, 3]

First two compassionate use case studies:

Case #1: 38-year-old with PSEN1 mutation and advanced AD

- Progressive improvements to mobility, speech, cognition and memory with monthly dosing

Case #2: 70-year-old with advanced AD

- Progressive improvements to memory, speech and cognition with monthly dosing
- "Clinical response after six treatments"

"NK cells can safely improve CSF levels of amyloid, α-synuclein, and tau proteins while also identifying and eliminating autoreactive T cells while sparing resting T cells, to reduce neuroinflammation"

Phase I trial findings:

- No serious adverse events (SAEs) or dose limiting toxicity (DLTs)
- Decreased AD biomarker levels in CSF
- 90% participants had stable or improved cognitive scores after 4 doses
- Ex vivo expanded autologous NK doses: 1 to 4 x 10^9 cells

Phase II trial findings (under US FDA IND, ongoing):

- Dose increased to 6 x 10^9 cells/3 weekly for 3-6 months
- **Reported findings to date: 12/13 showed stable or cognitive improvement, 1/13 non-responsive (2/3 moderate AD-mild continued for 12months)**

1. Gil *et al*. 2025, doi: https://doi.org/10.1002/alz.085846
2. NKGen Phase 2 trial news update
3. https://nkgenbiotech.com/wp-content/uploads/2024/12/NKGen-Corp-Deck-November-2024-Final.pdf

Leveraging Cartherics' cell therapy platform for neurodegenerative brain disorders

Seeking AUS$2-5M Seed Round to generate in vivo POC based on collaboration with a major pharma company

Evinco Tx legal status	**Wholly-owned subsidiary of Cartherics Pty Ltd, based in Australia**
Modality	iNK cell-derived EV (Exosomes)
Lead indication	Alzheimer's Disease (AD)
Current state of play and competition	• Most common form of dementia, people living with AD to increase with aging population • AD therapeutics market to reach USD19.3 billion by 2033[1] • Lack of disease-modifying therapy • **NK cell-based therapy first reported by NKGen Biotech now in Phase II** (Autologous NK cells) • The brain is normally immune privileged and NK cells are not known to traverse into the brain at large numbers but **may modulate neuroinflammation indirectly** • An ongoing challenge for therapeutics targeting brain disorders is effective brain-targeted delivery and retention for greater disease-modifying efficacy**; we plan to explore intranasal administration of iNK-EVs as a novel and effective way to deliver therapeutics into the brain**
Stage	• In vitro MOA data demonstrating microglia amyloid uptake and degradation, established by Cartherics

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1. Alzheimer's Disease market forecast

Steps Towards a New Therapy for Alzheimer's Disease

1. **Cartherics Pty Ltd manufactures iNK cells for cancer therapies – 20-40 billion cells each run.**

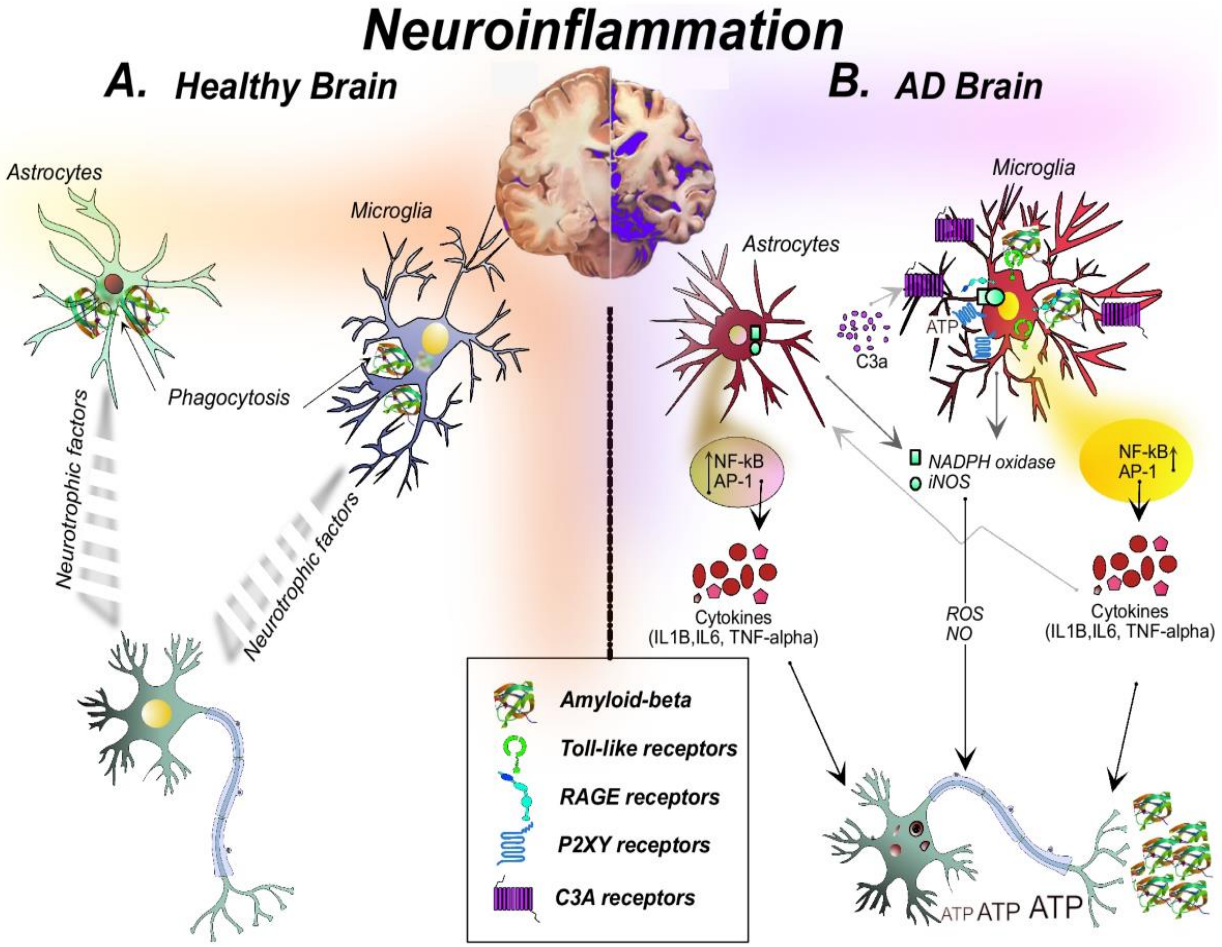
2. **Exosomes (called Extracellular Vesicles - EVs) are discharged by these cells and we have purified and characterized them – they are minute packages of the cell that are used for communication between cells (trillions of these EVs).**

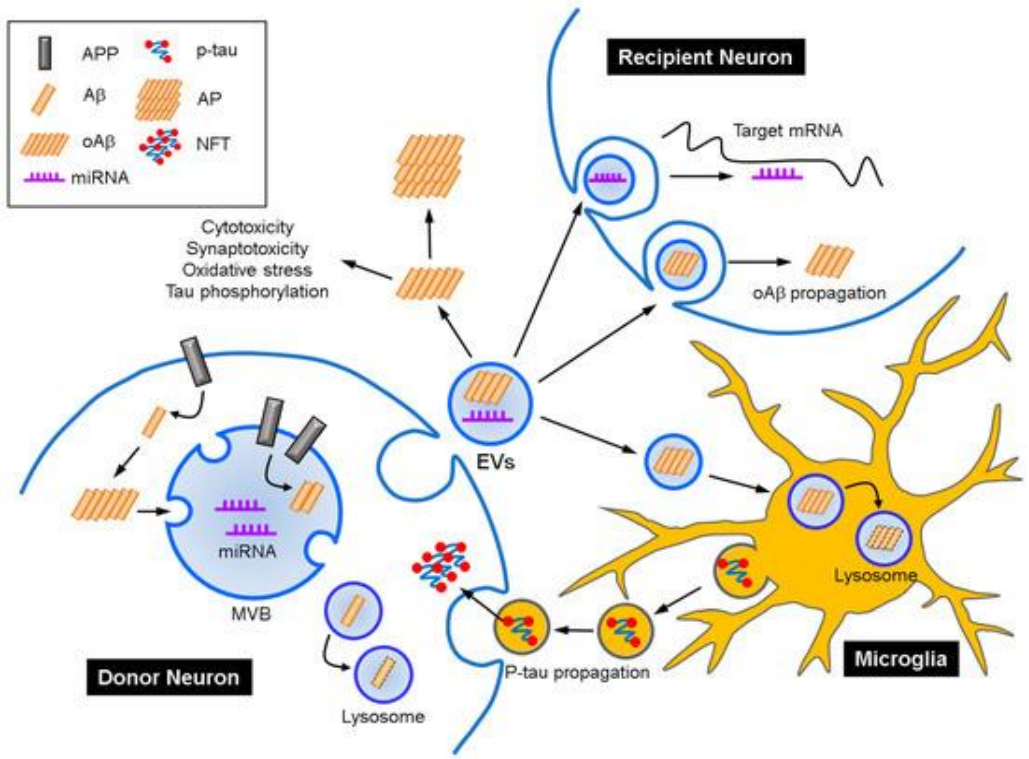
3. **A major pharma company has signed an agreement to partner with Evinco to guide the development of the R&D program to "proof of concept" for a therapy product (would attract major grant or Venture Capital investment).**

4. **A major US Venture Capital group has indicated interest in bringing a consortium of funders when we get to proof of concept.**

5. **Neurologists from Melbourne are very keen to do the early clinical studies and have plenty of patients who would be keen to try this type of therapy. They could do this as clinician sponsored studies.**

Alzheimer's Disease – Neuroinflammation Modified by NK cell EVs

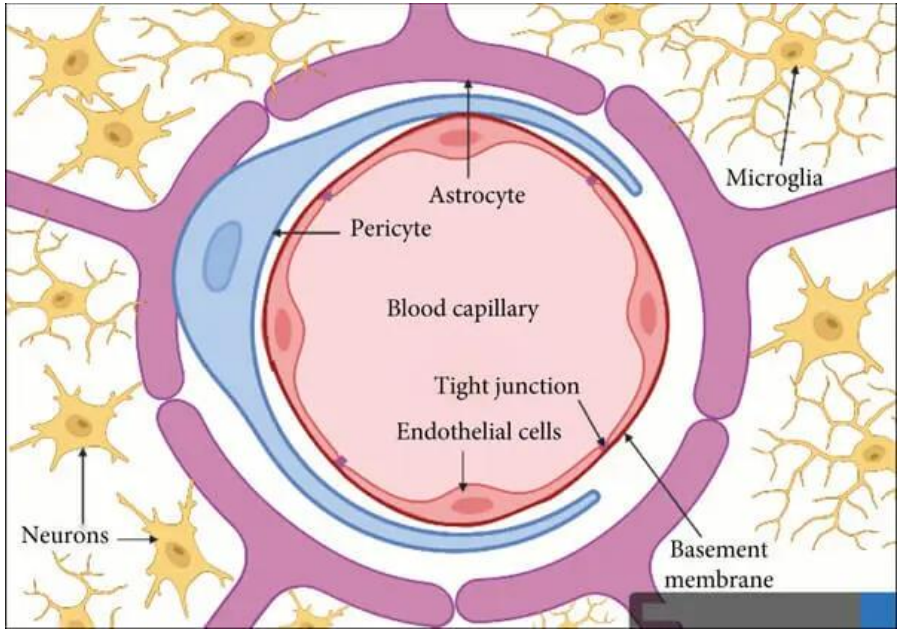




NK cell exosomes

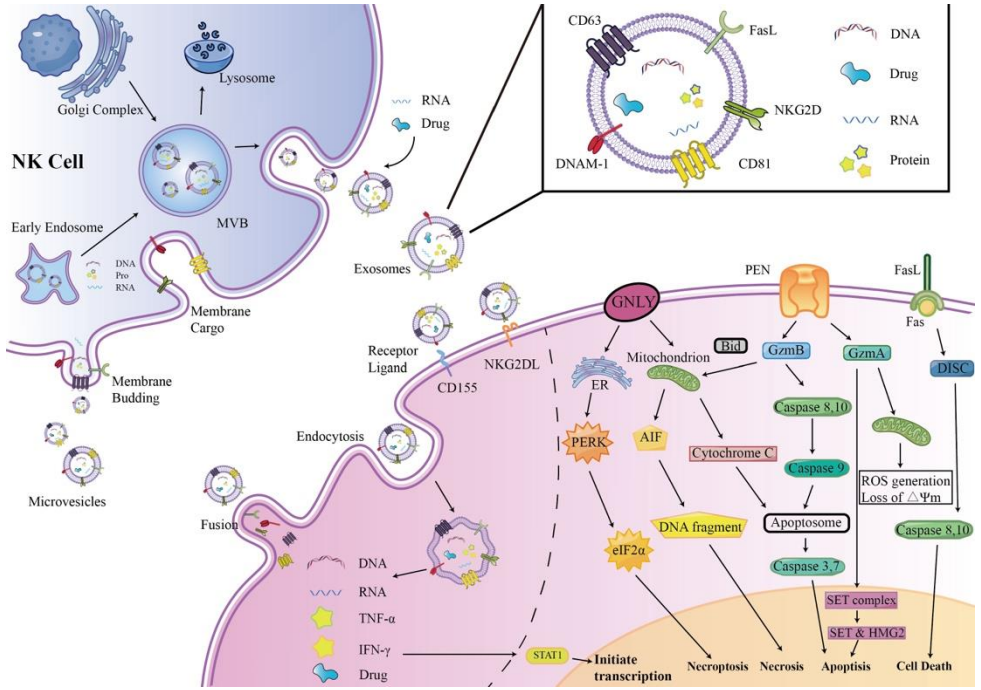
Proposed Mechanism of Action of NK cells on AD

NK cells are unable to directly access the brain

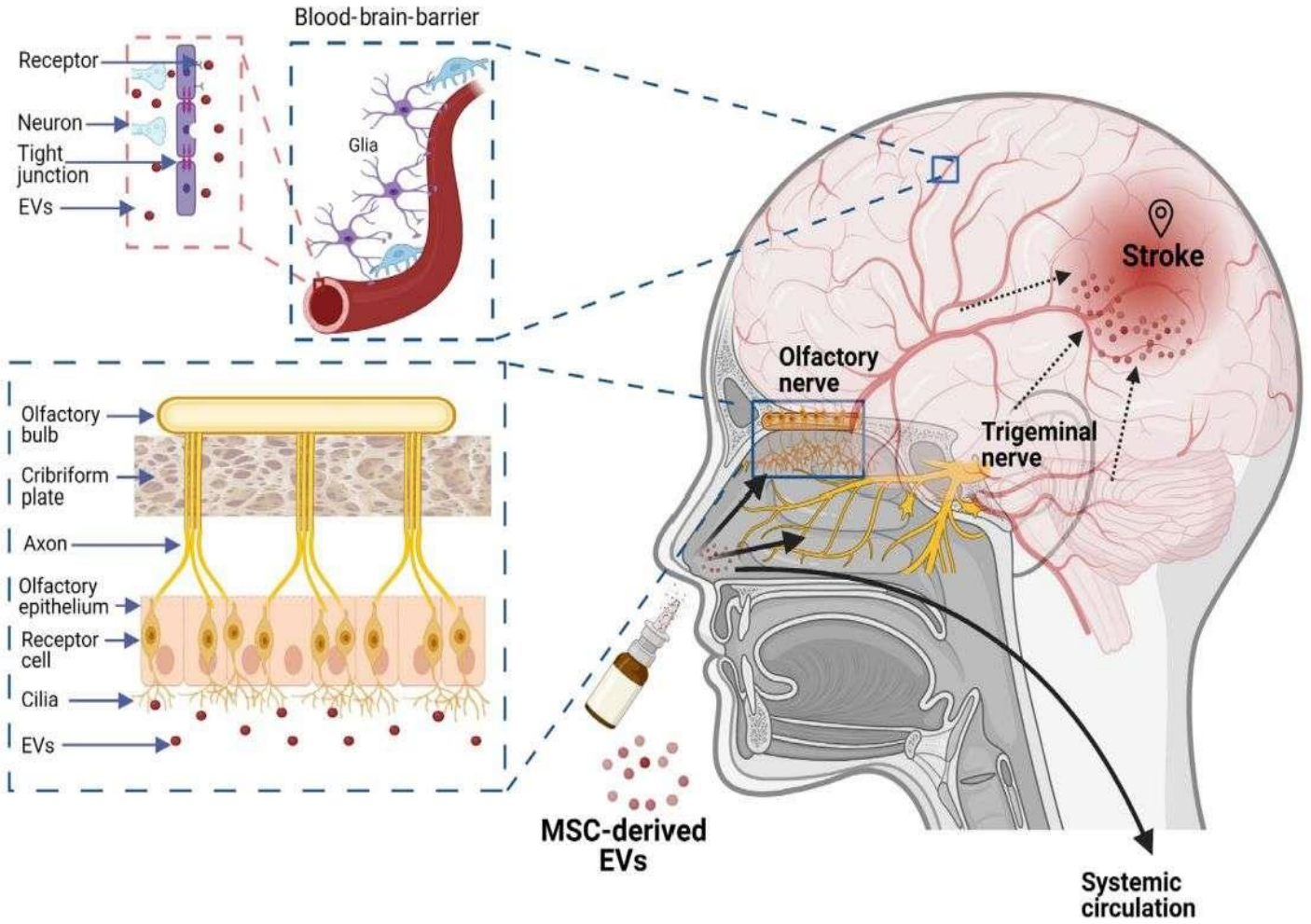


Effective blood brain barrier

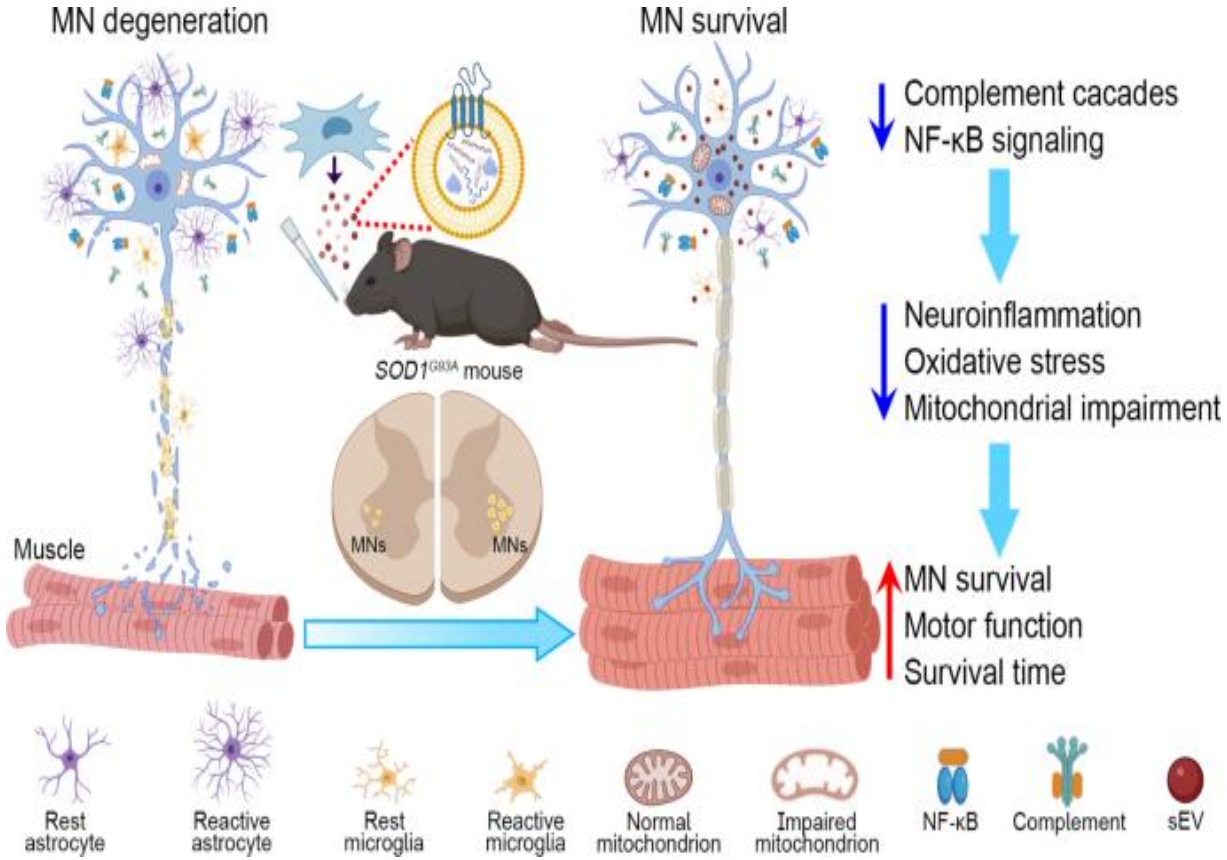
NK cells make EVs - exosomes

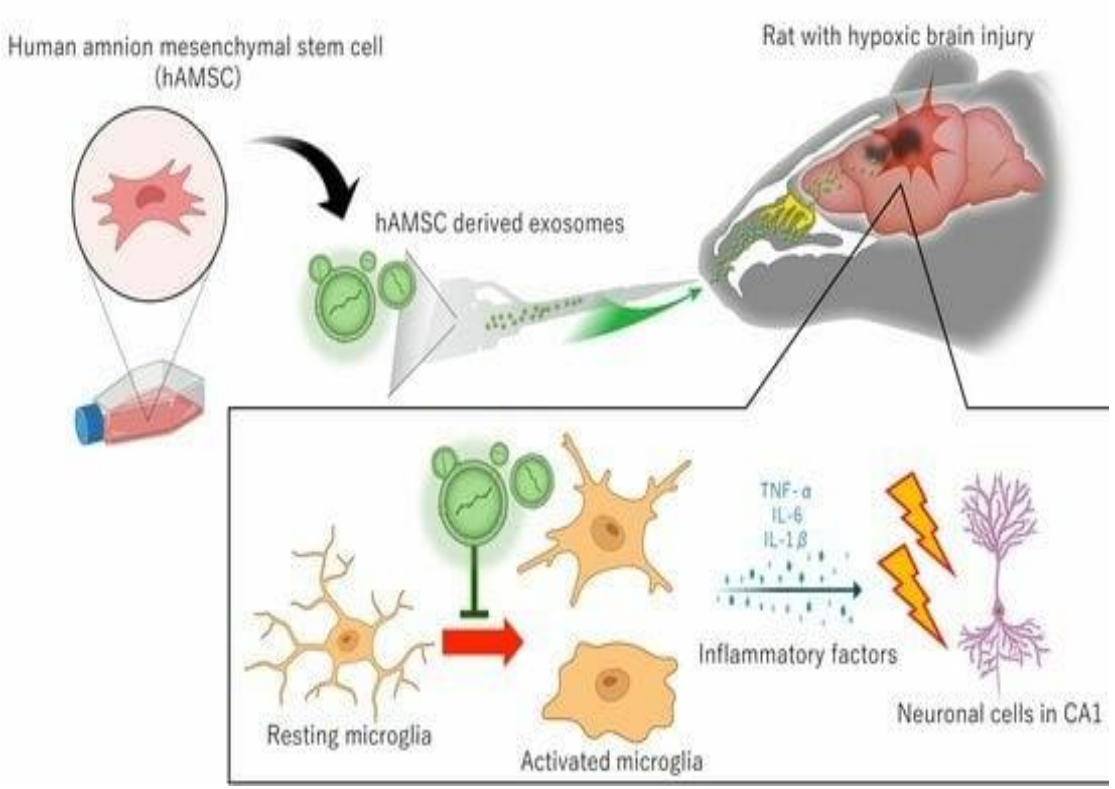


Nasal delivery of NK EVs direct to brain



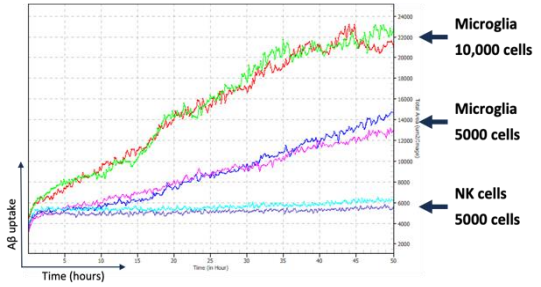
EVs used for Motor Neuron and TBI in rodent models





Differentiated approach to harness full potential of NK cells

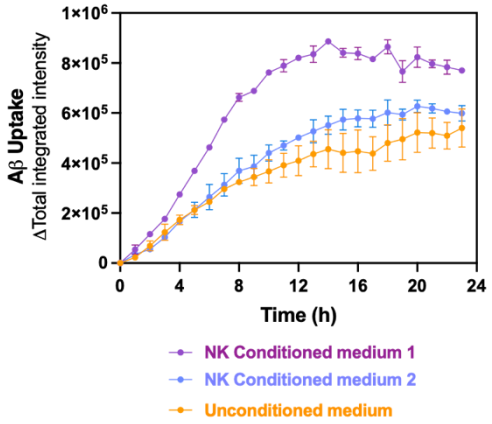
Microglia are more efficient at clearing protein aggregates than NK cells



Key findings:

- Microglia function as 'garbage collectors' of the brain, by modulating amyloid protein from becoming pathological plaques
- Microglia are brain-resident and more efficient at taking up amyloid aggregates, making them an important cell type to target

Indirect modulation of amyloid uptake through secretable factors

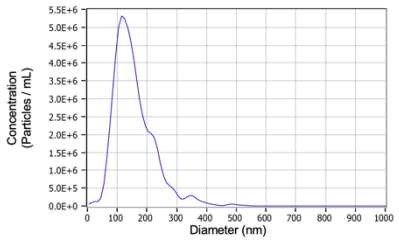


Key findings:

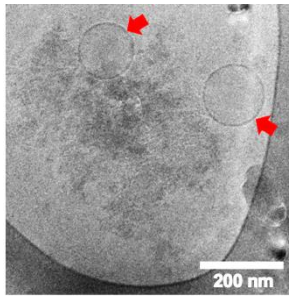
- Conditioned medium from PBMC-derived NK cells stimulated amyloid aggregate uptake differentially based on activation method
- First indication to show indirectly stimulation of microglia function by NK cells via secretable factors

Isolation and characterisation of EVs from iNK cells

EV particle size distribution



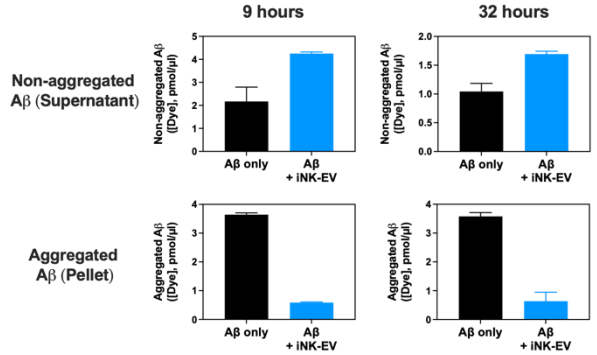
EV Cryo-EM imaging



EV and NK marker expression

- Western blot
- Flow cytometry
- ✓ EV and NK panel

iNK-derived EVs slowed down amyloid protein aggregation



Key findings:

- Astrocyte-derived EVs promoted amyloid aggregation[1], suggesting a potential role for EVs in regulating pathological protein aggregation
- In a cell-free state, monomeric amyloid protein was maintained in the monomeric state longer in presence of iNK-EVs
- After centrifugation, monomers remain in solution and aggregates will be pelleted

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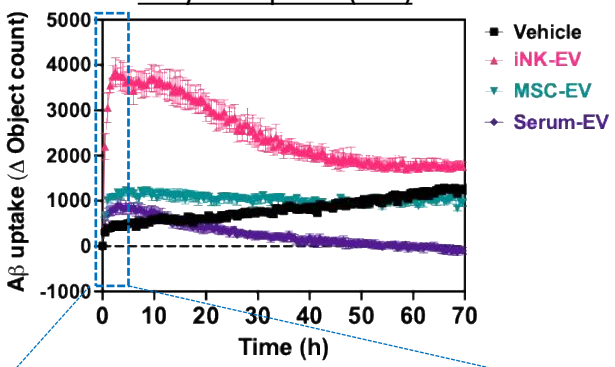
All data and findings presented on this slide were generated in-house by Cartherics Pty Ltd

[1]Dinkins et al. *Neurobiol Aging*. 2014 https://doi.org/10.1016/j.neurobiolaging.2014.02.012

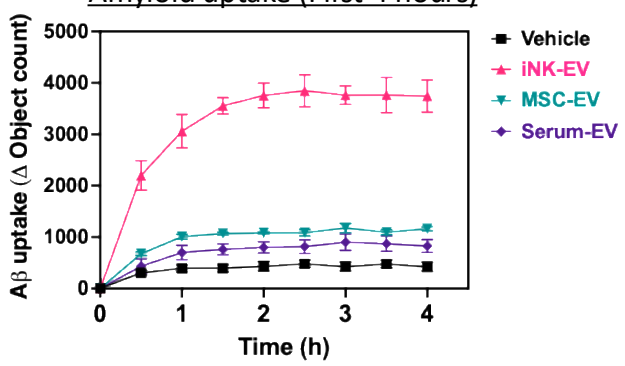
iNK-derived EVs promote microglial amyloid uptake & degradation

iNK-EV stimulated microglia to clear up more amyloid aggregate

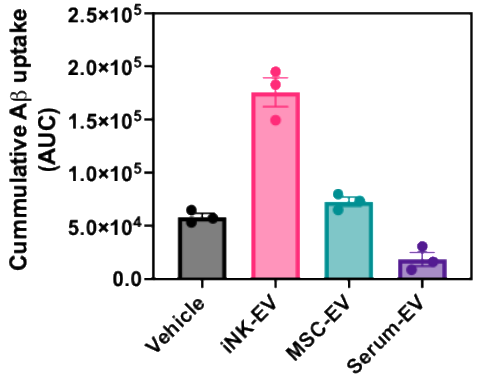
Amyloid uptake (Full)



Amyloid uptake (First 4 hours)



Amyloid clearance efficiency (AUC)

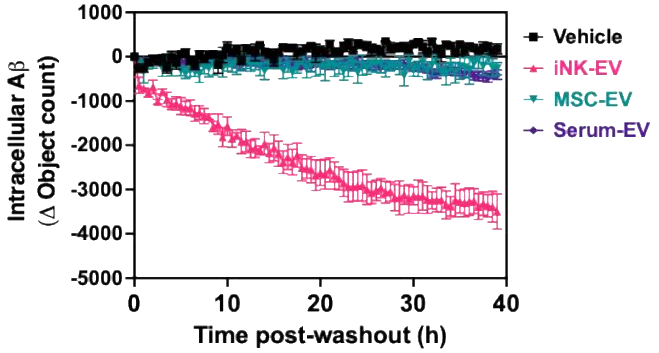


Key findings:

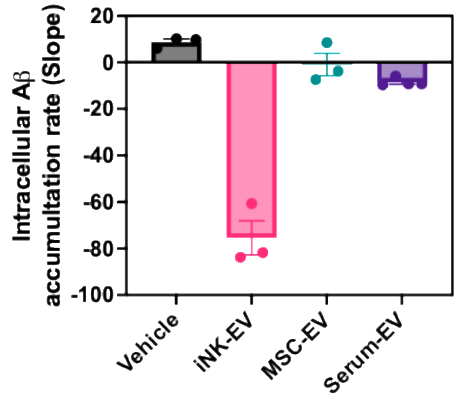
- iNK-EVs have a short action time, within the first 4 hours of treatment
- Short uptake burst was followed by steady plateau still higher than untreated microglia
- iNK-EVs stimulated a comparatively better amyloid clearing profile than other EV sources (MSC, human serum)

iNK-EV stimulated microglia to degrade internalised amyloid

Internalised amyloid levels



Amyloid degradation efficiency (Slope)



Key findings:

- To quantify amyloid degradation by microglia, remaining extracellular amyloid were washed out and new media added
- Internalised amyloid content was tracked over 40 hours
- iNK-EV treatment promoted amyloid degradation in microglia (Negative curve = reduction of amyloid)

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[1]Dinkins et al. *Neurobiol Aging*. 2014
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Forward thinking: Clinical utility of iNK-derived EVs

Current treatment regimen	Approved AD stage	Potential clinical utility of iNK-EV product candidate
First-line pharmacological treatments for AD: Cholinesterase inhibitors	Mild-to-moderate	• Donepezil, galantamine, rivastigmine • Explore **potential combination** to reduce efficacious dose of first-line drugs to reduce unfavourable side effects in existing drugs • **Potential to replace as a more targeted disease-modifying therapy**
First-line pharmacological treatments for AD: NMDAR/glutamate receptor antagonist	Moderate-to-severe	• Memantine • Explore **potential combination** to reduce efficacious dose of first-line drugs to reduce unfavourable side effects in existing drugs • **Potential to replace as a more targeted disease-modifying therapy**
Amyloid targeting therapies (Anti-amyloid antibodies)	Mild AD	• Donanemab • Anti-amyloid antibodies have amyloid-related imaging abnormalities (ARIA) and brain haemorrhages risks • If proven efficacious, iNK-EV product candidate have the **potential to replace** less tolerated anti-amyloid antibodies

Experienced Management Team, Advisors & Collaborators

Prof Alan Trounson AO
Executive Chair - CEO

California Institute for Regenerative Medicine (CIRM), Monash University

Dr Jing Yang Tee
Principle Research Scientist

Shenzhen Bay Laboratory

Dr Andrew French
Scientific Consultant

University of Melbourne

Dr Richard Boyd
Scientific Advisor

Professor of Immunology, Monash University

Prof Alice Pébay AM
Scientific Advisor

Dame Kate Campbell Fellow, University of Melbourne

Dr Nathalie Saurat
Group Leader, ARMI

Cambridge University, Memorial Sloan Kettering Cancer Center

Opportunity Summary

Who will it benefit?	Potentially people at all stages of AD (early AD to late AD), exact subgroups to be elucidated in clinical trials
How the treatment works?	Slows down protein aggregation, modulates brain immunity, reduces neuroinflammation, promote brain repair
Delivery method and duration?	Highest priority for intranasal delivery via nasal spray/nebulizer, but other routes of administration also to be explored
Potential side effects?	Safety and tolerance profile of iNK-EVs in animal models to be evaluated in Q3 2027 – Q1 2028; In-human safety profile to be evaluated in Phase I clinical trials.
Capital Needed	The program needs AU$2-3 million initial support 2026-27 (two years)

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Alan Trounson

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