

The Diabetes-Alzheimer's disease Connection and Targeting Beta Amyloid Production

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Understanding Alzheimer's disease and how risk factors promote disease progression.



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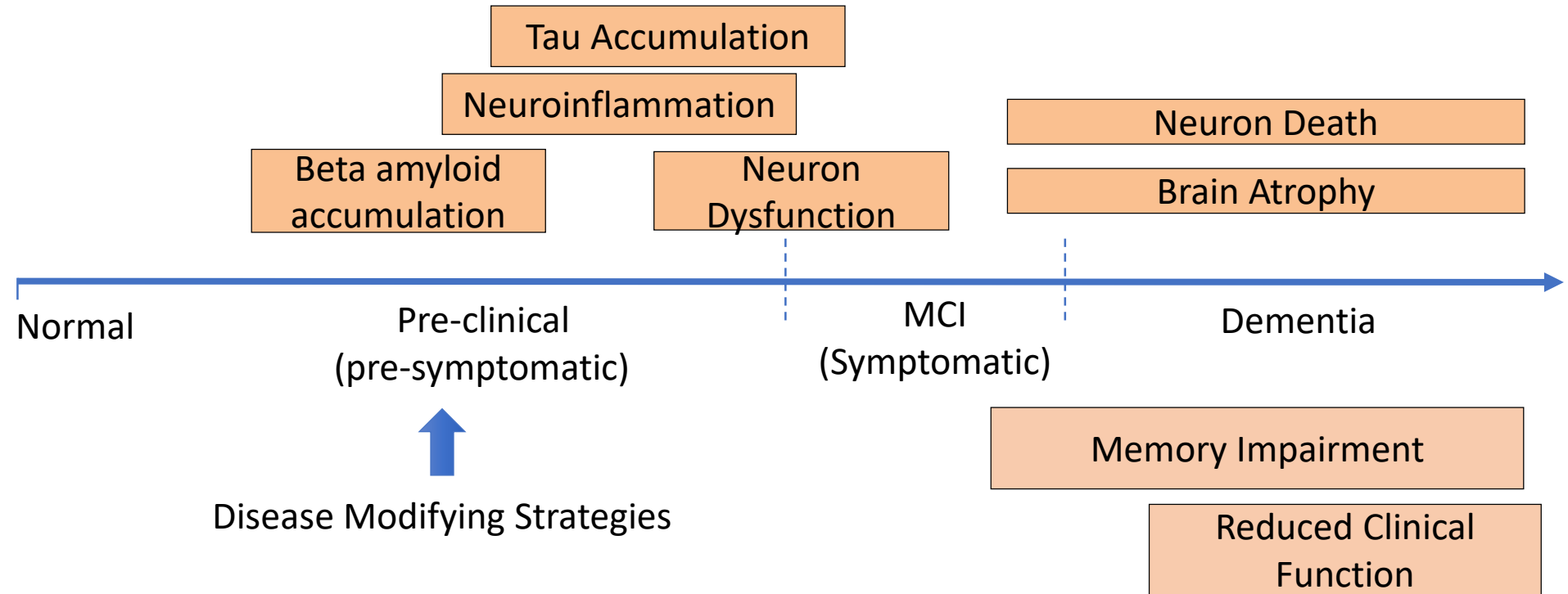
Funding



School of Pharmacy and Biomedical Sciences



Alzheimer's Disease progression occurs over decades



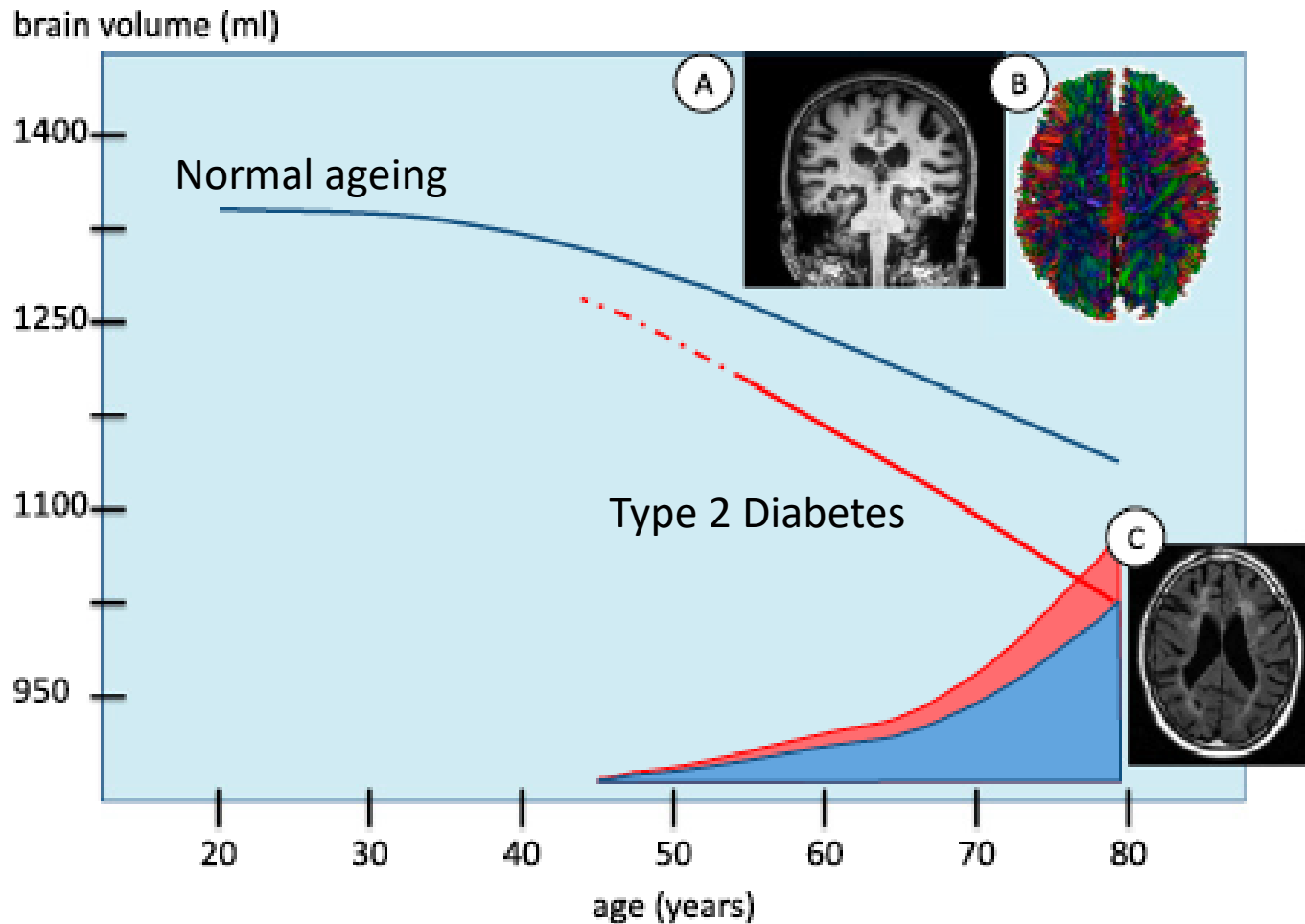
- Early diagnostic biomarkers
- Lifestyle modification
- **How risk factors promote disease progression.**
- Greater understanding of disease mechanisms and drug targets

Current treatments
"Temporary cognitive stabilisers"

Type 2 Diabetes- a Risk Factor for dementia

- Most common form of Diabetes and a chronic progressive disease commonly characterize by insulin resistance and high blood glucose levels.
- Currently 415 million people have Diabetes-world wide (1 in 11 of worlds adults). Predicted to increase to 642 million by 2040.
- Currently 1.7 million Australians with Diabetes at an annual cost of \$6 billion.
- 6th Leading cause of death in Australia
- Type 2 diabetes doubles the risk of developing dementia.

Brain Atrophy (shrinkage) in patients with type 2 diabetes



Geert Jan Biessels and Yael D. Reijmer, *Diabetes* 2014;63:2244–2252
Brain Changes Underlying Cognitive Dysfunction in Diabetes: What Can We Learn From MRI?,

Insulin resistance is associated with early changes in cognition and AD pathology



↑ Insulin Resistance associated with:

- Reduced Verbal Memory (Memory of events, recall of word lists)
- Reduced Executive Function (Organizational skills, Decision making).
- Reduced Global Cognition
- Increases in “abnormal” pTau



Miss Amy Woodfield

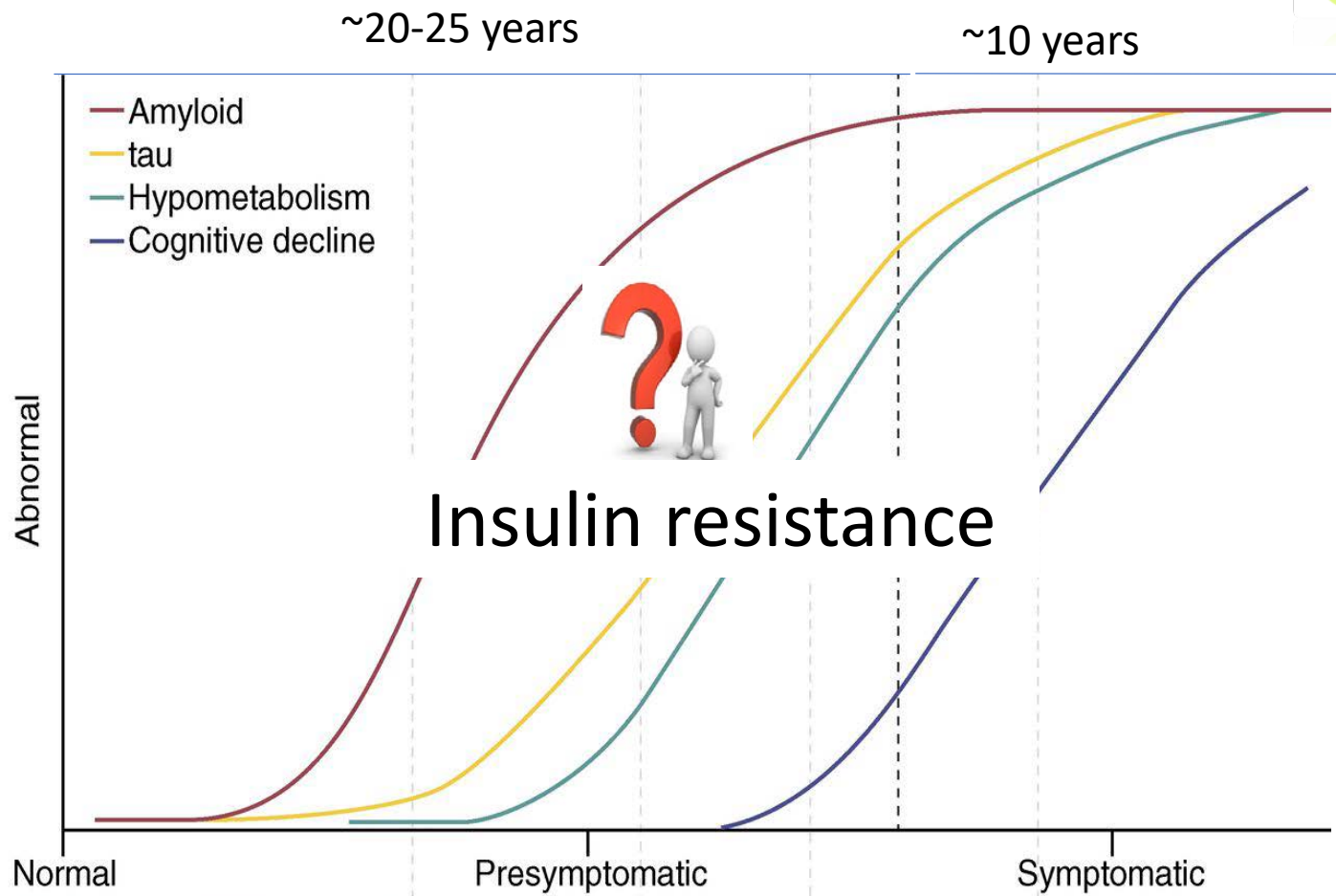


A/Prof Simon Laws



Dr Tenielle Porter

When does insulin resistance impact on cognitive functioning and the progression to AD?



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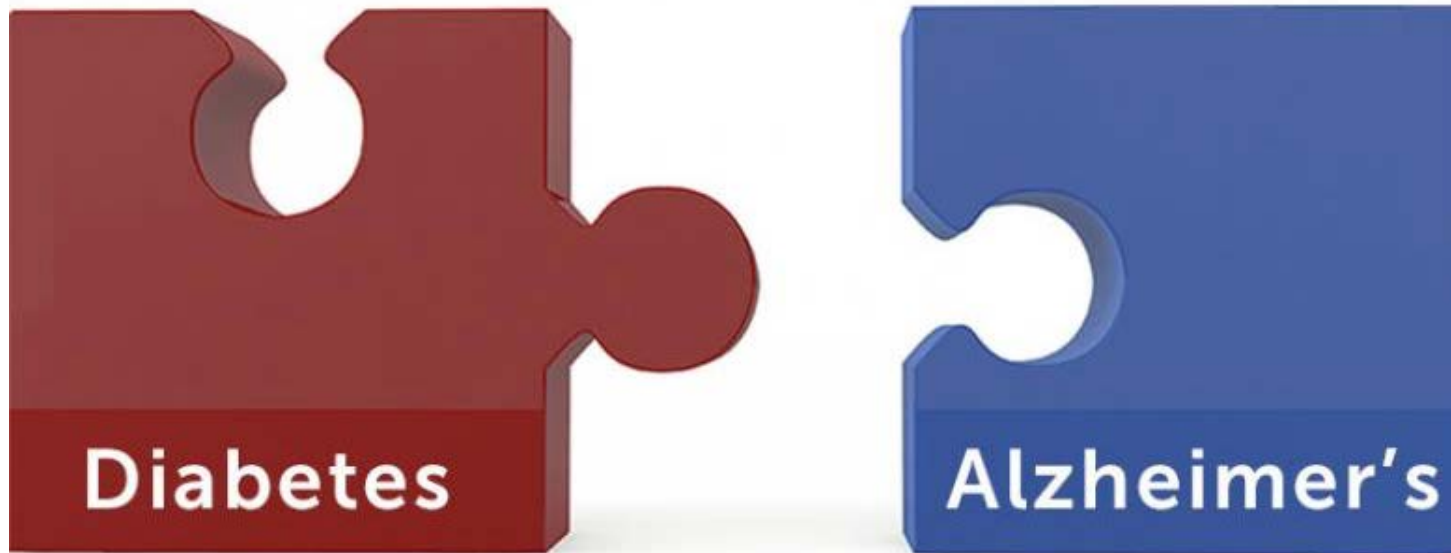
A/Prof Simon Laws



Dr Tenielle Porter

Molly Stanley et al. J Exp Med 2016;213:1375-1385

The Type 2 Diabetes-AD connection



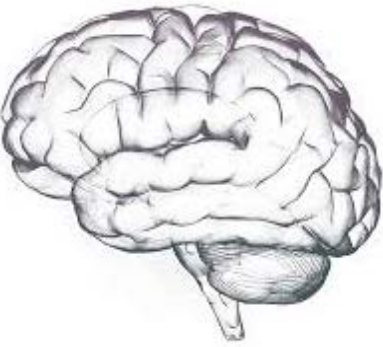
- Chronic diseases with slow progression
- Type 2 Diabetes increases risk of cognitive decline and Dementia
 - Brain atrophy (shrinkage)
 - Amyloid deposition
- Type 2 Diabetes promotes AD pathology (amyloid beta and Tau)
 - Inflammation
 - Impaired Metabolism
 - Insulin resistance
 - Lifestyle Risk Factors

Understanding how Type 2 Diabetes and AD are connected



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AD



Pathology ($A\beta$ /Tau)
Loss of neuron connections
Neuron Death
Cognitive Dysfunction

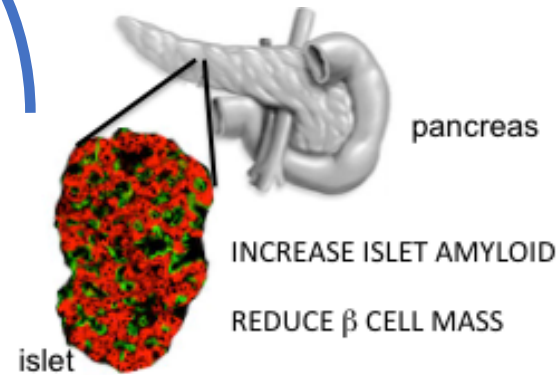
Reduced Insulin to the Brain
Reduced ability of the brain to respond to insulin.

Type-2 Diabetes



liver skeletal muscle adipose

Body Insulin Resistance



pancreas
islet
INCREASE ISLET AMYLOID
REDUCE β CELL MASS

Reduced Insulin levels

Beta amyloid /Tau



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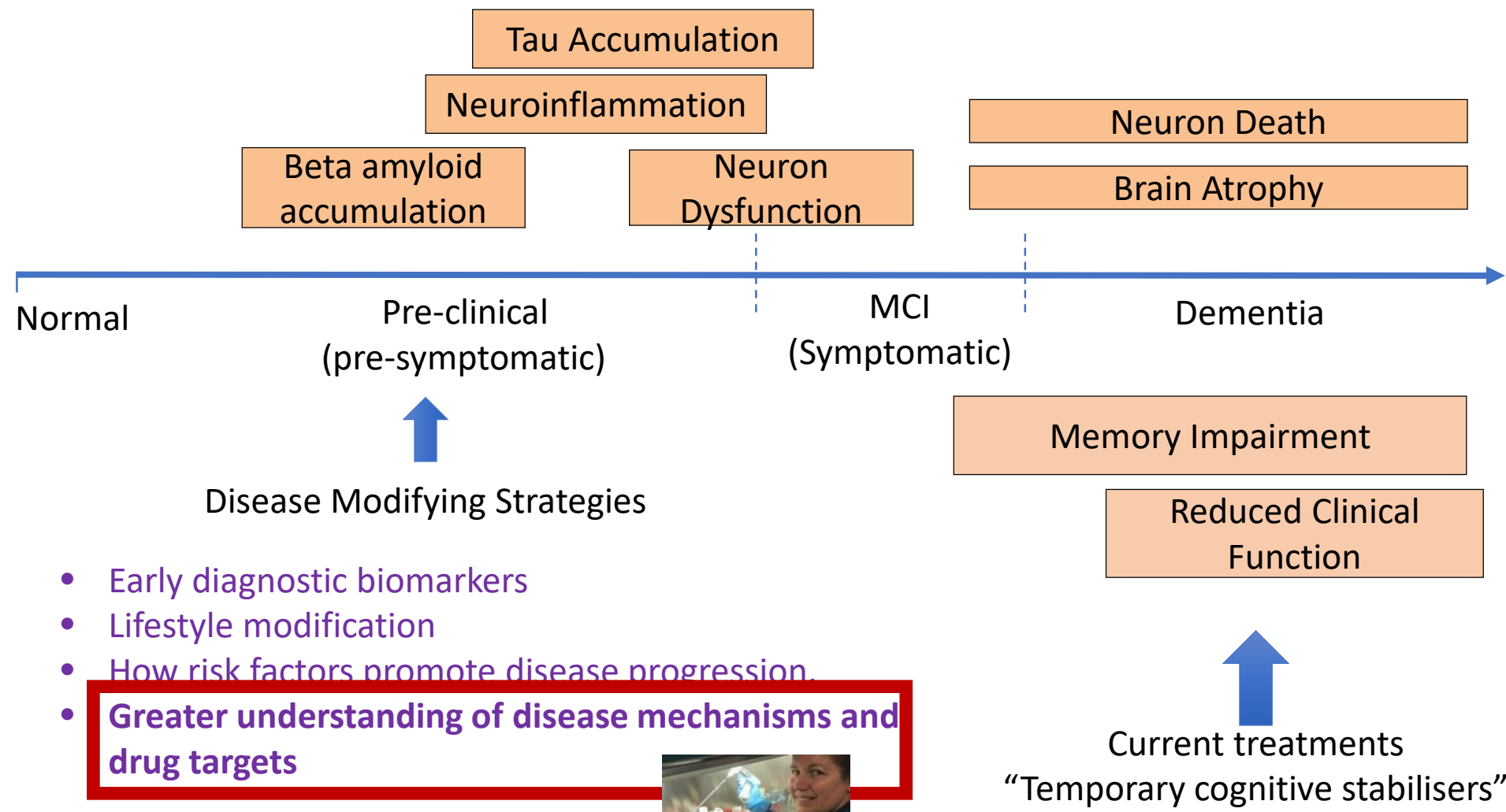


Professor Philip Newsholme (Curtin)



Dr Kevin Keane (Curtin)

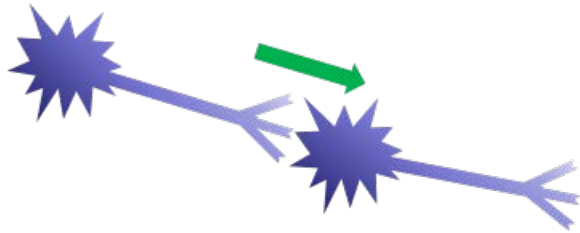
Alzheimer's Disease progression occurs over decades



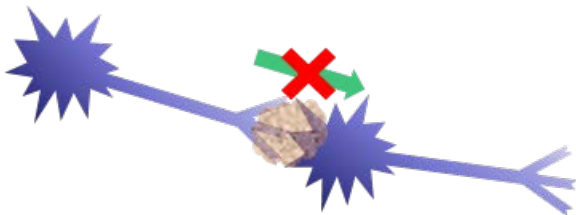
Miss Melissa Eccles

Targeting Beta Beta Amyloid Production

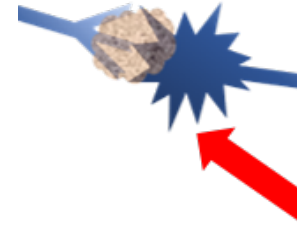
Message passed between
healthy brain cells



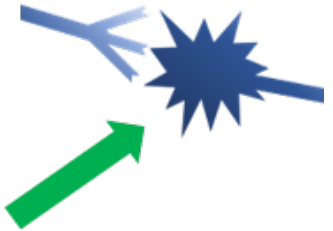
Beta Amyloid prevents message
passing across brain cells in
Alzheimer's



Long beta-
amyloid
builds up



Short beta-
amyloid is
protective



Enzyme cuts in
different positions

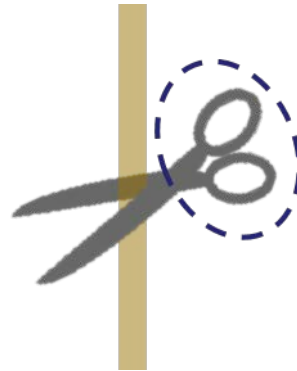


Targeting Beta Amyloid Production



Long vs Short

'Handles' determine
long vs short



Project goal:
Identify optimal
drug targets to
reduce long beta-
amyloid