National Centre for Neuroimmunology and Emerging Diseases

September 2021

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Our Mission

The National Centre for Neuroimmunology and Emerging Diseases (NCNED) is a research team located at Griffith University on the Gold Coast. Led by Professors Sonya Marshall-Gradisnik and Donald Staines, the team has a focus on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/ CFS).

Our mission is to translate research findings into preventative medicine, social and clinical care, and public health outcomes. By collaborating with local, national and international research institutes, we aim to create sustained improvements in health and health care for not only those affected by ME/CFS but also other immune disorders.

INTERNATIONAL ME/CFS CONFERENCE 2021: RID

The second ME/CFS International Conference 2021: RID-Research, Innovation and Discovery to be held at Sea World Resort and Conference Centre, Gold Coast, Queensland, Australia on the 16th and 17th of November 2021 is drawing closer. This will be a hybrid conference - a mixture of both in person and virtual presentations from national and international speakers. We are delighted to confirm the attendance of our key note speakers: Dr Elizabeth Unger, Centers for Disease Control and Prevention, USA; Dr Vicky Whittemore, National Institutes of Health, USA; Dr Avindra Nath, National institute of Neurological Disorders and Stroke (NINDS/NIH), USA; A/Prof Pawel Zalewski, Nicolaus Copernicus University, Poland; Professor Katsuhiko Muraki, Aichi-Gakuin University, Japan; Emeritus Professor Warren Tate, University of Otago, NZ; Dr Daniel Peterson, President of Sierra Internal Medicine in Incline Village, USA; Professor Livia Hool, University of Western Australia, Australia; Dr Jarred Younger, University of Alabama at Birmingham, USA; Dr Lucinda Bateman, Bateman Horne Center, USA; Professor Markus Barth, University of Queensland, Australia; Professor Julia Newton, Newcastle University, UK; Dr Sarah Knight, Murdoch Children's Research Institute, Australia; Professor Jonas Bergquist, Uppsala University, Sweden; Dr Nancy Klimas, Nova Southeastern University, USA; Dr Rosamund Vallings, Howick Health & Medical Centre, NZ; Professor James Baraniuk, Georgetown University Medical Center, USA; Dr Olga Sukocheva, Flinders University, Australia; Dr Gunnar Gottschalk, Simmaron Research Inc, USA; A/Prof Joshua Byrnes, Griffith University, Australia; Penelope McMillan & Geoffrey Hallmann, ME/CFS Australia; Kathy Dallest, National Advisory Advocacy Council for ME/CFS Research; together with NCNED researchers.

NCNED are pleased to announce that there will be two exciting awards presented at the RID Conference 2021 - a Student e-Poster Research Award in the amount of \$250 and a Best Early Career Researcher Award for \$250. Posters will be displayed at the conference and researchers are to deliver a short 1 minute presentation outlining their posters. The oral presentations for the Early Career Researcher Award will be delivered throughout the two day conference. This is an excellent opportunity for students and researchers to gain exposure for their research and expand their professional development opportunities and networks.

Please consider submitting an abstract for this Conference. The link can be found at: <u>https://forms.office.com/r/s9zquqFwCC</u>

To register, please click on the link https://app.secure.griffith.edu.au/griffithpay/RID-2021.html

RESEARCH VOLUNTEERS

NCNED is still looking for more participants for our Quality of Life and Burden of Illness associated with illness study. It is open to Australian residents aged 18-65 years old and will involve the completion of two online surveys. Participants will receive a \$5 Coles e-voucher and enter the draw to win \$50, \$75 and \$100 Coles e-vouchers drawn half-yearly.

NCNED is inviting patients formally diagnosed with ME/CFS and healthy controls (aged between 18 to 65 years old) to participate in continuing research using magnetic resonance imaging (MRI) of the brain. Interested participants will be asked to undergo MRI scanning with an advanced ultra-high field scanner (7 Tesla) for 60 minutes, and on the same day undergo a brief electroencephalogram (EEG) test for 15 minutes. The MRI Scanner is located at UQ, St Lucia so participants need to be able to travel to Brisbane to complete the scan. In addition to this, participants will complete 7 questionnaires for evaluation of fatigue symptoms, life quality, etc; wear a blood pressure cuff on their arm for 24 hours; and wear an activity monitor on their wrist for seven days to record physical activity, heart rate and sleep/wake information.

If you are interested in being part of these studies or would like more information, please contact NCNED on 07 56789283 or email ncned@griffith.edu.au.

ME/CFS

INTERNATIONAL

CONFERENCE

RID RESEARCH, INNOVATION

16-17 Nov 2021

National Centre for Neuroimmunology & Emerging Diseases Sea World Resort Conference Centre, Gold Coast, Old, Australia

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PUBLICATIONS



Dr Kiran Thapaliya, Dr Leighton Barnden and NCNED Researchers have published an important neuroimaging paper using diffusion tensor imaging (DTI). The findings were published in European Journal of Neuroscience.

This paper reports microstructural changes in the brainstem regions (mid-brain, pons and medulla) in ME/CFS in contrast to healthy controls. DTI parameters interaction-with-group regressions were abnormal for the clinical measures in both grey and white matter regions. Furthermore, we also demonstrated that only the stricter ICC case definition of ME/CFS could identify the neuropathology of this illness.

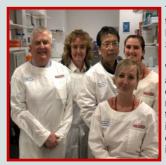
The information and link is below: "Diffusion tensor imaging reveals neuronal microstructural changes in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome". Authors: Kiran Thapaliya, Sonya Marshall-Gradisnik, Donald Staines and Leighton Barnden. Link to article: <u>https://onlinelibrary.wiley.com/doi/abs/10.1111/ejn.15413</u>

We are also pleased to announce an important article published in the Journal of Translational Medicine titled: 'The effect of IL-2 stimulation and treatment of TRPM3 on channel co-localisation with PIP2 and natural killer cell function in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) patients.' Authored by Natalie Eaton-Fitch, Helene Cabanas, Stanley du Preez, Don Staines and Sonya Marshall-Gradisnik. NCNED researchers have previously demonstrated impaired transient receptor potential melastatin 3 (TRPM3) ion channel and impaired calcium (Ca2+) mobilisation have been implicated in ME/ CFS pathology.

Link to article: https://doi.org/10.1186/s12967-021-02974-4

This new investigation built upon these previous novel findings. This important investigation examined natural killer (NK) cell function and the role of TRPM3 and co-localisation of the critical calcium-dependent signalling protein phosphatid/linositol 4,5bisphosphate (PIP2) with the regulatory cytokine IL-2. This study reported overnight IL-2 stimulation of NK cells effectively enhanced cytotoxicity in both ME/CFS and healthy controls cells, suggesting IL-2 remains effective and is preserved in NK cell function in ME/CFS patients. Furthermore, co-localisation of TRPM3 with PIP2 in NK cells was significantly reduced in ME/ CFS patients compared with HC following priming with IL-2.

This study provides important scientific information about the TRPM3 signalling pathway that is dependent upon sufficient Ca2+ influx and the presence of PIP2. These findings further identify the role of TRPM3 ion channel dysfunction in the pathomechanism of ME/CFS.



The NCNED team is pleased to announce a significant world-first publication in Frontiers in Immunology titled: "Potential therapeutic benefit of Low Dose Naltrexone in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Role of Transient Receptor Potential Melastatin 3 ion channels in pathophysiology and treatment" by Cabanas H., Muraki K., Eaton-Fitch N., Staines D. and Marshall-Gradisnik S.

We investigated TRPM3 function in ME/CFS patients already taking LDN using the natural killer (NK) cell model in a laboratory study. This is the first in vitro study confirming the efficacy and therapeutic benefit of LDN for ME/CFS patients by characterising the underlying regulatory mechanisms of LDN treatment involving TRPM3 and opioid receptor interaction in natural killer (NK) cells. Previous reports have been anecdotal for the clinical use of LDN and no scientific data to identify the cellular mechanism for this potential treatment have been previously published. These results confirm our previous investigations indicating ME/CFS is a channelopathy resulting from TRPM3 ion channel loss of function. This TRPM3 pathophysiology in ME/CFS is also identified as responsible for impaired Ca2+ signalling and Ca2+-mediated cell functions, including NK cell immune functions, thus validating its investigation in an NK cell model.

This publication is a significant and key step forward for ME/CFS patients. NCNED has demonstrated for the first time, that ME/CFS patients taking LDN have restored TRPM3-like ionic currents in previously impaired NK cells. This world-first scientific research study using the gold standard of Patch Clamp electrophysiology (PCE) confirms TRPM3 and opioid receptor interactions in the pathomechanism of ME/CFS, indicating the efficacy and therapeutic benefit of LDN for ME/CFS patients. Our data support the hypothesis that LDN has potential as a treatment for ME/CFS by characterising the underlying regulatory mechanisms of LDN treatment involving TRPM3 and opioid receptors in NK cells. Link to article: https://www.frontiersin.org/articles/10.3389/fimmu.2021.687806

WELCOME & WELCOME BACK



NCNED warmly welcomes Dr Jiasheng Su, Research Fellow, to the NCNED team. Dr Su's research focuses on the analysis of the functional MRI (fMRI) signals to study the pathophysiology of ME/CFS. Together with the NCNED team he will be working on the development of new medical imaging methods to map functional connectivity in the brain using ultra-high-field magnetic resonance imaging (MRI).



We are pleased to welcome back Ms Kay Schwarz who joined us during 2019-2020. Kay has returned to NCNED in the role of Centre Coordinator.

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