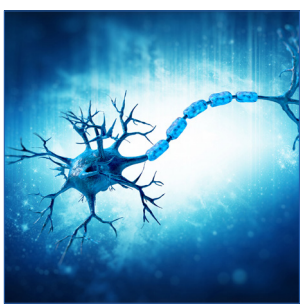
Keynote Forum
November 04, 2019

Neurology 2019




19th International Conference on

Neurology and Neurological Disorders

November 04-05, 2019 | Melbourne, Australia

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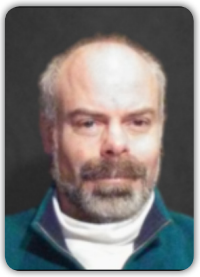

Gerald H Lushington

TheraPeptics, LLC

A glycated core of Neuropathology

What causes intractable neurological disorders such as Alzheimer's, Parkinson's and ALS? Are they primarily signal transduction pathologies? Forms of amyloidosis? Do they arise from rogue neuroinflammation? There is ample evidence for any of these etiologies, yet no single disease model has achieved clinical breakthroughs. Perhaps we must view these effects (protein dysregulation, aggregation, autoimmune dysfunction, etc.) as symptoms rather than root causes, and dig a bit deeper to identify a common pathological origin in order to discover better countermeasures.

Findings from recent publications hint at a plausible nexus for these etiologies. Specifically: 1) exposure to advanced glycation end-products (AGEs) impairs structural, enzymatic and signaling performance of various proteins, 2) AGEs tend to accelerate amyloid-related protein aggregation, and 3) glycated proteins trigger sustained inflammatory response. Much of this insight derives from studying peripheral diseases such as lupus, diabetes, arthritis, Crohn's, etc., but a compelling CNS link comes from the fourth observation that: 4) glycated proteins disrupt VEGF function, producing microvasculature that, in the choroid plexus epithelium, degrades the blood brain barrier. Taken together, this suggests a core molecular basis, amenable to structural biological characterization of the basis for how advanced glycation end-products may alter protein folding and function, hyper stimulate complement-related immune response, and produce small neurotoxic protein oligomers.

This talk will assess key observations in the neuropathology literature and apply structural biological concepts to rationalize them, en route to a framework for unraveling how glycation phenomena can help to unify disparate etiologies, and how the unified etiologies may be therapeutically exploited.

Speaker Biography

Gerald Lushington is a co-founder of TheraPeptics, LLC, a startup effort focused on applying artificial intelligence and bioinspiration for developing novel peptide formulations for antimicrobial, anticancer and immunotherapeutic medicines, as well as for a variety of analytical and diagnostic technologies. His other key biomedical interests include antiviral protease targeting and neuropathic mechanistic studies. His primary technical specializations are in informatics, modeling and visualization as applied to a diverse range of chemical and biological foci. He is Editor in Chief of the journal Combinatorial Chemistry & High Throughput Screening (Bentham Scientific) and serves on editorial boards of numerous other journals. He completed his PhD at the age of 26 years from the University of New Brunswick in Canada. He has over 200 publications that have been cited over 4100 times, amounting to an H-index of 35.

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Malcolm R Hooper

OXYMED, Australia

Hyperbaric Oxygen Therapy combined with (LOKOMAT) robotic exoskelton assisting Neuroplasticity in Brain and Spinal Cord disabilities

The Final Frontier-Repair and Functional Restoration Almost 20 to 30 per cent of the body's consumption of oxygen occurs within 3 to 5 per cent of the body mass – the brain and spinal cord structures. These structures are extremely sensitive to oxygen deficiency and benefit from oxygen repletion. The final frontier in the treatment of degenerative neurovascular disorders is focused on 'repair and functional restoration'. This involves the use of neural growth factors to promote axonal sprouting, activation of idling and non-functional neurons whilst promoting neovascularisation (new capillary formation) of the damaged (penumbra) areas.

Cells in a chronic hypoxic state overexpress pro-inflammatory cytokines including IL1, Il6, IL7, IL8, IL17, TNFa, MMP9, S100B. The smoldering 'cytokine storm' differs for each individual. Over expression of pro-inflammatory cytokines inhibit neuroplasticity and neurogenesis and promote secondary apoptotic cascades. The extent of both primary and secondary neurovascular deterioration can be significantly diminished with HBOT, which 'expands the therapeutic window'. "Hyperbaric Oxygen Therapy creates a 'fertile neurovascular platform' for emerging stem cell, immunotherapies and nanotechnology techniques. The impact and success of these and future procedures are dependent on the integrity of the underlying supporting neurovascular bed." (Hooper 2005).

The benefits of HBOT in rehabilitation is well documented. Hyperbaric tissue oxygenation results in increased blood flow by fostering the formation of 'new capillary dynamics' (neovascularization) into the damaged regions of the body. Hyperbaric tissue oxygenation accelerates neuroplasticity, activating damaged and dormant nerve cells (penumbra state). Increased Oxygenation significantly accelerates the rate of healing, stabilization and repair through numerous immune modulating effects, providing upregulation of anti-inflammatory cytokines, including: Granulocyte Macrophage Colony Stimulating Factor (GM-CSF), Interleukin-3 (IL3), Interleukin-4 (IL4), Interleukin-10 (IL10), Interleukin-13 (IL13), Interleukin-21 (IL21), Brain Derived Neural Growth Factors (BDNF, GDNF), Vascular Growth Factors (VEGF), TGFβ Signaling and IGF1. From the American Journal Physiology, Heart and Circulatory Physiology (2005): Stem Cell Mobilization by Hyperbaric Oxygenation reports a single two hour exposure to HBOT at 2 ATA doubles circulating CD34+ progenitor stem cells (primordial cells targeted to salvage and restore damaged structures). At approximately 40 hours of HBOT, CD34+ cells increase eight-fold (800 percent). LOKOMAT Robotic Gait Assisted Walking is a sophisticated exoskeleton technique where the patient is fitted with a harness, suspended from the wheel chair and strapped into the exoskeleton. The LOKOMAT kinetic settings can be varied and specifically adjusted throughout the training session to "match the specific requirements of the individual". Some patients have high level spasticity and others have a complete loss of tone. Robotic assisted training can be constantly adjusted to provide numerous accurate repetitions necessary to restore activity, especially walking function for neurologic patients. Improving a patient to the point that he or she no longer needs a wheelchair to move leads to reducing the economic burden associated wheel chair-associated complications that include pressure ulcers, circulatory disorders, osteoporosis and attendant care. LOKOMAT provides excellent opportunity to 'best-fit' a patient's specific capabilities and capacity to re-train function. LOKOMAT Gait Training not only improves the gait in neurological patients, it also positively effects cardiovascular performance and reductions in spasticity, bone loss and associated bladder or bowel complications. The combined benficial effects of Hyperbaric Oxygen Therapy and LOKOMAT Gait Training are explored in this presentation.

Speaker Biography

Malcolm R Hooper is the International Executive Director serving both the Hyperbaric Medicine International (HMI) and the International Hyperbaric Medical Foundation (IHMF). He is a regular speaker at international symposiums on the topic of Hyperbaric Oxygen Therapy applications in the modern era.

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Franz Grus

University Medical Centre Mainz, Germany

Autoimmune Biomarkers and AI algorithms could lead to new diagnosis and treatment options in Neurodegenerative diseases such as Glaucoma

Glaucoma is a chronic neurodegenerative disease and one of the leading causes of blindness. The elevated pressure cannot explain the disease in all patients. In glaucomatous human retinae, we could demonstrate some significant proteomic biomarkers by LC-ESI-MSMS and antibody microarrays. Several of those markers provide hints for an involvement of the immune system. Therefore, we used several bead-based mass spectrometric approaches for immunoproteomics. We could show alterations in serum antibody profiles of glaucoma patients against optic nerve and retinal antigens, upregulations (e.g. anti-HSP60, anti-MBP) and downregulations (e.g. anti-14-3-3) have been described. These markers were validated by antigen microarrays and are consistent in independent study populations. Additionally, the changes in antibody profiles could be used as highly sensitive and specific marker for diagnostics purposes. Using algorithm approaches from artificial intelligence and connections of different neural networks including deep learning approaches, we could demonstrate a sensitivity and specificity of more then 93%. Early diagnosis and intervention in risk patients would offer the chance of early treatment and to slow down the progression of disease. Furthermore, it could be shown that the intravitreal injection of some of these antibodies shows a neurorecovery in glaucoma animal models. We hypothesize that the homeostasis of the autoimmune system plays an important role in recovering and protecting those RGS in early damage. Using these markers could allow a beneficial translation into clinical routine for diagnosis and personal treatment.

Speaker Biography

Franz Grus is the Head of Experimental and Translational Ophthalmology. Currently, he is working at the Department of Ophthalmology, University Medical Centre Mainz, Germany. He is doing Research in Ophthalmology, Bioinformatics and Immunology. Furthermore, the research is focused on proteomics and immunoproteomics in ocular fluids and tissues acting as proteomics core unit with mass spectrometry and customized microarrays. He is also Consultant for pharma and start-ups. He Founded several companies e.g. focused on development of point-of-cares devices for diseaes such as glaucoma. He has several patent applications and approved patents.

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Hiroko Ikeshima-Kataoka

Keio University School of Medicine, Japan

Osteopontin has Neuroimmunological function for reactivation of Astrocytes and Microglial cells in stab wounded mouse Brain and LPS stimulated primary culture

Osteopontin (OPN) is an inflammatory cytokine inducer involved in cell proliferation and migration in inflammatory diseases, injuries or tumors. To clarify the functional role of OPN in reactivation of astrocytes during brain injury, we compared OPN-deficient (OPN/KO) with wild type (WT) mouse brains after stabbing wound injury on the cerebral cortex as a brain traumatic injury model. Furthermore, primary culture of astrocytes or microglial cells from either genotype of postnatal mouse brains was prepared and treated with lipopolysaccharide (LPS) to induce inflammation in the cells. By the immunofluorescent analysis on the injured brain sections, either astrocytes or microglial cell activation was attenuated in OPN/KO mice compared with WT mice confirmed with bromo-deoxy urine incorporation as a cell proliferation marker. Activation efficiency of astrocytes in primary culture was accessed using Western blotting analysis by examining the protein expression levels of glial fibrillary acidic protein (GFAP) and tenascin-C (TN-C), which are the markers for reactive astrocytes. The expression levels of both GFAP and TN-C were downregulated in the primary culture of astrocytes from OPN/KO mice compared to that from WT mice. Additionally, primary culture of astrocytes prepared from OPN/KO mice showed only 25% of normal shaped astrocytes in a flask were produced compared to that from WT mice. These data suggest that OPN is essential for proper astrocytic generation in vitro culture prepared from mouse cerebral cortex. Moreover, OPN is indispensable for astrocyte activation in the mouse brain injury model and in LPS stimulated primary culture.

Speaker Biography

Hiroko Ikeshima-Kataoka was graduated from Keio University School of Medicine (Dept. of Microbiology) and got Ph.D. on the functional analysis of calmodulin genes using transgenic mice. At the National Institute of Neuroscience, researched on the molecular mechanism of neuronal development using fly genetics. Then, promoted back to Keio University School of Medicine) and started to focus on the "reactive astrocytes" in injured mouse brain. At Jikei University School of Medicine, aimed on neuroimmunological analysis in mouse brain and primary culture. Promoted back again to Keio University School of Medicine (Dept. Pharmacology and Neuroscience) and found important molecules concerned in neuroimmunological functions of astrocytes. Now, using in vivo imaging on mouse to analyze functional role of "reactive astrocytes" at Waseda University, Faculty of Science and Engineering.

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