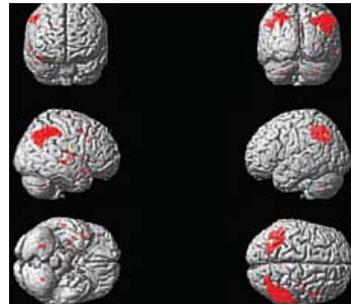
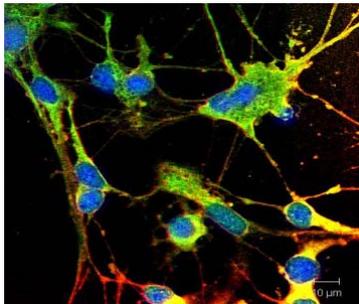
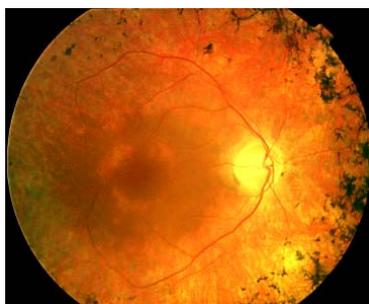


## Ageing Research in Trinity College

### 1. Trinity College Institute of Neuroscience & partner hospitals and centres

Trinity's ageing research is carried out primarily by researchers affiliated to the Trinity College Institute of Neuroscience (TCIN). This interdisciplinary research is carried out in a number of centres including TCIN, Mercer's Institute for Successful Ageing at St James's Hospital, Centre for Ageing, Neuroscience & Humanities at The Adelaide and Meath Hospital & St Patricks Hospital. Ageing Research is also strongly supported by our partner Schools of Psychology, Medicine, Genetics & Biochemistry. TCIN, Ireland's only dedicated brain research institute has over 40 associated Principal Investigators (PIs) and their research groups. Over half of our teams are engaged in research on ageing or neurodegenerative disease. The TCD ageing programme has attracted external funding of over €130 million in the past 10 years.



TCIN Images: (a) Ocular study (b) Neuronal study

(c) MRI study of cognitive impairment

TCIN houses Ireland's first whole body 3T and small bore 7T MRI scanners. The MRI suite, together with EEG and ERP facilities, clinical testing and neuropsychological evaluation suites for human patient work opens up a broad range of applications in neurophysiological, neuropathophysiological and neurocognitive research. The laboratories are engaged in research which ranges from molecular neurobiology and neurogenetics to behavioural neuropharmacology and *in vivo* electrophysiology. Preclinical research at the genetic, molecular and cellular levels, together with research involving neuroelectrophysiological and behavioural assessment, EEG and MRI, feeds through to clinical research. Clinical research combines behavioural assessment, EEG and MRI with epidemiological studies.



Examination of the eye for macular degeneration (TILDA)

## 2. Social Policy and Ageing Research

TCD has also been active in the social science & policy aspects of ageing and a number of research programmes are ongoing in the Social Policy and Ageing Research Centre (SPARC) including:

- Dementia Care Programme-The Prevalence of Cognitive Impairment in Nursing Homes
- Participation and inclusion of older people
- Long-term care- institutional and community approaches
- Older adults interacting with other age and population groups

## 3. Major clinical research projects

There are currently 3 major interdisciplinary projects in our Ageing research:

- (i) The Irish Longitudinal Study of Ageing ([TILDA](#))
- (ii) The GSK-Trinity Consortium in Neurodegeneration
- (iii) Technology Research for Independent Living ([TRIL](#))

A new initiative, Neuroenhancement for Inequalities in Elder Lives ([NIEL](#)) has just begun.

**TILDA** is a major inter-institutional initiative led by Trinity College Dublin, which aims to recruit a sample cohort of 8,000+ people from the age of 50, over a 10 year period. The study, which involves interviews on a two-yearly basis, collects detailed economic, health and social information on participants. Within this ongoing general study are nested studies which are designed to focus of neurocognitive function, and therefore there are identified cohorts of 'normal' ageing persons as well as persons with mild cognitive impairment and dementia, including Alzheimer's Disease (AD). Blood sample collection, for analysis of potential biomarkers, forms part of these studies.



**A health assessment exercise as part of the TILDA research programme**

**TRIL** explores the physical, social and psychological dimensions of ageing through comprehensive assessment of a large cohort of older Irish adults. The 5 strands of the study focus on Falls and Falls prevention, assessment of age-related changes in perceptual function, analysis of age-

related changes in cognitive function, social and mental health in the older person and wellness and exercise.

**The GSK-Trinity Consortium in Neurodegeneration.** The programme is designed to validate robust clinical end-points that can be used early in drug development to demonstrate pharmacodynamic activity of potential symptomatic and disease-modifying agents for Alzheimer's Disease (AD). The end-points are based on understanding the cognitive and neurophysiological impairments underlying normal ageing, mild cognitive impairment and Alzheimer's Disease and also on novel markers identified from preclinical models of ageing & AD.

#### 4. Clinical Readouts

The clinical readouts currently available for our research include:

##### (a) Neuroimaging and Electrophysiology

Structural MRI

EEG/ERP simultaneously acquired with fMRI;

Pupillometry

*Other electrophysiology:* Transcranial Magnetic/Direct/Alternating Current Stimulation

##### (b) Behavioural Assays

Analysis of cognition, affect, arousal

Novel cognitive assays (eg internationally used *Sustained Attention to Response Task*);

Training and self-administered cognitive enhancement protocols

Automated remote telephone-based cognitive assessment

##### (c) Biomarker discovery

In vivo human biomarkers of cognitive function

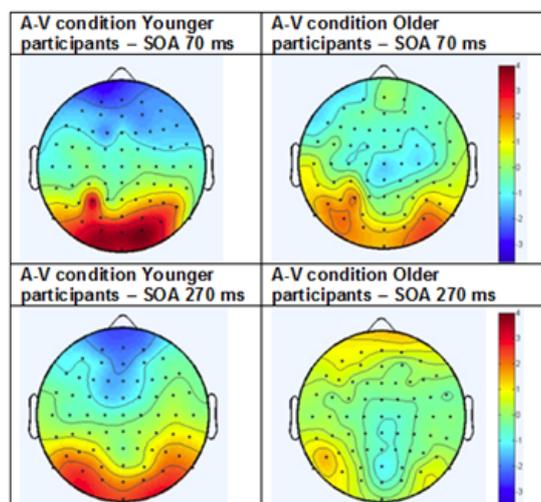
Markers in circulating cells (based on preclinical findings)

##### (d) Clinical cohorts

MCI, AD (and normal ageing), Depression



Walking gait analysis (TILDA)



A study of audio visual processing by EEG (TCIN)

## **5. Preclinical research programmes in Neurodegeneration and Ageing**

Trinity College has a strong record in the study of brain plasticity and how this opens up new ways of understanding the causes and potential treatments of cognitive decline in ageing and neurodegeneration. Preclinical work addressing the mechanisms underlying Alzheimer's Disease, including studies on amyloid  $\beta$ -protein and transgenic models, is being conducted in the laboratories of Rowan, Anwyl, Cunningham, Mills and Lynch. Several laboratories are involved in assessing neuroprotective strategies in the aged and stressed brain. These include the laboratories of Campbell, Connor, Kelly, O'Mara, Lynch and Harkin and active programmes in assessing the effects of potential therapeutic agents as well as exercise and novel environments. Preclinical models of ischaemia, multiple sclerosis, Parkinson's Disease, depression, macular degeneration and motor neuron disease are used in the laboratories of Lynch, Dev, Mills, Davey, Kelly, Connor, Harkin, Farrar, Humphries and Hardiman.

## **6. Preclinical Readouts and Models**

### **(a) Overall**

Integration of behaviour, cognition, neuropharmacology, neurophysiology, biomarkers.

Analysis of reflexes, cognition, affect, appetite, sleep. Structural and functional MRI imaging.

### **(b) Neurophysiology/Electrophysiology**

In vivo: Synaptic plasticity, EEG, neuronal ensembles

In vitro: Hippocampal slice recording, organotypic slices

### **(c) Behavioural analysis**

Novel object, water maze/water plus maze, automated delay non-match to sample, open field, forced swim test, novelty suppressed feeding, saccharin preference, elevated plus maze, voluntary/forced exercise.

Analytical techniques: FACS, PCR, ELISA, ING, signalling MRI,

### **(d) Cellular/molecular**

All standard technologies including cell culture, PCD, ELISA, FACS, IHC, confocal microscopy, live-cell imaging, HPLC.

### **(e) Animal models**

Aged mice and rats, LPS and A $\beta$ -induced changes, transgenic models of Alzheimer's Disease, ischaemia, multiple sclerosis, Parkinson's Disease, depression, macular degeneration, behavioural stress and motor neuron disease. Transgenic/knockout animal models of neuroinflammation.

## **7. Overall scope of Trinity College's Ageing research program**

-Multidisciplinary Ageing research programmes

-Preclinical studies and models

-Clinical studies and populations

-Medical & Optical Imaging

-Assistive Technologies

-Nutrition, Pharmacology & Therapeutics

-Cellular & Molecular

-Research programs & partners including EU, GE, GSK, HRB, INTEL, SFI, TRIL, TILDA, NEIL

-Dementia Care Programme

-Participation and inclusion of older people.

-Long-term care: institutional and community approaches.

-Older adults interacting with other age and population groups

## 8. Important links:

<http://www.neuroscience.tcd.ie>

<http://www.tcd.ie/Neuroscience/niel>

<http://sparc.tcd.ie>

<http://www.misa.ie>

<http://www.tilda.ie>

<http://www.trilcentre.org>

<http://www.ageandknowledge.ie>

## 9. Statement of PI Interests

### (i) Clinical and human studies

'Rose Anne Kenny's research focuses on the relationship between neurocardiovascular instability and brain ageing in the context of syncope, falls and frailty.' ([rkenny@tcd.ie](mailto:rkenny@tcd.ie))

Brian Lawlor's research focuses on improving our understanding of the psychological, social and biological aspects of Alzheimer's disease with a view to developing novel treatment strategies for this neurodegenerative disorder.' ([blawlor@stpatsmail.com](mailto:blawlor@stpatsmail.com))

'Desmond O'Neill's work focuses on stroke, dementia and ageing: health services, gerontological and cognitive aspects, and sub-topic interests in a) stroke/neurodegenerative diseases and driving/transport, b) neuroimaging and cognition in older people.' ([des.oneill@amnch.ie](mailto:des.oneill@amnch.ie))

'Ian Robertson's research focuses on identifying and remediating cognitive impairment in ageing and other conditions using novel combinations of behavioural, brain stimulation and pharmacological therapies.' ([ian.robertson@tcd.ie](mailto:ian.robertson@tcd.ie))

'Paul Dockree's research focuses on understanding cognitive dysfunction following Traumatic Brain Injury (TBI) and developing new translational methods to improve patient recovery from cognitive disabilities.' ([dockreep@tcd.ie](mailto:dockreep@tcd.ie))

'Thomas Frodl's research focuses on functional, microstructural and molecular brain changes in stress-related psychiatric disorders, ageing and during psycho- and pharmacotherapy.' ([thomas.frodl@tcd.ie](mailto:thomas.frodl@tcd.ie))

'Orla Hardiman's research focuses on clinical, epidemiologic, and complex genetic aspects of neurodegenerative diseases, identifying new therapeutic targets and disease-specific biomarkers, and providing well-phenotyped patient cohorts for early-phase clinical trials.' ([ohard@iol.ie](mailto:ohard@iol.ie))

'Colin Doherty's research interests are translational aspects of epilepsy, dementia, genetics and brain imaging.' ([codohert@tcd.ie](mailto:codohert@tcd.ie))

'Gary Donohoe's research focuses on genetic aspects of neurocognitive deficits associated with psychiatric disorders and cognitive remediation for these deficits.' ([donoghug@tcd.ie](mailto:donoghug@tcd.ie))

'Declan McLoughlin's research focus is developing molecular biomarkers to aid diagnosis and long term management of depression in parallel with randomised controlled trials to improve therapy.' ([d.mcloughlin@tcd.ie](mailto:d.mcloughlin@tcd.ie))

'Richard Reilly's research is focused on signal processing for new neurodiagnostics, neural prostheses and therapeutic neuromodulation devices.' ([richard.reilly@tcd.ie](mailto:richard.reilly@tcd.ie))

'Arun Bokde's group investigates the how large scale neural networks in the brain support cognitive function and how breakdown in such networks lead to cognitive impairment with particular focus on neurodegeneration.' ([bokdea@tcd.ie](mailto:bokdea@tcd.ie))

'The goals of Fiona Newell's research are to understand how multisensory information is integrated for the coherent perception of objects, persons and places, and to elucidate the brain mechanisms underlying these processes.' ([fiona.newell@tcd.ie](mailto:fiona.newell@tcd.ie))

### (ii) Preclinical studies

'Shane O'Mara's research focuses on the relations between cognition, synaptic plasticity and behaviour, in the context of brain ageing and depression.' ([shane.omara@tcd.ie](mailto:shane.omara@tcd.ie); [shane.omara@gmail.com](mailto:shane.omara@gmail.com))

'Thomas Connor's research is focused on the role of inflammation in the neurodegenerative process, and in the development of psychiatric disorders including depression and anxiety' ([connort@tcd.ie](mailto:connort@tcd.ie))

'Áine Kelly's research group investigates neuroprotective strategies that may prevent cognitive impairments associated with the ageing process.' ([aikelly@tcd.ie](mailto:aikelly@tcd.ie))

'Christian Kerskens is interested in the physical basis of physiology. He focuses on transport and diffusion processes.' ([christian.kerskens@tcd.ie](mailto:christian.kerskens@tcd.ie))

'Gavin Davey's research focuses on energy metabolism in the brain and the involvement of mitochondrial dysfunction in the neurodegenerative process.' ([gdavey@tcd.ie](mailto:gdavey@tcd.ie))

'Colm Cunningham's research addresses the influence of both systemic and CNS inflammation in episodes of delirium and on the progression of chronic neurodegeneration.' ([cunnico@tcd.ie](mailto:cunnico@tcd.ie))

'Michael Rowan's group studies the mechanisms underlying the regulation of synaptic plasticity during learning and in models of stress and Alzheimer's disease.' ([mrowan@tcd.ie](mailto:mrowan@tcd.ie))

'Aileen Lynch's research investigates the mechanisms which modulate blood-brain barrier permeability, particularly in the context of the ageing brain' ([amlynch@tcd.ie](mailto:amlynch@tcd.ie))

'Pete Humphries research interests are in human molecular and medical genetics, and especially degenerative diseases of the retina. Current research is directed toward the molecular pathologies associated with such conditions, in addition to developing translational molecular therapies involving neuronal barrier modulation technologies for optimizing systemic low molecular weight drug uptake by the retina and brain.' ([pete.humphries@tcd.ie](mailto:pete.humphries@tcd.ie))

'Veronica Campbell's group is investigating the cellular mechanisms involved in neurodegeneration and neuroprotection.' ([vacmpbll@tcd.ie](mailto:vacmpbll@tcd.ie))

'Marina Lynch's research is designed to examine the impact of ageing on synaptic function with emphasis on understanding the role of microglia' ([marina.lynch@tcd.ie](mailto:marina.lynch@tcd.ie))

'Kumlesh Dev investigates molecular mechanisms regulating receptor trafficking to develop novel drug targets and therapies for neurodegenerative diseases, with a particular focus on Multiple Sclerosis.' ([kdev@tcd.ie](mailto:kdev@tcd.ie))

'Julie Kelly's research focuses on investigating the roles of neuropeptides in the central nervous system (CNS) and development of neuropeptide-based therapeutics for CNS disorders.' ([kellyja@tcd.ie](mailto:kellyja@tcd.ie))

'Andrew Harkin's research, in the area of neuropharmacology, is focused on the neurobiology of depression, the development of novel antidepressants and the adverse effects of drugs of abuse.' ([aharkin@tcd.ie](mailto:aharkin@tcd.ie))

'In a simple, defined neural circuit, Mani Ramaswami's group studies in vivo mechanisms of implicit, inhibitory learning of relevance to autism and schizophrenia.' ([mani.ramaswami@tcd.ie](mailto:mani.ramaswami@tcd.ie))

'Daniel Ulrich's research focuses on the role of sleep in modifying synapses in the brain and how this is affected by age.' ([ulrichd@tcd.ie](mailto:ulrichd@tcd.ie))



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