Keynote Forum
October 16, 2017

Neuro 2017

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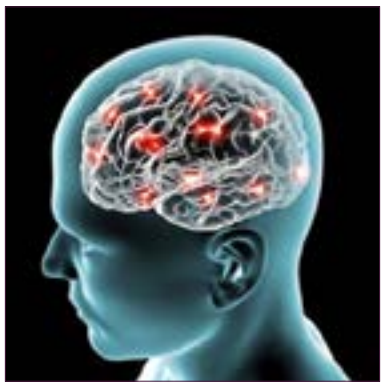


17th International Conference on
NEUROLOGY AND NEUROSCIENCE &
4th International Conference on
MENTAL HEALTH AND PRIMARY CARE

October 16-18, 2017 | Toronto, Canada

M Raafat El-Gewely

UiT-The Arctic University of Norway, Norway

Lessons learned from the study of non-malignant meningioma tumors profiling

Meningiomas represent the most common primary tumors of the central nervous system. Meningiomas originate from the arachnoid tissue and are classified into grades I to III according to the WHO system, with grade III is malignant. The proliferation rate in meningioma increases from grades I to III. The majority of clinically encountered meningiomas is benign, and corresponds to grade I. These tumors have a slow growth rate and generally are with minimal risk. Since most of our knowledge about tumors are based on malignant tumors, thus investigating and comparing elements of transcriptional expression profiles in these slow growing non-malignant tumors with those of malignant tumors would help clarify tumorigenesis and growth, as well as revealing the presence of molecular elements that must be expressing and are preventing non-malignant tumors from progressing to malignancy. With a focus on the profiling of micro RNAs and putative mRNA targets, deep sequencing of small RNA libraries from two human meningioma biopsies grades I and II were compared to excess dura controls. Validation of the differentially expressed microRNAs and putative mRNA targets in more patient tumors and controls was by RT-qPCR. The tumor suppressors' miR-143, miR-193b and miR-451 were lower in the tumors than the control. Surprisingly, microRNAs, miR-34a and miR-218 were at a higher level in tumors than controls. Cancer-promoting miR-21 RNA was expressed to a much lower level. Observed over-expression of p63 and cyclin D1 were also observed in cancerous tumors, while tumor suppressors PTEN and E-cadherin were at high level. In conclusion, non-cancerous meningiomas share important biomarkers with cancerous tumors, at least miRNAs promoting the formation of tumors. However, these non-malignant tumors also express other biomarkers preventing progression to cancer. Expanding this study and including other benign and non-malignant tumors should be investigated.

Speaker Biography

M Raafat El-Gewely currently is Professor Emeritus, Institute of Medical Biology, University of Tromsø, Norway. He served as Professor of Biotechnology, 1988-2012 (Appointed by king Olav of Norway); Director of Biotechnology Center, University of Tromsø 1989-1999, Assoc. Research Scientist, Department of Biological Chemistry, U. of Michigan Medical School. Ann Arbor, Michigan1983-1988; Visiting Scholar at Dept. of Cellular and Molecular Biology, University of Michigan, 1977-1983. He also served as Visiting or Adjunct Professor at several universities including UCSD Med School, Institute for Systems Biology (ISB), Adjunct Professor at Dept. of Biotechnology, University of Aalborg, Denmark, Dept. of Microbiology and Immunology, Medical School, University of Michigan; Dept. of Biological Chemistry, Medical School, University of Michigan, Chief Editor of "*Biotechnology Annual Review*" (1995- 2009). He has extensive research experience in in Molecular Biology, Recombinant DNA and Genetic & Protein Engineering Technologies with numerous publications; developing therapeutics using a novel alternative approach to gene therapy and genetic control of protein folding (patents). He is focused on the utilizations of modern tools in translational applications in medicine.

e: raafat.el-gewely@uit.no

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Tatsuo Ido

Gachon University, Republic of Korea

Radiopharmaceuticals for PET imaging of brain functions

PET (Positron Emission Tomography) is one of the most effective methodologies for the functional and molecular imaging of human brain with high sensitivity and quantitative measurement. This consists from the coincident matrix detection technique and the in-vivo positron tracer. In 1976, the first brain regional glucose consumption mapping in human had been succeeded with ^{18}FDG in collaboration among of Brookhaven National Laboratory, NIH and Pennsylvania University. These regional glucose consumption mapping had led to understanding the function of central nerves system (specially, sensor cortex and mortar cortex). In 1982, the first neuro-receptor imaging (Dopamine D2) human brain in-vivo with ^{11}C-methylspiperon was succeeded in the collaborative work between Johns Hopkins Medical School and Uppsala University. This was the starting point of the molecular imaging by PET. After this, the compounds related to signal transduction (agonist, antagonist) were labelled with ^{11}C or ^{18}F and applied to determination of synapse activity. Dopaminergic, Serotonergic, Cholinergic, Histaminergic, GABAergic, Glutamatergic receptors can be determined by this method. Also positron labelled MAO inhibitor and ACh-esterase inhibitor are applied to diagnosis of Parkinson's disease (PD) and Alzheimer's diseases (AD). Recent highlight works in Brain PET research are the imaging of amyloidal plaque and active tau protein for AD patient. ^{11}C- and ^{18}F-labelled thioflavin analogs have been developed as amyloidal plaque marker. Active tau protein image by ^{18}F-THK compound (quinoline derivative) is closer related to cell denature than amyloidal plaque image. Another highlight work is the imaging of neuro-inflammation that may be important to find tissue denature at early stages in PD, AD and other neurodegenerative diseases. For this purpose, TSPO (translocator protein) ligand (phenoxy phenyl acetamide and oxo purine derivatives) is labelled with ^{11}C and ^{18}F. Development of PET methodology requires both factors such as the progressing of detection equipment and the finding of new radiopharmaceuticals which are suitable for functional imaging and molecular imaging.

Speaker Biography

Tatsuo Ido is a Chair Professor and the Director of Theragnostic Compound R&D Center, Neuroscience Research Institute, Gachon University (Republic of Korea) and Emeritus Professor of Tohoku University (Japan). He had completed his PhD of Pharmaceutical Sciences at Graduate School of Tokyo University (Tokyo, Japan) in 1970. He has investigated PET radio-pharmaceuticals for near 50 years at National Institute of Radiological Sciences (Chiba, Japan), Brookhaven National Laboratory (Long Island, USA) and Tohoku University (Sendai, Japan). In 1976 at BNL, he had succeeded first synthesis of ^{18}FDG and applied to human brain functional study. After retired as Professor of Tohoku University, he had continued his research work as Professor of High Energy Biomedical Research Center of Fukui University (Fukui, Japan). From 2007 to 2012, he had leaded stable supply of radioisotopes in Japan at Japan Radioisotope Association as Executive Director. From 2013 until present, he is working continuously in developing new PET radiopharmaceuticals in Neuroscience research field.

e: ido@gachon.ac.kr

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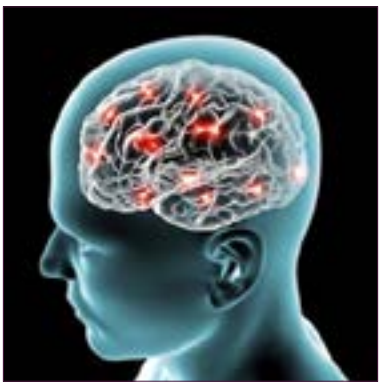


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Takehiko Fujino

Kyushu University, Japan

Efficacy and blood plasmalogen changes by oral administration of plasmalogen in patients with Alzheimer's disease

Reduced levels of plasmalogens (Pls), a special class of glycerophospholipids, have been reported in the brains and the blood of patients with Alzheimer's disease (AD). Therefore, we have assessed the efficacy and safety of scallop-derived Pls in patients with AD. The results were as follows: The multicenter, randomized, double-blind, placebo-controlled trial in patients with mild AD and mild cognitive impairment; Of 328 patients enrolled, 276 patients completed the trial. They orally received either 1 mg/day of Pls or placebo. In mild AD patients, Wechsler Memory Scale- Revised significantly improved among females and those aged below 77 years in the treatment group. Non-controlled trial in patients with moderate to severe AD; 53% of 57 patients with moderate AD and 28% of 18 patients with severe AD showed a significant improvement of Mini Mental State Examination after the oral administration of 1 mg Pls daily for three months. All patients with mild to severe AD showed the reduced levels of erythrocyte membrane and plasma Pls. Oral administration of purified Pls derived from scallop increased the levels of Pls in the peripheral blood. The improvement of cognitive functions correlated with the increase of erythrocyte membrane Pls. These findings suggest that oral administration of scallop-derived purified Pls improve cognitive functions of AD patients.

Speaker Biography

Takehiko Fujino is an Emeritus Professor of Kyushu University. He has graduated from Medical School of Kyushu University, Japan, in 1964. He is strongly interested in the Integrated Medicine, especially in the correlation between brain and other organs although his specialty was initially Cardiology of Internal Medicine. He has advocated a new concept "Brain Fatigue", from which many kinds of diseases might be induced, and developed "BOOCS: Brain-Oriented Oneself-Care System", a new method for removal of "Brain Fatigue" in 1994. It has been known that many kinds of disorders such as metabolic syndrome, depression and dementia were improved and then the death rate of those patients decreased by "BOOCS" method. As one of those researches, he has studied the correlation between plasmalogen and "Brain Fatigue".

e: fujino-t@boocsclinic.com

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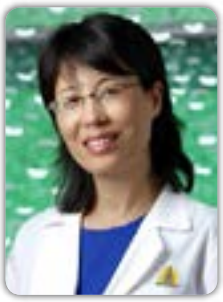

Wenzhen Duan

Johns Hopkins University, USA

Therapeutic target and biomarker development in Huntington's disease

Most neurodegenerative diseases, including Alzheimer's, Parkinson's, and Huntington's disease (HD), have converging pathogenesis, such as formation of abnormal protein aggregates and mitochondrial dysfunction in the nervous system. Unfortunately, despite tremendous efforts by many scientists and increasing knowledge about disease mechanisms, we still lack disease-modifying treatments for any of these diseases. While these diseases affect different areas of the brain and are distinct at the cellular and molecular levels, they share underlying similarities. Thus, development of treatment for any one disease has the potential to accelerate the path to treatment for related neurodegenerative diseases. Research into potential therapies for HD is particularly attractive because it is a genetically homogeneous disease for which numerous well-established animal and cell-based models exist. HD is an autosomal dominant disease caused by a CAG repeat expansion in exon 1 of the huntingtin gene. The HD gene encodes the protein huntingtin (Htt), whose polyglutamine expansion is believed to mediate the cytotoxic effects of HD. Therefore, HD serves a model for both neurodegenerative diseases and polyglutamine diseases. Our laboratory aims to develop therapeutic targets and biomarkers for neurodegenerative diseases, with a focus on HD. I will discuss our recently identified therapeutic targets as well as biomarkers which have high potentials to be translated into clinical application. Drug discovery has been revolutionized in the past decade. However, despite technological advances because of substantial investment, the number of new drug approvals remains stagnant and the cost of bringing a drug to market is higher than ever. This highlights the persistence of a model of drug development that has not adapted to changes in science and public perception of drug companies. I will use Huntington's disease as an example to discuss the challenges and opportunities in the translational neurobiology and drug development.

Speaker Biography

Wenzhen Duan is an Associate Professor of Psychiatry and Neuroscience, Johns Hopkins University School of Medicine, has completed her PhD in Neuropharmacology at Peking Union Medical University, China in 1998. She is the current Director of Laboratory of Translational Neurobiology at Johns Hopkins University School of Medicine. She is internationally known for her work on translational research in neurodegenerative diseases, particularly in Huntington's disease. She is a pioneer in developing multimodal micro-MRI biomarkers for preclinical studies of neuroprotective therapeutics. Her laboratory identified key molecular targets for therapeutic intervention for HD and conducted preclinical therapeutic trials. She has published over 70 research articles and reviews. She is recognized by national and international organizations and serves in Review Committee for science foundations in the USA such as NIH as well as outside US, including UK, Austria, Swiss, Italian, and other European science foundations.

e: wduan2@jhmi.edu

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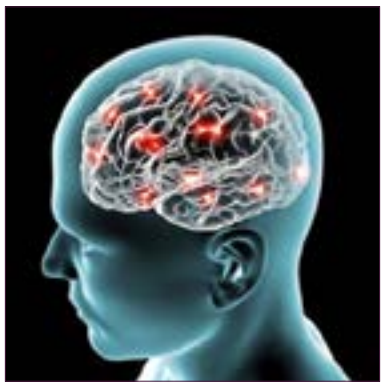


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Vijay Sharma

Washington University School of Medicine, USA

Interplay between Intuition and Design of PET Tracers to Counteract Challenges for Imaging Alzheimer's Diseas

Alzheimer's disease (AD) is a devastating neurodegenerative disorder characterized by progressive decline in cognitive functions. For therapeutic interventions (antibodies; anti-amyloid disease modifying drugs and small organic molecules; BACE 1 Inhibitors) to be effective, drugs need to be administered at earliest stages prior to clinical manifestation of the disease. For stratification of patients likely to be benefitted from a given mode of treatment, it is imperative to diagnose AD at prodromal stages for offering significant help to effected individuals. To accomplish this objective, Florbetapir, Flutemetamol, and Florbetaben have gained FDA approval for Aβ imaging. Although promising for visualizing compact plaques in vivo, these agents also show high nonspecific white matter retention, cross reactivity with other β-sheet structures (myelin binding protein), and are unable to detect oligomers and diffuse Aβ plaques. To achieve an accurate quantification of Aβ pathophysiology non-invasively, a highly specific (at a molecular level) yet sensitive 18F-PET agent, potentially capable of binding to both fibrillar and diffuse plaques, to enable ultrasensitive detection capability (at prodromal stages of the disease) would be desired. To accomplish this objective, our lab has rationally designed a novel heterocyclic fluorescent molecule (named Fluselenamyl) belonging to an entirely new class of molecules that shows concentration dependent and saturable binding, with Kd values of 1.4±0.35nM and 2.9 ±1.35nM, to AD homogenates and preformed Aβ1-42 fibrils, respectively. The agent detects both fibrillar plaques and displays cerebral amyloid angiopathy (CAA) ex vivo in the hippocampus regions of brain sections in APPsw+/-/PS1 mice, while also exhibiting high sensitivity for detecting diffuse plaques, compact plaques, and vascular deposits (CAA) in human tissues. Further, the PET tracer 18F-Fluselenamyl demonstrates an extremely high first pass extraction in brains (8.86 ± 0.32 %ID/g %ID/g; 2 min post tail-vein injection) of FVB mice, and followed by a washout (25% faster than 18F-Avid 45) in absence of targeted plaques. Compared with FDA approved tracers undergoing facile metabolism in vivo, 18F-Fluselenamyl remains non-metabolized in human serum up to 3h. Additionally, multiphoton microscopy in live APPsw+/-/PS1 (15 months old) mice demonstrates that Fluselenamyl traverses the blood brain barrier (BBB) instantaneously to label plaques in brain parenchyma and blood vessels (CAA). Furthermore, microPET/CT imaging shows higher brain uptake of the radiotracer (30 min post-tail-vein injection), and its retention in the cortex of transgenic mice compared with their age-matched Bl6 counterparts, consistent with the binding of the tracer to Aβ plaques, which also correlates with ex vivo autoradiography and immunohistochemistry. While dosimetry studies in mice (n=40), using MIRD methodology indicate an effective dose equivalent of ^{18}F-Fluselenamyl to an allowable maximum injection of 20 mCi in humans, the radiotracer also penetrates primate brain (5%ID/g), and clears to background levels in the absence of targeted plaques. Finally and importantly, Fluselenamyl provides a highly specific molecular signature for AD (displays no cross-reactivity with biomarkers of other neurodegenerative diseases); while also detecting diffuse and compact plaques in an ^{11}C-PIB PET imaging negative, but an Aβ+ AD case. Some of these aspects would be compared with the existing state-of- the art in Neuro2017.

Speaker Biography

Following post-doctoral training with Prof. Jim Wuest in University of Montreal, Quebec, Canada, Dr. Sharma joined in August 1994 Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis. He is currently a tenured professor within departments of Radiology, Neurology, and Biomedical Engineering. Dr. Sharma is also a founding member of the ICCE institute, member of Siteman cancer center, and director of the radiopharmaceutical sciences in Molecular Imaging Center, AMGEN faculty mentor, and program director of MIR summer research program. He is a NIH funded principal investigator for over 20 years in biomedical research. Dr. Sharma serves on review panel of over 40 plus biomedical journals in interdisciplinary sciences, editorial boards, grant review panels for National Institutes of Aging (NIA), Mental Health (NIMH), Allergies and Infectious Diseases (NIAID), Centers for Excellence & Commercialization of Research (CECR, NSERC, Canada), and Killam Faculty Fellowship Awards (NSERC, Canada), national foundations, and AXA Research Fund, Paris, France. At School of Medicine, Dr. Sharma directs a research program focused upon design and development of PET tracers for biomedical imaging in neurodegenerative diseases, interrogating roles of adenosine binding cassette (ABC)-family of transporters in chemotherapeutic resistance including blood brain barrier, cancer biology, and cardiovascular diseases.

e: sharmav@wustl.edu