

# **IBRO-MENA 7<sup>th</sup> International workshop (virtual) on Food and Brain Health**

**&**

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### **April 7-8, 2021**

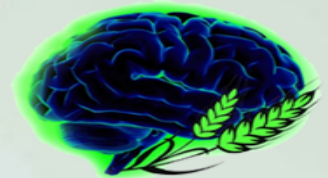
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# **IBRO-MENA 7th International Workshop on Food and Brain Health**

**& How to publish books and write articles by Springer**

# **IBRO-MENA 7th International Workshop (Virtual): Food and Brain Health & How to Publish Books and Write Articles by Springer**

April 7-8, 2021 – Sultan Qaboos University, Sultanate of Oman

## **1. Mechanisms of Molecular Mimicry Involving the Microbiota in Neurodegeneration: Results from Animal Models and Prospects for Gene Therapy**

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Parkinson's disease (PD), Alzheimer's disease, amyotrophic lateral sclerosis and related conditions all involve the formation of transmissible self-propagating prion-like proteins. The formation of amyloids by these proteins involves autocatalytic, noncovalent production of Beta-pleated structures which are transmitted between organisms, as well as between body regions. *The initiating factors responsible for creation of these misfolded nucleating factors are unknown.* Amyloid patterns of protein folding are highly conserved through evolution and are widely distributed in the world. Similarities of tertiary protein structure may be involved in the creation of these prion-like agents through molecular mimicry. The largest opportunity for exposure of humans to foreign antigens is in the gut, which contains 1-2 Kg of bacteria per person and > 100 times more nucleotide sequences than our DNA. These commensal organisms include bacteria and fungi that make functional amyloid proteins. Cross-seeding of altered proteostasis and oxidative stress may be induced by extracellular amyloid proteins made by bacteria in our microbiota. To uncover the initiating factors responsible for protein misfolding and neuroinflammation in PD we studied aged Fischer 344 male rats which develop AS deposits in gut neurons with age (~24 months) (Chen et al, *Sci Rep*, 2016). Rats exposed to bacteria producing curli had more deposition of aggregated AS in neurons in both gut and brain (striatum and hippocampus), more microgliosis in brain (neocortex, hippocampus, and striatum) and more brain expression of interleukin-6, toll-like receptor 2 and tissue necrosis factor than rats exposed to either mutant bacteria unable to synthesize curli or to vehicle alone. We also found that exposure of AS expressing *Caenorhabditis elegans* to curli producing bacteria caused AS aggregation and deposition. A recent study in PD model mice provides support for these findings (Sampson et al *Elife*, 2020). These results suggest that bacterial amyloid may work as a trigger to initiate aggregation of AS and related proteins through cross-seeding and enhance immune responses to amyloid proteins. The potential for development of new preventive or therapeutic measures targeting the microbiota is great, as they can be altered through diet, prebiotics, probiotics, antibiotics or transplantation. Thus “*gene therapy*” altering the genes of our partner organisms can be accomplished. The role of the microbiota in neurodegenerative disorders deserves further investigation.

## **2. Network Meta-analysis of Alcohol Modulation of Amyloid Precursor Protein in Alzheimer's Disease**

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Increased alcohol use has been reported during the COVID-19 pandemic in the US. Heavy alcohol use increases the risk of Alzheimer's disease (AD). However, the underlying mechanisms are not addressed. During the lockdown with no access to both *in vivo* and *in vitro* facilities, network meta-analysis was conducted to address the mechanisms underlying alcohol modulation of amyloid precursor protein (APP) in Alzheimer's disease (AD).

The key chemical of alcohol beverages is ethanol (EtOH), and acetaldehyde is its key toxic metabolite. QIAGEN Ingenuity Pathway Analysis (IPA) bioinformatics tool was used to investigate and compare the holistic impact of EtOH and acetaldehyde on AD. An extensively researched biomarker of AD pathologies is amyloid-beta of which the precursor protein is APP. Molecules associated with APP or EtOH were collected from the QIAGEN Knowledge Base, and 313 molecules were overlapping between the molecule sets. Using the “Pathway Explorer” tool, 40 of the 313 molecules were found to change due to EtOH exposure and influence APP and were compared with acetaldehyde-mediated molecule expression changes. A pathway analysis of the findings related to these 40 molecules showed that EtOH increases APP expression at a confidence of  $p = 0.056$  (z-score = 1.91, two-tailed). Among the top 10 IPA canonical pathways, ranked by the Benjamini-Hochberg corrected Fisher’s Exact Test, identified through the “Core Expression Analysis” feature of IPA, revealed that neuroinflammation was associated at the highest confidence ( $p=5.97E-73$ ). Our study suggests involvement of the neuroinflammation pathway in alcohol modulation of APP as a potential causal factor in AD.

### 3. Mediterranean Diet and Brain Nutrition: What Consequences on NeuroCognition?

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The Mediterranean diet is characterized by the abundant consumption of olive oil, high consumption of plant foods (fruits, vegetables, pulses, cereals, nuts and seeds); moderate consumption of fish, seafood, yogurt, cheese, poultry and eggs; and low consumption of red meat and processed meat products. High consumption of dietary fiber, low glycemic index and glycemic load, anti-inflammatory effects, and antioxidant compounds may act together to produce favorable effects on health status. In fact the Mediterranean dietary patterns comply better with recommended nutrient and micronutrient intakes. It is now well documented that the Mediterranean diet (MD) was associated with reduced mortality and lower risk for metabolic chronic diseases besides its low ecological, carbon and water footprints due to its high share of plant-based foods. MD could increase longevity with better quality of life. With regard to brain nutrition and its consequences on neuro-cognition, lately many studies and meta-analyses have reported good that good adherence to MD is associated with low incidence of chronic neurodegenerative diseases (i.e. Parkinson and Alzheimer) by suppressing oxidative stress and neuroinflammation in neurodegenerative diseases as well as signal transduction. Our talk will focus on the relationship between the Mediterranean Diet and its components on the brain with some focus on neuroprotection.

### 4. Indian Traditional Medicine and Brain Health

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Indian traditional medicine remains the most ancient medication practice around the globe. In several studies, it has been proved that active components in the plants of Indian origin treat cognitive and neurodegenerative disorders. Inflammation, oxidative stress, and protein aggregation are the main sources of neurodegenerative disorders which inevitably lead to neurocognitive disorders. The popularity of Indian Traditional Medicine is increasing due to its perceived effectiveness, safety, and affordability. Recent popular Indian medicinal plants that are used for brain health includes Ashwagandha (*Withania somnifera*), Turmeric (*Curcuma longa*), Brahmi (*Bacopa monnieri*), Chirata (*Swertia chirata*), Balsampear (*Momordica charantia*) and Indian gooseberry (*Momordica charantia*). Ashwagandha is known to have ameliorative effects on diverse neurodegenerative disorders. Bacosaponins in Brahmi are potent neuroprotectants which inhibits Amyloid-beta aggregation, diminishes ROS, causes neuroinflammation, and further improves memory and learning behavior. Curcuminoids dwindle the amyloid-beta aggregation in Alzheimer’s disease. Our laboratory uses *Caulobacter crescentus* (asymmetric dividing bacteria) and DH5 $\alpha$  (symmetrical dividing bacteria) as experimental model organisms for

aging-related studies. We are investigating the comparative efficiency of fresh garlic and aged garlic and *Annona muricata* fruit extract against the oxidative stress-induced replicative-aging in bacterial model.

## 5. Trans-differentiation Potential of Mouse Mesenchymal Stem Cells Towards Neuronal Lineage Through Targeting *Wnt* Signalling Pathway

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Till date to repair and restore these lost function of neurons, numerous approaches were addressed but the retaining activities of those cells were not well distinguished. The lack of effective treatments, including disease-modifying therapies and the characteristic of neurodegenerative disease pathology, make these diseases appropriate candidates for cell therapy. Our current study focused on using small molecules Quercetin and Niclosamide that are potent inhibitors of *Wnt* signalling pathway by targeting TCF/Frizzled receptors as downstream targets that might aid in trans-differentiation of mouse mesenchymal stem cells (mMSCs) into neuronal-like cells. The differentiation potential of mMSCs was confirmed by the formation of cell body, nissil body formation, and gene expression analysis of neuronal-specific genes like *CHAT*, *MAP2*, *NeuN*. The morphological similarities and significant upregulation in neurite growth potential after treatment with Quercetin and Niclosamide confirmed the trans-differentiation potential of mouse mesenchymal cells. These cell-permeable small molecules have exhibited to facilitate cell reprogramming and promote neural differentiation of mMSCs. Additionally, the mechanisms underlying neurodegeneration are poorly understood, thus making the target-based drug screening strategies rather difficult. With the realization of inducing easily accessible cells, such as mMSCs, to inaccessible cells lost neuronal cells in the degenerative diseases, these results may contribute to potential cell replacement therapies. However, further studies are yet to be carried out to understand the mechanism of these small molecules in modulating the *Wnt* signalling pathway to transdifferentiate MSC's to the neuronal cells.

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## 6. Streptokinase – An Efficient Clot Buster with Ameliorated Therapeutic Potential

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Stroke is ranked as the third leading cause of death worldwide, and around 15 million people suffer stroke every year. Among them, almost 50% die, and others are disabled permanently. A cerebral stroke occurs when there is a sudden interruption or blockage of oxygen supply and nutrients to the brain cells. It is manifested either due to blockage of blood artery or bleeding from the damaged artery. This results in blood spills into or around the brain cells, leading to oxygen and nutrient deficits in the brain cells, causing brain damage or death. While medical conditions like diabetes, high blood pressure, elevated cholesterol, and heart disorders can increase the chances of stroke; life-style changes, healthy eating habits, and routine exercises can lower the risk of stroke. During the inceptive years, complex and costlier surgical interventions were used to clear blood clots. However, thrombolytic therapy has revolutionized the treatment regime for the dissolution of blood clots or thrombus. Among various clot-busters, Tissue plasminogen activator (tPA), Alteplase, Tenecteplase, and Streptokinase are commonly used worldwide. Streptokinase, because of its bacterial origin, is associated with few disadvantages: high immune reactivity, fibrinogen degradation, and low circulatory half-life (approximately 10-15 minutes). To overcome

these challenges, we have engineered SK-variants through site-specific PEGylation, which resulted in an extended half-life and reduced immune-reactivity to meet the clinical requirements. These engineered SK-variants with favorable properties can be used as the next generation thrombolytics for the treatment of CVDs and stroke.

## 7. Identification of Novel Nrf2 Activators from the Roots of *Valeriana officinalis*

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Nrf2 (NF-E2-related factor 2) is a transcriptional regulator of cellular responses against environmental stresses. Nrf2 induces the expression of detoxification enzymes (such phase II enzymes) such as glutathione S-transferase (GST) and metabolic pathway enzyme for glutathione synthesis. Therefore, Nrf2 activators might be used to stimulate the body's anti-defense mechanisms. Our study was focussed on the discovery of novel Nrf2 activators from medicinal plants. Initially, a variety of commercially available ethanolic extracts were screened for Nrf2 activity using a Nrf2-luciferase reporter cell line, and *Valeriana officinalis* root was identified as one of the most potent samples. Then, six sequential extracts of the root were prepared and investigated for Nrf2 activity. Among the sequential extracts, the dichloromethane extract was most active and chosen for further purification by HPLC. From the isolated peaks, four known compounds (Isovaltarte, Valtrate, Jatamanvaltrate-P and Valerenic acid) were identified as Nrf2 activators by NMR and LC/HRMS analysis using the Nrf2 luciferase reporter cell line. As GST is among the Nrf2 upregulated genes, changes in GST activity upon incubation with the isolated Nrf2 activators were determined in a HepG2 cell line. All four compounds increased GST activity significantly. Our results suggest that Isovaltarte, Valtrate, Jatamanvaltrate-P and Valerenic acid are the main Nrf2 activators contained in *Valeriana officinalis* root. Our finding might expand the medical use of this medicinal plant beyond its current use as a sleep aid.

## 8. Neuroethics, Precision Medicine: Trends & Challenges Relevant to Brain Health

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Precision medicine and AI have the potential to transform healthcare. Excitement about the promises of these fields is abounding. However, fulfilling this promise and the delivery of effective patient-centered care in an equitable and timely manner will not be straightforward. Innovations within the healthcare system are challenging at the best of times which means that substantial process and infrastructure changes will be needed. One essential tool to achieve this goal is an integrated and comprehensive pathway for healthcare data storage, analysis, and utilization. Additionally, substantial collaboration between the various stakeholders in healthcare is critical to ensure complete rollout of patient-centered care and P4 medicine. A separate presentation will deal with the interdisciplinary field of Neuroethics. The discussion will focus on issues raised by our enhanced and continuously improved understanding of neuroscience, the brain and our ability to monitor and influence it.

## 9. Food to Enhance Happiness

Blessy Prabha Valsaraj,<sup>1</sup> Judie Arulappan,<sup>2</sup> P Valsaraj<sup>3</sup>

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It is interesting to understand that the food we eat can regulate our emotions and mental health. The right choice of food can keep people happy. This knowledge can be utilized effectively in treating depression and managing

anger. The session is aimed at enumerating the foods that boost happiness, reviewing the evidence of food that help in preventing depression and recommending food for attaining better emotional health and happiness. People who had sufficient fruit and vegetable intake had a 0.187 higher happiness score than those who had insufficient fruit and vegetable intake. It is found that people who eat nuts, fruit, vegetables, and fish have a significantly lower incidence of depression than those who eat sweets or processed foods. Depression is more commonly seen among people who ate more sweets and processed foods compared with who ate mainly whole foods. The session will be review on evidence emphasizing wise choice of food to enhance the happiness and to curtail depression among the population.

## **10. Effect of *Nigella sativa* on Anxiety in Post-Graduation Students: Intervention Study through Multigrain *Nigella sativa* cookies**

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Anxiety disorder are the most common of all the mental health disorders in human and animals which may lead to wide range of problem. *Nigella sativa* L. (Family: Ranunculaceae) commonly known as black cumin is an annual herb. Recent studies have demonstrated the pathogenesis of anxiety is linked to oxidative stress and decrease antioxidant capacity and *Nigella Sativa* seeds have a potent antioxidant activity. The principles in *Nigella Sativa* seeds are Thymoquinone, Carvacrol, T-anethol, and 4-terpineol, they possess antioxidant activities and prevent oxidative Injuries. 450 post-Graduate students who belonged to the age group of 21-25 years and who belonged to different socio-economic statuses along with satisfying the criteria for the research, volunteered to participate in observational study, where anxiety test was conducted with the help of STAI questionnaire. 60 students with high anxiety were then considered to participate in the stage 2 of the study (interventional) where they were divided into 2 groups- Control and experimental. Experimental group was provided with the Multi-flour cookie incorporated with 500mg *Nigella Sativa* seeds for 4 weeks. Using a semi-structured questionnaire, the Height, weight, hip circumference, waist circumference was measured, and the BMI and Waist hip ratio and anxiety scores were calculated To administer the *Nigella sativa* to the participants, 4 different sample lotes of cookies with various combination of flours with *Nigella sativa* were prepared. As per the sensory evaluation of four products: Product 1((Refined flour cookie) Product 2(Multi-grain cookie) Product 3(Green gram flour cookie) and Product 4 (Multi-flour cookie),\_it was found that product 4 (Multi-flour cookies) is most accepted among the evaluators compared to Product 1,2 and 3. The mean value of texture, appearance and smell was greater in Product 4, whereas mean value of taste and content is greater in Product 1 and 3 respectively. As the multi flour *Nigella sativa* cookies is considered more acceptable through sensory tests, it was recommended to use in the study. In order to ensure the product safety, the multi-flour *Nigella sativa* cookies were subjected to microbiological lab testing. The result revealed no growth of microbes even after 9<sup>th</sup> day of shelf life of product.2. To assess the effect of *Nigella sativa* cookies on anxiety the cookies were provided to the participants during the study. In state anxiety inventory (current anxiety), there is a decrease in the mean of anxiety in experimental group from pretest (52.76) to post test (42.80), whereas there is no significant difference in the mean of control group from pretest (55.03) to post test (52.88). The pre state anxiety inventory (AI) p value shows 0.254 which is not significant. The post state AI shows <0.001 which is highly significant at 1% level. Which states that there was a difference in anxiety level from pre to post in experimental group. The pre-Trait anxiety inventory (general anxiety) does not show significant difference between the 2 group. The post Trait anxiety inventory shows

decrease in the mean of experimental from (58.50) to (42.66) than control from (53.46) to (52.43). This shows that there is a decrease in anxiety of experimental group by 15.84. The pre trait AI shows p value 0.003 which is significant at 5% level where as the post trait AI shows <0.001 which is highly significant at 1% level. From the 450 samples selected, conducting a State and Trait Anxiety Inventory (AI) test, 73 had high state anxiety and 73 had high trait anxiety at the beginning and 30 among them were grouped as experimental and 30 were grouped as control. After four weeks of intervention of cookies containing 500 mg of *Nigella sativa* seeds there was a statistically significant variation between experimental groups with a drop of Anxiety level from the mean (52.7) to (42.80) in state AI and slightly drop of anxiety level from the mean (55.03) to (52.88) in control which shows no significant variations. and there was a statistically significant variation between experimental groups with a drop of Anxiety level from the mean (58.8) to (42.66) in trait AI and slightly drop of anxiety level in control from the mean (53.46) to (52.43) in Trait (AI) which shows no significant variations. It is observed that the effect of *Nigella sativa* on anxiety as measured by STAI showed statistically significant difference between Pre and Posttests. This demonstrates that there might have been reduction in anxiety. Therefore, *Nigella sativa* might be a potential source for developing new products for treating anxiety.

## 11. Alpha 7 Acetylcholine Receptor: An Immune Link between Gut and Brain

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Healthy food habits have beneficial effects on physical and mental health. Food we eat determines the beneficial and detrimental effects on organs, especially - the gut and brain – via the immune system. This system mediates the responses that are generated from the enteric nervous system (ENS) pass to the central nervous system (CNS) through the gut-brain axis. An ion-gated channel, alpha7 acetylcholine receptor, which is an essential part of the cholinergic anti-inflammatory mechanism, plays an important role in the regulation of inflammation in the gut and brain through vagus nerve. Vagus nerve upon electrical or chemical stimulation releases acetylcholine to activate  $\alpha 7$ AChR in macrophages, thereby modulating inflammation. As an example, we show that lipopolysaccharide-induced inflammation upregulates  $\alpha 7$ AChR and releases inflammatory molecule (TNF $\alpha$ ) in macrophages. And the stimulation of  $\alpha 7$ AChR by its agonist, GTS-21, activates anti-inflammatory pathway and decreases increased levels of TNF $\alpha$ . We also show that binge alcohol consumption perturbs gut microbiome and transform commensal bacterial population into pathogenic and produces gut microbiome-derived metabolites, which are associated with the changes in behavior and brain function. Taken together, we suggest that coordination between CNS and ENS, mediated by immune system, is crucial to keep the gut and brain healthy. This coordination can be attained by making right choices of healthy and whole foods in the diet.

## 12. Evaluation of Neuroprotective Effects of Polyphenol Enriched Blueberry in Sleep Restricted Animals

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The present study aims to evaluate the neuroprotective effects of polyphenol enriched blueberry (PEB) extract in sleep restricted mice. Animals were sleep restricted using modified multiple platform method for 21 days and treated with PEB 100 and 200mg/kg, p.o for 21 days. On day 22, cognitive assessment was performed using Novel object recognition test (NORT) and stepdown latency. At the end of the study animals were euthanized, plasma and brain were collected. Plasma was analyzed for the antioxidant enzyme levels like superoxide dismutase (SOD), reduced glutathione (rGSH) and lipid peroxidation (LPO) contents. Hippocampal tissue was analysed for kynurenic acid content and protein expression levels of cytokines TNF $\alpha$ , IL-1 $\beta$  and NF $\kappa$ B. The results showed recovery of memory in PEB treated animals. PEB increased SOD, rGSH and decreased LPO,

increased kynurenic acid and downregulated inflammatory markers. The study reveals the neuroprotective role of polyphenol enriched blueberry extract in sleep restricted animals.

### **13. Functional Foods, Micronutrients and Epilepsy**

Mohd. Farooq Shaikh, Ph.D.

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Epilepsy is a serious neurological disorder that affecting more than 50 million people globally. Common antiepileptic drugs (AEDs), currently prescribed to epileptic patients, are ineffective in alleviating their burden, with nearly 30% of them. Many epileptic patients are suffering from uncontrolled seizures, and some are living with AED-induce comorbidities like neuropsychiatric disorders and infertility. Dietary interventions such as functional foods, ketogenic diet and micronutrients have gain more attention as a possible therapy for epilepsy due to their protective effects against seizures. It is important to generate more evidences on the effectiveness and safety of these treatment options.

### **14. The Role of Diet and Micronutrients in Parkinson's Disease**

Norlinah Mohamed Ibrahim

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Nutrition is an important aspect in PD regardless of stage. Micronutrients form an important part of our diet and is necessary for the optimal cell functioning. Adequate intake, and absorption ensures that all individuals obtain the required micronutrients for cell function. In Parkinson's disease (PD), there is progressive degeneration of dopaminergic cell death, which leads to complex motor and non-motor symptoms. While genetic cause has been identified in 20% of all PD cases, gene-environment interactions play an important role in the sporadic cases. Dietary factors have been linked to pathogenesis of PD – theory of gene-environment interaction. Epidemiological studies, in vitro and human studies have explored the link between nutrition, particularly the role of dietary components, nutritional supplements or phytochemicals in PD. Some dietary components are believed to be neuroprotective, while others confer a risk, suggesting that there is a complex interplay between differing dietary constituents and PD. Although, there is no direct cause and effect link between nutritional deficiency and the development of PD, neuroprotective effects of nutritional supplements and phytochemicals have been shown in a number of animal studies, but not in human studies. Dietary factors may have an effect in the neuronal function in PD through various mechanisms: 1. Deficiency of crucial nutrients for cell functioning 2. Diets leading to an increase in oxidative stress causing reduced neuronal survival 3. Diets leading to an alteration in gut microbiome (gut dysbiosis).

### **15. Assessment of the Activity of Biomolecules as Anti-inflammatory and Anti-depressant using Kynurenine Pathway Molecules.**

Gilles J. Guillemin, Ph.D.

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The kynurenine pathway (KP) of tryptophan metabolism is one of the major regulatory mechanisms of the immune response. Activation of the KP is implicated in the pathogenesis of a wide range of neuroinflammatory diseases. Several pro-inflammatory mediators can activate indoleamine 2,3 dioxygenase (IDO-1) one of the first and regulatory enzymes of the KP. A prolonged activation of the KP leads to production and accumulation of several neuroactive metabolites including the potent excitotoxin quinolinic acid (QUIN). Over the last few years, together with our collaborators, we have shown that the KP is activated and especially QUIN level increases in



neuropsychiatric disorders (depression, suicidality...). QUIN is only produced by activated monocytic cells (macrophages and microglia). Many biomolecules are known for their anti-inflammatory activity and often used as complementary treatment for various diseases. Other natural compounds are used as surrogate anti-depressor treatment. We demonstrated that, *in vitro*, QUIN production by activated human primary macrophages can be used as an accurate biomarker to assess anti-inflammatory activity and anti-depressor potential.

## 16. mTORC2-PKC Epsilon in Alcohol Use Disorder

Jayakumar Moorthy

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PKC epsilon (PKC $\epsilon$ ) has been shown to regulate various behavioral changes related to alcohol dependence at the preclinical level by phosphorylating other proteins at specific locations. Existing literature suggests PKC $\epsilon$  undergo autophosphorylation at S729, while more recent findings have implicated an upstream kinase mTORC2 in phosphorylation of PKC $\epsilon$  at S729. *In vitro* studies have shown PKC $\epsilon$  to interact with mTORC2 through mSIN1 (a subunit attached to mTOR core protein). Hence, in this study, we assessed the gene, protein expression and protein interaction between mTOR, mSIN1, total PKC $\epsilon$ , and phosphorylated PKC $\epsilon$  (S729) in the amygdala during various stages of alcohol consumption. Rats were assigned to 5 groups (n=6 per group); control (rats fed with non-ethanol containing modified liquid diet (MLD) for 28 days), acute ethanol (rats fed with control diet for 28 days and injected with acute ethanol (2.5 g/kg, 20 % v/v, intraperitoneal) on day 28, chronic ethanol group (rats fed with control diet for 7 days, and followed by ethanol-containing MLD for 21 days, ethanol withdrawal (rats fed with control (7 days) ethanol-containing diet for 21 days, and followed by withdrawal of ethanol from MLD on day 28 and injected with saline on day 28, ethanol withdrawal + ethanol (MLD feeding regimen was similar to ethanol withdrawal group, except on day 28 the rats were injected with acute ethanol instead of saline). Throughout the study, parameters such as body weight changes, MLD intake, ethanol intake, and serum ethanol level were assessed. Serum ethanol level was significantly higher in acute, chronic, EW, and EW+EtOH compared to control (P<0.01). The serum ethanol level of the chronic group was higher than the rest of the ethanol-fed groups. Oral intake of ethanol was similar in chronic, EW, and EW+EtOH groups. The RT-PCR analysis revealed a decrease in PKC $\epsilon$ , sin1 and mTOR mRNAs in the acute group (p<0.05). Similar changes were observed in the chronic group for sin1 and mTOR expression (p<0.05). Whereas, PKC $\epsilon$ , mTOR and sin1 mRNA were upregulated in EW and EW+EtOH groups (P<0.05). There was a significant increase in the protein expression of mTOR, total PKC $\epsilon$ , phosphorylated PKC $\epsilon$  (S729), and sin1 in chronic, EW and EW+EtOH groups. Acute ethanol challenge significantly increased the interactions between mTOR/PKC $\epsilon$  and mTOR/phosphorylated PKC $\epsilon$  (S729). The interactions between mTOR/Sin1, mTOR/PKC $\epsilon$ , and mTOR/phosphorylated PKC $\epsilon$  were reduced in chronic ethanol, EW, and EW+EtOH groups. Our results indicate that increase in expression of phospho-PKC $\epsilon$  (Ser729) during the late stages of AUD is not directly mediated by mTORC2, but most likely due to an increased reserve pool of PKC $\epsilon$  available to be phosphorylated.

## 17. Nutrigenomics and Brain Health

Mohamed Salama, MD

Associate professor, I-GHHE, the American University in Cairo, Egypt AND Atlantic Senior Fellow, Global Brain Health Institute, Trinity College Dublin, Ireland

Recent research has reignited interest not only in the genetic risk factors associated with some neurodevelopmental deficits, but also in the role of nutrition and how different genetic make-up may contribute to the biological response to different dietary styles in some disease profiles of neurodevelopmental disorders. Several nutrients and genetic profiles have been proposed to demonstrate such models, yet many controversies still exist. This lecture provides a brief overview of the nutrigenomics of brain disorders explaining some proposed links, biological mechanisms of action and finally by providing examples of common disorders; PD and AD.

## **18. The Epigenetics of Diet and Drugs in Pregnant Women and Impacts on the Developing Fetus**

Farah Zahir

University of British Columbia, Vancouver, Canada

Epigenetic regulation is a molecular mechanism that is known to be a significant contributor to neurodevelopmental disorders (ND), and also offers a means to explain how environmental exposures can impact genetics. It is recognized that environmental exposures contribute to etiology of ND, especially complex ND such as Autism Spectrum Disorders. We discuss the impact of maternal exposures during pregnancy to certain drugs and dietary intake on the developing fetus. We find that exposure to certain drugs during gestation are associated with a higher risk of ND, while other dietary compounds may offer promise to rescue related epigenetic regulatory insults. While more work is needed, this area of research has important implications in understanding, prevention and treatment of ND.

## **19. Diet and ADHD**

Judie Arulappan

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Attention-deficit/hyperactivity disorder (ADHD) is a debilitating mental health problem hampering the child's development. The underlying causes include both genetic and environmental factors and may differ between individuals. Children with ADHD are at risk for impaired academic performance, social isolation and peer problems, substance abuse, aggressive behavior and delinquency. Recent research has shown that suffering from ADHD may result in decreased life expectancy with more than double the risk of premature death from unnatural causes, like accidents, compared to people without ADHD. In sum, ADHD seriously affects the quality of life of child, parents and siblings, incurs high economic costs and is a long-term burden on families and society.

The current multimodal standard of ADHD therapy consists of pharmacological treatment and/or behavioral or psychosocial therapy. Deficiencies in certain types of foods can worsen symptoms of ADHD in children and adults. The effect of food on ADHD is hypothesized that both artificial food additives and foods rich in salicylates might be 'important etiologic agents' of the hyperkinetic syndrome. The efficacy of diet treatments in ADHD was evaluated in few studies. Foods rich in protein can have beneficial effects on ADHD symptoms. Protein can prevent surges in blood sugar, which increase hyperactivity and impulsivity. Eating several servings of whole grains, which are rich in fiber, each day, will prevent blood sugar levels from spiking. When the children with ADHD eats a well-balanced diet, including vegetables, complex carbohydrates, fruits, and plenty of protein, the behavior tends to be more consistently under control. Low iron levels correlate with cognitive deficits and severe ADHD. Zinc regulates the neurotransmitter dopamine and may make methylphenidate more effective by improving the brain's response to dopamine. Low levels of this mineral correlate with inattention. Studies suggest that giving children who have low levels of B vitamins a supplement improved IQ scores and reduced aggression and antisocial behavior. Omega-3s are believed to be important in brain and nerve cell function. A new study found that daily doses of omega-3s reduced ADHD symptoms by 50 percent.

An extract made from French maritime pine bark, pycnogenol was found to improve hyperactivity and sharpen attention, concentration, and visual-motor coordination in students with ADHD after one month. The more sugar hyperactive children consume, the more destructive and restless they exhibit. Studies published in *The Lancet* suggest that some children with ADHD are adversely affected by food additives. A recent study indicates that artificial food coloring and flavors, as well as the preservative sodium benzoate, make some kids without ADHD hyperactive. According to studies, gluten, wheat, corn, and soy cause some children to lose focus and become more hyperactive. A healthful diet may reduce symptoms of ADHD by reducing exposure to artificial colors and

additives and improving intake of omega-3 fats and micronutrients. In addition, it certainly will improve overall health and nutrition, and set the stage for a lifetime of good health.

## **20. Docosahexaenoic Acid as a Potential Regulator of Brain Cancer or Cancer Metastasis to the Brain**

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The neuronal membranes contain phospholipids that are predominantly rich in docosahexaenoic acid (DHA), the most unsaturated of the long-chain omega-3 fatty acids. The importance of DHA in learning, intelligence, Alzheimer disease, stroke, and traumatic brain injury has been highlighted in several excellent, recent studies however, its role in primary brain tumor development and metastasis from the cancers of other organs has not been so apparent. The importance of DHA in brain function was only realized in the late 1980s and early 1990s; but Stein et al. developed an interest in the fatty acid composition of brain tumors as early as 1963, and subsequently reported that transmissible glial tumors implanted in mice intracerebrally or subcutaneously contained 70-80% less DHA than normal brain tissues. Another study also found significantly low levels of total omega-3 fatty acids and DHA in 19 patients with gliomas and meningiomas compared to control human brain tissues. The DHA in phospholipids was also found to be significantly reduced (by 60-70%) in human neuroblastoma cells compared to human and rat cerebellum tissue. We have also found low DHA levels in gliomas (unpublished data) in comparable ranges as reported by Martin et al. Furthermore, a study published in 2003 on childhood cancer among Alaska Natives, who primarily eat food from marine sources rich in omega-3 fatty acids and DHA, reported almost 10 times less incidences of neuroblastomas compared to the US white population. These observations imply that a deficiency of omega-3 fatty acids, particularly DHA, may be linked to the development of brain tumors. Consistent with these findings, prophylactic treatment with DHA delayed neuroblastoma development and inhibited the growth of established tumors in a mouse xenograft model. These observations clearly suggest a profound role of DHA in regulating brain structure and metabolism that may offer a protection against developing primary brain tumors or metastasis from other cancerous sites to the brain. The brain is relatively protected from metastasis because its microvascular endothelial cells provide an active permeability barrier and transport system known as the blood-brain barrier (BBB). An impairment in the BBB has been reported in cancer patients who developed metastasis to the brain. DHA has been shown to play a role in maintaining the integrity of the BBB. These observations suggest that DHA deficiency creates a permissive environment for brain tumor growth and/or helps tumors metastasize to the brain from other primary sites, such as the breast, whereas improving the DHA concentration in the brain may protect the brain from tumor development as well as brain metastasis from other organs.

## **21. Role of Probiotics in Modulating Acrylamide Induced Developmental Toxicity in *Drosophila melanogaster***

Swetha Senthil Kumar, Bulla Humpy, Pallavi Dan and Sahabudeen Sheik Mohideen

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The presence of acrylamide in the environment is startlingly high due to its occurrence in the effluents of paper, textile, dye and cosmetics industries. Though, the most crucial point of consideration is its presence in high temperature processed foods that are rich in starch and asparagine. This has led to a series of toxicological investigations regarding the effects of dietary acrylamide, several model organisms like *Drosophila melanogaster* and rats were extensively used to analyze the induced toxicity. Acrylamide was found to adversely affect the development and neuronal health in these organisms, hence effective mitigation strategies like using phytochemicals, chitosan, antioxidants, enzymes, etc. have been investigated so far. However, in this study, we explored the effect of probiotic bacteria, *Lactobacillus fermentum* as a potential treatment for dietary acrylamide induced toxicity. Probiotics are known as functional foods due to their beneficial effects on the host physiology

as they modulate the gastrointestinal system and essentially the xenobiotic metabolism. Their effect on the metabolism is of key importance in the *Drosophila* model as it involves the insulin/insulin-like signalling pathway. This pathway has also been noted to be involved in vitellogenesis, development and progression of oogenesis. Thus, we would like to analyze the possibility of probiotics to attenuate the acrylamide induced developmental toxicity in *Drosophila melanogaster*.

## 22. Edible Bird's Nest: Tasteful and Favorable Neuroscience

Wael MY Mohamed. MD, Ph.D.

Department of Basic Medical Science, Kulliyah of Medicine, International Islamic University Malaysia (IIUM), Kuantan, Pahang, Malaysia and Clinical pharmacology department, Menoufia Medical School, Menoufia University, Egypt

Alzheimer's disease (AD) is one of the leading causes of dementia characterized by loss of memory and cognitive skills. Until now there is no available curative treatment for AD and the only available option is symptomatic treatment. There are many evidence showing that oxidative stress precedes the beginning of the development of AD. The continuous reduction of cerebral blood flow resulting from chronic cerebral hypoperfusion leads to the overproduction of reactive oxygen species that triggers inflammation, causing cognitive decline. Till now, there is no cure for AD and the only option is symptomatic treatment. Recent alternative medicines have underscored the neuroprotective and antioxidant ability of the edible bird's nest (EBN). Nevertheless, there has been minimum studies explored the effect of EBN in reduction of AD. The current work discusses the effects of EBN on hippocampal neurons mainly in CA1 hippocampal region in chronic cerebral hypoperfusion rat model. EBN may be used as adjuvant treatment with any cognitive enhancer Drugs (CED) in patients with AD or Dementia to minimize its dose hence, it minimizes CED side effects and delays drug resistance. Further, EBN can be taken prophylactically as daily dietary supplementation, it is a natural product and has no side effects with no harm for longer usage.

## 23. How to Get Your Book Idea Published?

Aakanksha Tyagi,

Senior Editor (Books), Life Sciences, Springer Nature

Selecting the right publisher is one of the most important decisions an author will make. At Springer, we recognize that our authors are at the heart of what we do and we are committed to providing the resources, support and advice authors need to help them succeed. Our quest is to always help our authors discover, distribute the hot topics in respective research areas. With my talk I will take you in brief journey to explore the process of getting your book ideas published. Partner with Springer and publish your work with confidence.

## 24. Publishing Ethics- Guidelines Proposed by Ethics

Bhavik Sawhney

Editor (Books), Biomedicine, Springer Nature

Integrity is doing the right thing, even if nobody is watching!

Scientific research has had its credibility damaged at various times in history because of ethical breaches in its research and publication practices. Today the field is experiencing an emerging crisis in values caused by increasing pressure to publish, conflicts of interest, and ethical committee restrictions on research. Most of the cases are due to a lack of knowledge rather than intentions. So, I will take the audiences through the different publishing ethics in the course of the talk, which are guided by a committee of publishing ethics. Through my talk, I would like to highlight the relative seriousness of ethical misconduct and how to prevent these kinds of problems before they arise.

## 25. Should Authors market Their Book - Publicizing Your Book for Greater Reach and Visibility?

Madhurima Khalia,  
Editor (Books) Biomedicine, Springer Nature

While the publisher's marketing team is busy introducing your book to its targeted audience through a variety of channels, there are many ways for authors to use social media to help with their book's promotion. Personal branding is an important tool for maximizing the visibility of your book in the market. Maximum reach of your book entails concerted efforts. Learn how to Generate Interest for your book much before it is published?

## 26. Should Books also be Published in Open-Access?

Jagjeet Kaur  
Editor (Books), Medicine and Life Sciences, Springer Nature

In my presentation, I will be addressing an exciting question, "Should books also be published in Open-Access?" and sharing some highlights of the open access book program at Springer Nature. I will talk about the basics and the benefits of open access publication, followed by information about OA Books Publishing at Springer Nature, OA Book Series and Partnerships, and OA Funding and Support Service at Springer Nature.

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