2\textsuperscript{nd} Translational Strategies for Therapeutic Discovery in Dementia Conference

February 1, 2013
NUS Centre for Life Sciences Auditorium
Singapore
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<td>1430 - 1500 hrs</td>
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<td><strong>Chairperson : Prof David Townsend</strong></td>
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<td>1500 - 1600 hrs</td>
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**Prediction of PiB (-) Subcortical Vascular Dementia Using Clinical And MRI Variables**

*Professor Duk L. Na, M.D.*

*Department of Neurology, Sungkyunkwan University, Samsung Medical Center, Seoul, Korea.*

Geon Ha Kim\(^a\), Jae Hong Lee\(^b\), Sang Won Seo\(^a\), Ji Soo Shin\(^a\), Chi Hun Kim\(^a\), Young Noh\(^a\), Hanna Cho\(^a\), Seung Jun Oh\(^c\), Jae Seung Kim\(^c\), Duk L Na\(^a\)

\(^a\) Department of Neurology, Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea

\(^b\) Department of Neurology, University of Ulsan college of Medicine, Asan Medical Center, Seoul, Korea,

\(^c\) Department of Nuclear Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea,

Corresponding author: Duk L. Na, M.D. Department of Neurology, Sungkyunkwan University, Samsung Medical Center, 50 Ilwon-dong, Gangnam-gu, Seoul 135-710, Korea.

Tel.: +82-2-3410-3591/-3599, Fax: +82-2-3410-0052, E-mail: dukna@skku.edu

**Background and Objective:** Subcortical vascular dementia (SVaD) is considered the most common type of vascular dementia and often shows a slow progression simulating Alzheimer’s disease (AD). It is difficult to separate SVaD from mixed AD with cerebrovascular disorder because they share some clinical manifestation and MRI findings. However, it is important to differentiate between them since the prognosis and the therapeutic approach could be different. The purpose of this study, therefore, was to investigate if there were clinical and MRI variables that may help to discriminate \(^{11}\text{C}\)-Pittsburgh compound B (PiB) (-) SVaD from PiB (+) SVaD and to propose a new criterion for predicting PiB (-) SVaD.

**Methods:** We measured brain amyloid deposition using PiB positron emission tomography (PET) in 77 (men: women=32:45; mean age 73.6 ± 7.0 years) patients with SVaD. They all met the DSM-IV criteria for vascular dementia and had “severe” white matter high signal intensities without territorial infarction or macrohemorrhage on MRI. The clinical and MRI variables, which were statistically different between the two groups, were considered to be a component for combined criteria for PiB (-) SVaD. The ideal cut off values were selected from all cut points with the highest Youden’s index.

**Results:** Using the highest Youden’s index, we identified four variables that discriminated PiB(-) from PiB(+) SVaD: age, number of lacunes, and medial temporal atrophy (MTA), and presence of apoE4 allele. With the combination of these values, we can provide different sensitivity and specificity for PiB(-) SVaD.

**Conclusion:** The combination of clinical and MRI variables such as age, the number of lacunes, MTA and ApoE may help to differentiate PiB(-) SVaD from PiB (+) SVaD with various sensitivity and specificity.
Predicting Regional Neurodegeneration from the Healthy Brain Functional Connectome

Dr Helen Juan Zhou
Duke-NUS Graduate Medical School, Singapore

Neurodegenerative diseases target large-scale neural networks. Emerging network-sensitive neuroimaging techniques have allowed researchers to demonstrate that the spatial patterning of each disease relates closely to a distinct functional intrinsic connectivity network (ICN), mapped in the healthy brain with task-free or “resting-state” functional magnetic resonance imaging (fMRI). Our previous work on task-free fMRI suggested that behavioral variant frontotemporal dementia and Alzheimer’s disease featured divergent functional changes within the two major networks (the default mode network and the salience network), consistent with known reciprocal network interactions and the opposite symptom-deficit profiles of the two disorders. Collectively, these findings raise mechanistic questions about why each disease adopts a network-related spatial pattern and whether and how connectivity in health predicts regional neurodegeneration severity in disease, with a view to develop early intervention methods. In this talk, our recent work on predicting neurodegeneration from the healthy brain functional connectome will be discussed. Four competing mechanistic hypotheses have been proposed to explain network-based disease patterning: nodal stress, transneuronal spread, trophic failure, and shared vulnerability. We used task-free fMRI and ICN methods to test model-based predictions of how intrinsic connectivity in health predicts region-by-region vulnerability to disease. For each of the five neurodegenerative diseases, specific regions emerged as critical network “epicenters” and graph theoretical analyses in healthy subjects revealed that regions with higher total connectional flow and, more consistently, shorter functional paths to the epicenters, showed greater disease-related vulnerability. These findings best fit a transneuronal spread model of network-based vulnerability. Further developed and tested in longitudinal dataset, brain functional connectome signatures from multimodal neuroimaging data may provide simple, inexpensive, and non-invasive biomarkers for differential diagnosis, disease monitoring, behavior prediction, and treatment planning in dementia.
Association of Retinal Imaging With Neuroimaging and Cognition

Dr Kamran Ikram
Singapore Eye Research Institute & National University Health System, Singapore

The retina provides a unique window to assess vascular health non-invasively and directly in vivo. Advances in fundus photography and retinal image analysis techniques have enabled the objective and accurate assessment of both qualitative and quantitative retinal vascular abnormalities. As the retina shares many features with the brain including embryological origin, anatomical and physiological characteristics (such as blood-tissue barrier), the retina may in particular provide insights into vascular pathology in the brain. Over the last few decades, there is increasing evidence that retinal microvascular abnormalities including retinopathy signs and retinal vascular calibers are associated with age-related vascular pathology in the brain including not only clinical outcomes such as stroke and cognitive impairment, but also subclinical MRI-defined changes, including cerebral infarction, white matter lesions and cerebral atrophy. However, thus far the full potential of retinal image-analysis techniques remains undetermined. With the continuous development and advancement of retinal imaging techniques, there still remains scope for improvement in the quantification of retinal microvascular parameters, which may be utilized as non-invasive biomarkers for cerebrovascular diseases. This presentation provides an overview on the associations between novel retinal imaging markers with neuroimaging and cognition.
Alzheimer’s disease (AD) is a devastating neurodegenerative disease that comprises the majority of all cases of dementia and currently affects over 36 million people worldwide. There are two types of AD – (1) familial AD (FAD), which comprises about 5% of all AD cases and is inherited, (2) sporadic AD (SAD), which comprises 95% of all AD cases and has no obvious genetic basis. Currently, there is no effective disease-modifying therapy for AD and current treatments provide only temporary symptomatic relief. AD is characterized by the presence of amyloid-beta (Aβ) plaques and hyperphosphorylated tau-containing neurofibrillary tangles (NFTs) in the brain. Research has demonstrated that Aβ is cardinal in the toxicity observed in AD and this has resulted in the inception of the amyloid cascade hypothesis, the major basis in AD research. The amyloid cascade hypothesis is clearly supported by a myriad of in vitro and in vivo models and has elucidated many important discoveries regarding AD disease progression. However, aside from the genetic cases, the amyloid cascade hypothesis is unable to account for why there is a sudden increase in AD pathology in the SAD cases. Since SAD comprises the majority of all AD cases, this highlights the urgent need for new animal models to investigate the putative driving mechanisms propagating AD disease onset. Epidemiological studies have shown that type 2 diabetes (T2DM) is a risk factor for AD but it is still unclear why that is the case. Even though the impairment of the insulin signaling pathway has been suggested to play a role in T2DM and AD, the fact that not all T2DM patients develop AD suggest that impairment in the insulin signaling pathway is not sufficient to account for this increased risk. Amylin is a peptide that is found to accumulate in the pancreata of T2DM patients; in a process akin to the one Aβ undergoes to form plaques in AD brains. We have previously demonstrated that amylin is able to exert neurotoxicity via the same mechanisms as Aβ. We will build upon this previous knowledge to study whether other aspects of T2DM promotes AD pathology via in vitro and in vivo approaches at the Memory and Ageing Cognition Centre (MACC) to study the possible effects of T2DM on AD pathology.
Genome Wide Microarray Approaches Toward Biomarkers Discovery in Dementia

Dr Mitchell Lai  
National University of Singapore, Singapore

Neurodegenerative dementias such as Alzheimer’s disease and vascular dementia are complex diseases whose pathogenesis involve multiple proteins and pathways. With the advent of genome wide microarray platforms, such complex interactions are now more amenable to systematic study and characterization as a first step towards uncovering novel biomarkers which may aid in improving diagnosis, prognosis as well as provide further insights into disease processes. Here, I will give an overview of the various microarray based studies current underway at MACC as well as highlight the strengths and limitations of these approaches.
Neurochemical Studies of Dementia: Clues for New Biomarkers

Professor Paul T Francis
King’s College London, Wolfson Centre for Age-Related Diseases, London UK

Following the licensing of cholinesterase inhibitors and memantine for the symptomatic treatment of Alzheimer’s disease (AD) and other forms of dementia such as dementia with Lewy bodies (DLB) and Parkinson’s disease dementia (PDD), the dominant theory for the development of new medications for AD has been the amyloid cascade hypothesis. There have been no similar widely supported theories to underpin drug development in DLB/PDD. With the possible exception of solanezumab, a range of compounds have been tried in AD but have proved ineffective in slowing disease or treating symptoms. It is now considered that in AD tau represents a better, more tractable target but clearly drugs in this area are some way off and will require long and expensive trials. Given the overlap of pathology between many AD cases and DLB/PDD it remains possible that compounds that are effective in AD may have benefit in these other conditions. Given the lack of success, this leaves many people with dementia of all forms and their carers dealing with the day-to-day problems that come with these devastating conditions. The purpose here is to review the biochemical evidence we have to identify suitable new treatment targets for relieving the symptoms of dementia. It is arguable that for the foreseeable future, better, safer symptomatic treatments will be an important part of the landscape even when disease modifying treatments are available. Such treatments need to be developed for cognition but, perhaps more pressing for successful alleviation of behavioural symptoms and changes in mood that are often characteristic of dementia.

An important aspect of the drug development process is the identification and use of biomarkers for both efficacy and target engagement in both humans and model systems. To some extent cognition and behavioural symptoms are their own biomarkers in man but there are difficulties back-translating many specific human cognitive functions and behaviours to animals. One way around this is to identify biochemical and pharmacological targets that relate closely to specific cognitive functions or behaviours and assess the extent to which potential candidate compounds engage with those targets.

This presentation will examine biochemical markers of neuronal function and their relationship to both cognitive and behavioural symptoms in AD, DLB and PDD cases at post-mortem and discuss ways in which these might provide treatment targets and yield biomarkers against which candidate compounds could be assessed both in animal models and in people with dementia.
Degenerative Protein Post-Translational Modifications in Human Disease and Ageing

A/Professor Newman Sze
School of Biological Sciences, Nanyang Technological University, Singapore

Degenerative protein post-translational modifications (DPTMs), e.g. oxidation, carbonylation, glycation, deamidation, racemization, are attributed to many critical events in disease initiation, progression and ageing. These undesirable DPTMs impart deleterious structural and functional changes to proteins that accumulate in long-live cells such as neuron and cause various degenerative diseases and ageing. Despite the obvious biological importance of the DPTMs, the molecular basis of the DPTMs process in relation to disease and ageing has not been extensively explored thus far because of the technical challenges in studying DPTMs. To elucidate the roles of DPTMs in diseases and ageing, we developed proteomic methodologies to in-depth proteome-wide investigate DPTMs in in-vitro cell line and in-vivo animal models, and in clinical samples. Results revealed potential novel biomarkers, and new insight of disease mechanism.
Imaging Cortical Microinfarcts and Cerebrovascular Lesions in Dementia

Professor Geert Jan Biessels
Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht, The Netherlands

Autopsy studies report vascular pathology in the majority of patients with dementia, also in those with a clinical diagnosis of Alzheimer’s disease. Vascular pathology in dementia is potentially preventable, but we need more sensitive tools to study its etiology and to evaluate the effects of treatment. In this respect, microvascular lesions, in particular microinfarcts and microbleeds are of interest, because they appear to be very common, but may escape detection on regular clinical brain MRI. Ultra high field strength MRI scanners may offer a breakthrough in the detection of microvascular lesions, due to their high spatial resolution and high sensitivity to susceptibility effects. Our group studies small vessel disease on 7T MRI, focusing on microvascular lesions (i.e. microbleeds and microinfarcts), as novel imaging markers of the vascular burden in ageing-related cognitive decline and dementia.

In my presentation I will provide an overview of recent studies that use state of the art MRI techniques to assess the vascular burden in dementia. I will address MR angiography, intracranial vascular wall imaging and advanced techniques to study the microstructural integrity of the cerebral white matter, in particular diffusion tensor imaging. A particular focus of the presentation will be on microbleeds and cortical microinfarcts.

Suggested references:

Brain Morphological Shape Markers for Alzheimer’s Disease and Vascular Dementia

Dr Qiu Anqi
Division of Bioengineering, National University of Singapore, Singapore

Structural magnetic resonance imaging (MRI) techniques have been widely used to investigate imaging markers associated with psychiatric disorder and neurodegenerative diseases. In this talk, I will move away from traditional volumetric analysis to sophisticated morphological shape analysis for subcortical structures assessed using conventional T1-weighted MRI. I will demonstrate it in early detection of mild cognitive impairment (MCI), Alzheimer’s disease (AD), and vascular dementia (VaD) using the datasets of ADNI, South Korean ADNI, and Singapore Memory Aging Cognition Study.
Development of Arterial Spin Labeling Perfusion MRI for Translation Study of Dementia

Dr Chuang Kai-Hsiang
Singapore Bioimaging Consortium, Agency for Science Technology and Research, Clinical Imaging Research Centre & National University of Singapore, Singapore

The measure of cerebral blood flow (CBF) has provided essential information of cerebrovascular function for the diagnosis and prognosis of stroke. Furthermore, CBF is tightly coupled with cerebral glucose metabolism and hence allows mapping brain activation under a task or a drug, as well as the diagnosis of various neurological diseases. Conventionally, CBF is measured by injecting exogenous contrast agents, such as Gd-chelates or $^{15}$O-water, together dynamic imaging of the tracer kinetics. Arterial spin labeling (ASL) MRI, by magnetically labeling blood water spin as a freely diffusible endogenous tracer, allows noninvasive, quantitative and repeated measurement of CBF. Although low sensitivity and technical difficulty had hindered its application in early years, with recent advances in pulse sequence and high-field MRI, ASL has been started to be applied in large-scale studies including the Alzheimer’s Disease Neuroimaging Imitative (ADNI). We have been developing ASL for human and animal studies to facilitate translation from mouse model to patient. Longitudinal study in transgenic mice expressing human ApoE genes showed reduction of CBF in cortex and hippocampus. In human, global and regional reduction of CBF can be detected between AD, mild cognitive impairment, and normal control subjects. Whether reduced CBF contributes the neurodegeneration or is the result of degeneration is a topic of ongoing study.
Professor Duk L. Na

Date of Birth: Nov. 28, 1956

Gender: Male

Nationality: Korean

Current Address: Department of Neurology,
Samsung Medical Center,
Sungkyunkwan University School of Medicine
50 Ilwon-dong, Kangnam-ku, Seoul, 135-710, Korea
Tel: 82-2-3410-3591, 2378, 3599
Fax: 82-2-3410-0052
E-mail: dukna@skku.edu, dukna@naver.com

Education:

Date | Experience
--- | ---
Sep. 1989 - Aug. 1992 | Ph.D. in College of Medicine, Korea University, Seoul, Korea
Mar. 1987 - Feb. 1989 | Postgraduate Master Course (Neurology), College of Medicine, Seoul National University, Seoul, Korea
Mar. 1978 - Feb. 1982 | College of Medicine, Seoul National University, Seoul, Korea
Mar. 1976 - Feb. 1978 | Premedical School, College of Natural Science

Degree and Qualification

Dates | Experience
--- | ---
Aug. 31. 1992 | Ph.D. conferred by Korea University, Seoul, Korea
Feb. 26. 1989 | M.S., conferred by Seoul National University, Seoul, Korea
Feb. 26. 1989 | Board of Neurology (No.221), granted by Ministry of Health and Social Affairs, Republic of Korea
Feb. 28, 1982 | M.D.(No 24781), granted by Ministry of Health and Social Affairs, Republic of Korea

Professional Qualifications:

Date | Qualifications
--- | ---
Sept. 2009 - Present | Chairman, Department of Neurology
Mar. 2002 - Present | Professor, Department of Neurology

Sungkyunkwan University School of Medicine, Seoul, Korea
**Associate Professor, Department of Neurology**  
Sungkyunkwan University School of Medicine, Seoul, Korea

Neurology Staff in Samsung Medical Center, Seoul Korea

Research and Clinical fellow (Behavioral Neurology and Clinical Neuropsychology) at University of Florida, Gainesville, Florida

Research and Clinical fellow (Behavioral Neurology and Dementia) at University of Western Ontario, London Canada

Clinical Assistant Professor, Seoul National University Hospital

Fellowship in Neurology, Seoul National University Hospital

May. 1986 - Feb. 1989  
Residency, Neurology, Seoul National University Hospital

Medical officer, Republic of Korea, Army forces

Internship, Seoul National University Hospital, Seoul, Korea

Publications (International Journals only):


Dr Helen Juan Zhou

Title: Assistant Professor  
Official mailing address: 8 College Road, #06-33, Singapore 169857  
Contact No: +65 66012392  
Email: helen.zhou@duke-nus.edu.sg

Current position and employment history:

- 08/2011 – present, Assistant Professor, Neuroscience and Behavioral Disorders Program, Duke-NUS Graduate Medical School, Singapore
- 01/2011 – 07/2011, Associate Research Scientist, Phyllis Green and Randolph Cowen Institute for Pediatric Neuroscience, Child Study Center, New York University, NY, USA
- 10/2008 – 12/2010, Post-doctoral fellowship, Memory and Aging Center, Department of Neurology, University of California, San Francisco, CA, USA
- 03/2007 – 09/2008, Research fellow, Computational system biology program, Singapore-MIT Alliance, Singapore

Academic qualifications:

- Postdoctoral fellowship, Memory and Aging Center, Department of Neurology, University of California, San Francisco, CA, USA, 2008-2010
- Ph.D., School of Computer Engineering, Nanyang Technological University, 2004-2007
- B. Eng, Accelerate Bachelor Program (3.5 years), 1st class honor, School of Computer Engineering, Nanyang Technological University, 2000-2003

Publications:

- Zielinski BA, Gennatas ED, Zhou J, Seeley WW. Network-level structural covariance in the developing brain.


Scientific Awards and Research Achievements:
- Nominee for Lee Kuan Yew Gol Mud Medal and the Institution of Engineers Singapore Gold Medal, School of Computer Engineering, Nanyang Technological University, Singapore, 2004
- Student award, 2nd IAPR International Workshop on Pattern Recognition in Bioinformatics, 2007
- Paper was selected for highlights in 62nd Annual meeting of American Academy of Neurology, 2010
- Travel award from 7th International conference on frontotemporal dementias, Indianapolis, USA, 2010
Dr Mohammad Kamran Ikram

Department/Institution: Department of Ophthalmology, National University Health System

Mailing Address: 1E Kent Ridge Road, NUHS Tower Block, Singapore 119228

Email: kamran_ikram@nuhs.edu.sg

Contact No.: (65) 6772 3979; (65) 8126 1594

Current Position(s):
Assistant Professor & Lee Kuan Yew Fellow, Department of Ophthalmology, National University of Singapore
Principle Investigator Neuro-epidemiology Theme, NUHS Memory Aging & Cognition Centre (MACC)
Adjunct Clinician Scientist, Singapore Eye Research Institute
Senior Clinical Fellow, Department of Medicine (Neurology), NUHS

Academic Qualifications:

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<tr>
<th>Year</th>
<th>Institution</th>
<th>Degree/Discipline</th>
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<tr>
<td>1999</td>
<td>Netherlands Institute for Health Sciences</td>
<td>M.Sc. (Epidemiology)</td>
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<tr>
<td>2001</td>
<td>Erasmus Medical Center/Erasmus University</td>
<td>M.D.</td>
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<tr>
<td>2005</td>
<td>Department of Epidemiology, Erasmus Medical Center</td>
<td>Ph.D.</td>
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<tr>
<td>2010</td>
<td>Department of Neurology, Erasmus Medical Center</td>
<td>Neurologist</td>
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Research Interests:
Retinal vascular disease, epidemiology, cerebrovascular diseases, dementia, novel ocular imaging

Selected Publications:


Recent Scientific Awards:
2012 NMRC Clinician Scientist Award (Investigator Category)
2012 NUHS Clinician Scientist Program Award
2012 Young Investigator Award by the Asian Pacific Society of Hypertension and Hypertension Sydney 2012
2011 National Veni award by the “Netherlands Organization for Scientific Research”, the Netherlands
2011 Lee Kuan Yew Postdoctoral Felowship Award, Singapore
Dr Andrea Lim Yu-An

Contact No: 9150-1051

Office Mailing Address:
#09-02T, Centre for Translational Medicine (CeTM), 14 Medical Drive, Singapore 117599

Current Position:
(June 2012~) Research Fellow in YLLSoM @ NUS.

Academic qualifications:
(2006-2009) PhD, University of Sydney
(2005-2005) Honours of Science, University of Melbourne
(2002-2004) BSc (Majors in Neuroscience and Immunology), University of Sydney

Research interests:
Alzheimer’s disease, diabetes mellitus, mitochondrial dysfunction, amyloid-beta, amylin, neurotoxicity.

Experiences:
(1) Postdoctoral Research Associate, University of Sydney (2010-2011).
(2) Host of Research Topic and Associate Editor of Frontiers Journal (Feb 2012~),
(3) Grant reviewer for Czech Science Foundation (main public funding agency in the Czech Republic)(Oct 2012~).

Publications:

Peer-reviewed Journal Publications
1. Lim YA, Murray LA, Lai MKP, Chen CC (2013). NeuroAid™ and Amyloid Precursor Protein Processing. Cerebrovascular Diseases (Accepted)

Monograph:
Dr Mitchell Lai

Office: Dept. Pharmacology, Yong Loo Lin School of Medicine, National University of Singapore, Kent Ridge, Singapore 117597.
Email: mitchell_lai@nuhs.edu.sg

A. EDUCATIONAL QUALIFICATIONS
1995: BSc (Biological Sciences), University of Alberta, CANADA
2003: PhD (Neurochemistry), University of Sydney, AUSTRALIA

B. PROFESSIONAL EXPERIENCE
2012-present: Assistant Professor, Dept. Pharmacology, National University of Singapore
2010-present: Co-Investigator, Memory, Aging and Cognition Centre, National University Health Systems
2011-2012: Research Assistant Professor, Dept. Pharmacology, National University of Singapore
2004-2010: Principal Research Scientist, Dept. Clinical Research, Singapore General Hospital

C. RESEARCH INTERESTS
- Neurochemistry of dementia
- Biomarkers for dementia
- Novel dementia therapeutics

D. SELECTED PUBLICATIONS


Professor Paul T Francis

BSc PhD

Work address:
Wolfson Centre for Age-Related Diseases, Guy's Campus, King's College London, St Thomas Street, London SE1 1UL,
☎️+44 (0)207 848 6269, Fax +44 (0)207 848 6240, paul.francis@kcl.ac.uk

Academic Background

1976-1979 BSc Physiology and Biochemistry, University of Reading, Reading, UK
Degree: 2(i).
1984 Doctor of Philosophy
Title of Thesis: The role of the monoamine neurotransmitters in the control of luteinizing hormone release in the domestic fowl (Gallus domesticus).

Professional Experience

1982-86 Post-Doctoral Research Fellow, Institute of Neurology, Department of Neurochemistry.
1986-90 Post-Doctoral Research Fellow, Institute of Neurology, Department of Neurochemistry.
1990-95 Honorary Lecturer in Neurochemistry (Brain Research Trust).
1994 - Recognised Teacher, University of London
1995- 2004 Senior Lecturer in Biochemistry, Division of Biochemistry and Molecular Biology, UMDS.
2004-2008 Reader in Neurochemistry, University of London.
2007- Directed Brains for Dementia Research, a £2.3M initiative by Alzheimer Research Trust and Alzheimer’s society
2008 - Professor of Neurochemistry

Current Grants

- Alzheimer’s Society/Alzheimer’s Research UK, £3.2m Brains for Dementia Research 2013-2018
- Safra Foundation, £270,000 (with Prof Clive Ballard) Models of Lewy body dementia and Parkinson’s disease dementia 02/2012-01/2017.
- Alzheimer Society/BUPA, £245,215, 11/10-10/13. PI (with Dr Hortobagyi and Dr Attems, NCL co-applicants). Biochemical investigations of behavioural disturbance in Lewy body dementia. Staff: Dr Julie Vallortigara.
- Government of the Kingdom of Saudi Arabia, £72,000, PhD studentship for Mrs Amani AlGamdhi. 10/10-09/14.
- Alzheimer Society & Alzheimer Research UK PI (with Prof Lovestone and Dr Al-Sarraj) Establishment of Brains for Dementia Research, £2.5M, 2008-2013. Personal grant £825,000.

Publications in refereed journals


A/Professor Newman Sze

Address: School of Biological Sciences, NTU, 637551.
Email: sksze@ntu.edu.sg;
Contact No: 6514-1006 (O); 9183-9800 (HP); Fax: 6791-3856

Current Position:
Associate Professor, Nanyang Technological University, Singapore; Director, Proteomics Facility, Nanyang Technological University. (100% full time appointment in Singapore.)

Academic Qualifications:
1990-1995 Ph.D., University of Hong Kong, Hong Kong
1987-1990 B.Sc.(First Class Honours), University of Hong Kong, Hong Kong

Research Interests:
We conduct multi-dimensional research that falls within the frame of proteomics and clinical application. Our goal is to develop new methods in proteomic technology to uncover answers pertaining to biological and biomedical questions that are difficult or impossible to be studied with use of traditional biochemical and molecular biology methods. Our proteomic methods are being successfully employed to decipher human diseases and biomarkers including cardiovascular diseases and stroke.

Selected Publications Most Closely Related To The Proposal:
Professor Geert Jan Biessels

Current position: Professor of Neurology, Cerebrovascular Disease & Cognition
Program leader Utrecht Vascular Cognitive Impairment research group;
http://www.uu.nl/vkc/vci
Section Cerebrovascular disorders, Department of Neurology and Neurosurgery, Rudolf Magnus Institute of Neuroscience, UMC Utrecht
Head of Department Prof GJE Rinkel

Work address:
Department of Neurology G03.228
University Medical Center Utrecht
PO Box 85500, 3508GA Utrecht, the Netherlands
g.j.biessels@umcutrecht.nl
Phone +31 88-7558600; Fax +31 30-2542100

Academic education/Positions after PhD
• Master's Degree: Utrecht University 1986-92 Medicine, 1990-92 Medical Biology; cum laude
• Medical Degree: Utrecht University 1995
• Doctorate Medicine: Utrecht University 1997; thesis: Cerebral function in diabetes mellitus
• 1998-2004: Resident in Neurology, UMC Utrecht, head of department Prof Dr J van Gijn
• From 2004: Neurologist, UMC Utrecht
• 2004: fellowship at the Alzheimer Centre of the VUMC Amsterdam, Prof Dr P Scheltens
• From 2011: Head of section General Neurology of the department of Neurology UMC Utrecht
• Form July 2012: Professor of Neurology, UMC Utrecht

My research line focuses on the role of vascular disease in cognitive decline and dementia, referred to as “vascular cognitive impairment” (VCI). In this context, we have extensively studied cognition and dementia in people with diabetes. We have established the severity and course of development of cognitive decrements in diabetes and prediabetic stages, the relation with vascular disease, and identified brain MRI correlates of impaired cognition. We apply new brain MRI techniques, including advanced volumetric measurements and assessment of microstructural cerebral white matter integrity, with Diffusion Tensor Imaging (DTI). We also develop high-resolution 7T MRI for application in VCI, allowing detection of vascular brain lesions with unprecedented detail.

The VCI program involves 20 UM CU staff members and 18 PhD students from the departments of neurology, neuropsychology, radiology, image sciences, geriatrics, epidemiology, primary care medicine, and rehabilitation medicine. There are intensive (inter)national collaborations

Honors and awards
• 1998: Dutch Association for Pharmacology, best thesis: Cerebral function in diabetes mellitus
• 1999: Neurodiab prize for preclinical science. Neurodiab is the official diabetic neuropathy study group of the European Association for the Study of Diabetes (EASD).
• 2010: Nederlandse Hartstichting, Clinical Established Investigator Fellowship

Publications (recent key publications from over 140 peer-reviewed papers and book chapters)
Dr Qiu Anqi

Department of Bioengineering,  
Clinical Imaging Research Centre  
National University of Singapore  
9 Engineering Drive 1, Block E3 #03-12,  
Singapore, 117574  
Email: bieqa@nus.edu.sg  
http://www.bioeng.nus.edu.sg/~cfa

Education

2006   Ph.D. in Electrical and Computer Engineering     the Johns Hopkins University
2005   M.S. in Applied Mathematics and Statistics         the Johns Hopkins University
2002   M.S. in Biomedical Engineering                    University of Connecticut
1999   B.S. in Biomedical Engineering                    Tsinghua University

CURRENT POSITIONS

2007-present Assistant Professor at department of bioengineering of NUS
2009-present Joint Assistant Professor at Clinical Imaging Research Center
2008-present Adjunct Assistant Professor at Singapore Institute for Clinical Science
2007-present Visiting Professor at Johns Hopkins University

SCIENTIFIC AWARDS

Young Investigator Award, National Univ. of Singapore, 2010

PUBLICATIONS

Dr Kai-Hsiang CHUANG

Office Mailing Address: Singapore Bioimaging Consortium. 11 Biopolis Way, #02-02, Singapore 138667.
Contact No : Tel: +65-64788764 / Fax: +65-64789957.
Email : chuang_kai_hsiang@sbic.a-star.edu.sg

Current positions:
April 2009 – present: **Head**, MRI Group, Singapore Bioimaging Consortium, A*STAR.
April 2009 – present: **Adjunct assistant professor**, Department of Physiology, Yong Loo Lin School of Medicine, NUS.
July 2009 – present: **Research Scientist**, Clinical Imaging Research Centre, NUS.

Professional Experiences

<table>
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<tr>
<th>Employment History</th>
<th>Appointments</th>
<th>Institution</th>
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<tr>
<td>2008-2009</td>
<td>Group Leader</td>
<td>Laboratory of Molecular Imaging, Singapore Bioimaging Consortium, A*STAR, Singapore</td>
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<tr>
<td>2003-2007</td>
<td>Research Fellow</td>
<td>National Institutes of Health, Bethesda, Maryland, USA</td>
</tr>
<tr>
<td>2002-2003</td>
<td>Associate MR Scientist</td>
<td>Dept of Radiology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan</td>
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Academic qualifications

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<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<tr>
<td>National Taiwan University, Taiwan</td>
<td>BS</td>
<td>1991-95</td>
<td>Electrical Engineering</td>
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<td>National Taiwan University, Taiwan</td>
<td>MS</td>
<td>1995-97</td>
<td>Biomedical Engineering</td>
</tr>
<tr>
<td>National Taiwan University, Taiwan</td>
<td>PhD</td>
<td>1997-2001</td>
<td>Biomedical Engineering</td>
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Research interests

MRI; functional imaging; neural plasticity; neurodegeneration; brain development;

Publications of direct relevance to the study


**Scientific Awards**

2006 Fellows Award for Research Excellence, NIH, USA

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Ms Jean Toh (National University of Singapore)
Mr Abdul Aziz Bin Salim (National University of Singapore)
Ms Lynn Yap Jing Ting (National University of Singapore)
Ms Jasinda Lee (National University of Singapore)
Ms Chai Yuek Ling (National University of Singapore)
Mdm Salmah Yassin (National University of Singapore)

Organizers

A/P Christopher Chen Li Hsian Director
Memory Aging & Cognition Centre, NUHS

Dr Mitchell Lai Department of Pharmacology,
National University of Singapore

The Secretariat
Yudi Wisantoso
Siobhan Li Peipei