

Joint Event on



International Conference on

**CANCER THERAPY AND ONCOLOGY**

and

International Conference on

**NEUROLOGY AND BRAIN DISORDERS**

June 21-22, 2018 | Osaka, Japan

**DAY 1**

**Scientific Tracks & Abstracts**

Cancer Summit & Neuro Congress 2018

# Day 1

# SESSIONS

June 21, 2018

Cancer Therapy | Organ Specific Cancers | Cancer Management & Prevention

## Session Introduction

### Session Chair

**Zongbing You**  
Tulane University School  
of Medicine, USA

**Title: IL-17-MMP7-EMT axis as potential druggable target in the prevention and treatment of prostate cancer**

Zongbing You, Tulane University School of Medicine, USA

**Title: FXD3: A promising biomarker for cancer treatment**

Chia-chi Liu, University of Sydney, Australia

**Title: Prognostic association of plasma cell free DNA based androgen receptor amplification and circulating tumor cells in pre-chemotherapy metastatic castration resistant prostate cancer patients treated with abiraterone acetate**

Manish Kohli, Mayo Clinic, USA

**Title: Dead-box RNA helicase DP103 enhances YAP sumoylation for YAP-TEAD dependance and statin sensitivity in triple negative breast cancer**

Alan Prem Kumar, Cancer Science Institute of Singapore, Singapore

**Title: Therapeutic targeting of TFF3 inhibits oncogenesis in colorectal cancer**

Rumei Chen, National University of Singapore, Singapore

# CANCER THERAPY AND ONCOLOGY

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# NEUROLOGY AND BRAIN DISORDERS

June 21 - 22, 2018 | Osaka, Japan

Zongbing You, Allied J Med Res 2018, Volume 2

## IL-17-MMP7-EMT AXIS AS POTENTIAL DRUGGABLE TARGET IN THE PREVENTION AND TREATMENT OF PROSTATE CANCER

### Zongbing You

Tulane University School of Medicine, USA

**T**h17 cells are a subset of T helper cells secreting interleukin-17 (IL-17A and IL-17F). We have systematically investigated the role of IL-17 in prostate cancer. We found that IL-17 receptor C (IL-17RC) expression was up-regulated in human prostatic intraepithelial neoplasia (PIN), hormone naïve prostate cancer, and castration-resistant prostate cancer. Using an Il-17rc;Pten (Phosphatase and tensin homolog) double knockout mouse model, we found that IL-17 promoted development of hormone-naïve and castration-resistant prostate cancer through multiple mechanisms, including: 1) directly stimulating expression of cytokines, chemokines, and growth factors; 2) directly inducing inflammatory cell infiltration; 3) increasing the ratio of immunosuppressive immune cells; 4) increasing angiogenesis; 5) enhancing cellular proliferation; and 6) inhibiting cellular apoptosis. Using an Mmp7;Pten double knockout mouse model, we found that MMP7 promoted prostate adenocarcinoma through induction of epithelial-to-mesenchymal transition (EMT). IL-17 induced MMP7 and EMT in human prostate cancer cell lines, while siRNA knockdown of MMP7 inhibited IL-17-induced EMT. Selective inhibitor of MMP7, inhibitor of Th17 cell differentiation, and anti-IL-17A neutralizing antibodies were able to partially inhibit prostate cancer formation in the Pten knockout mice. These findings demonstrate that IL-17-MMP7-EMT axis plays an important role in prostate cancer development, indicating IL-17-MMP7-EMT axis as a potential target for developing new strategies in the prevention and treatment of prostate cancer.

## BIOGRAPHY

Zongbing You received his MD at the age of 23 years and PhD at the age of 28 years from West China University of Medical Sciences, Chengdu, China. He is a tenured Associate Professor and Vice Chair for Research as well as Director of the Two-Year Research Master's Degree Program in the Department of Structural and Cellular Biology at Tulane University School of Medicine, New Orleans, Louisiana, USA. He has published 80 publications and edited a professional book. His research interest is in inflammation and prostate cancer.

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## FXVD3: A PROMISING BIOMARKER FOR CANCER TREATMENT

### Chia chi Liu

Sydney Medical School - University of Sydney, Australia  
Kolling Medical Research Institute - Royal North Shore Hospital, Australia

**E**asy access to the Na<sup>+</sup>-K<sup>+</sup> pump in the cell surface membrane and the critical dependence of cell survival on the pump has made it is an attractive therapeutic target in cancer. Use of cardiac glycosides have been explored but has turned out to have limited utility due cardiac toxicity of the drugs. As an alternative we have examined if targeting FXVD proteins that associate closely with the Na<sup>+</sup>-K<sup>+</sup> pump molecular complex might be useful. FXVD3 is of interest because it is markedly over-expressed in several common cancers and we have shown that several FXVD proteins, including FXVD3, are critical for reversal of glutathionylation of the β1 Na<sup>+</sup>-K<sup>+</sup> pump subunit, an oxidative modification that inhibits pump activity. We hypothesized that FXVD3 protein overexpression protects pump function against inhibition by the high levels of oxidative stress in cancer cells typically encounter and a reduction in FXVD3 expression levels would sensitize cells to chemotherapy and radiotherapy that largely induce cell kill by increasing oxidative stress. In light of the reported treatment resistance of overexpressing FXVD3 cancers, results suggest silencing wild type proteins may greatly strengthen the efficacy of treatments that increase oxidative stress within tumors. Such increases are commonly seen with radiotherapy and chemotherapeutic agents. This ongoing study endeavors to develop amalgamated novel treatments for cancer patients while alleviating side effects associated with traditional therapy; advance diagnosis and improve overall patient well-being.

## BIOGRAPHY

Chia chi Liu is Senior Research Fellow and Molecular Biologist with expertise in oxidative protein chemistry at University of Sydney. She was a Biochemistry Lecturer in Taipei Medical University Taiwan. She completed MSc in Cell and Molecular Biology at Taipei Medical University Taiwan, followed by second MSc in Biotechnology, University of New South Wales. She then completed her PhD within the Department of Chemistry and Biomolecular Science, Macquarie University. Her core focus is investigating the relationship between oxidative stress and the sodium pump function. Her research interests include the development of new diagnostic methods for oxidative damage of the pump; the discovery of new drugs for heart disease; and the design of novel therapeutic proteins for cancer treatment.

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Note:

**PROGNOSTIC ASSOCIATION OF PLASMA CELL FREE DNA BASED ANDROGEN RECEPTOR AMPLIFICATION AND CIRCULATING TUMOR CELLS IN PRE-CHEMOTHERAPY METASTATIC CASTRATION RESISTANT PROSTATE CANCER PATIENTS TREATED WITH ABIRATERONE ACETATE**

**Manish Kohli**

Mayo Clinic, USA

**Background:** The prognostic significance of plasma cell-free DNA (cfDNA) androgen receptor amplification (ARamp) in metastatic castration resistant prostate cancer (mCRPC) stage is not known.

**Methods:** As part of a prospective study in mCRPC stage, concurrent collection of plasma and circulating tumor cell (CTC) counts was evaluated for determining prognostic value of plasma cfDNA ARamp. Specimen collection was performed twice, after progression on androgen deprivation therapy (baseline) and then repeated after 12 weeks. QuantStudio3D digital PCR. system (dPCR) was used to determine plasma cfDNA AR copy number variations (CNVs) and Cell search assay for enumerating CTC counts. Association of baseline cfDNA ARamp status/CTC counts with overall survival (primary goal) was evaluated using Kaplan–Meier method and log-rank test ( $p \leq 0.05$  for significance) and Receiver Operator Curves (ROC) for ARamp status and CTCs  $\geq 5$ . A multivariate analysis was also performed using Cox regression models that included ARamp, CTC counts, volume of metastatic disease, cfDNA amount, Gleason score and PSA levels.

**Results:** ARamp was detected in 19/70 patients of baseline plasma specimens. At the time of analysis, 28/70 patients had died (median study follow-up 806 days (IQR: 535-966)). ARamp was associated with poor overall survival (2 year OS of 35% vs. 71% in non-ARamp; log-rank  $p$ -value=  $<0.0001$ ). Baseline CTC count  $\geq 5$  (vs  $< 5$ ) was also associated with poor survival (2 year OS of 44% vs 74%); log-rank  $p=0.001$ ). ROC analysis demonstrated area under the curve (AUC) of 0.66 for ARamp and 0.68 for CTC counts based prognosis ( $p=0.84$  for difference). The best two variables included for multivariable analysis were ARamp and CTC  $\geq 5$ , however the two factor model was not significantly better than using ARamp alone for predicting survival (HR=5.25;  $p=0.0002$ ).

**Conclusions:** Plasma cfDNA ARamp has clinical utility as an independent prognostic factor in mCRPC stage.

**BIOGRAPHY**

Manish Kohli holds an academic rank of Professor and Consultant in Oncology at Mayo Clinic. He has participated extensively in cancer clinical research for the past 15 years. During this time, he has initiated therapeutic trials, recruited several hundred patients for intervention and non-intervention cancer biomarker-based clinical trials and published results of several of these studies. During the course of this research effort, he interacted with multi-disciplinary teams which involved working with geneticists, laboratory scientists, bio-statistical and bio-informatic colleagues, study personnel among others. His early publications were focused on clinical research, mainly in prostate cancer therapeutics. These publications helped advanced therapeutic science in particular with the establishment of docetaxel chemotherapy in castrate resistant prostate cancer in 2004. Subsequently, he built upon these research experiences in developing genomic-based biomarker profiling in advanced prostate/kidney cancer therapeutics as a tool towards developing a precision medicine that is based on cancer's genetic landscape. In this regard, he initiated the building of prospective clinically annotated bio-repositories, which have uniform processing protocols for obtaining quality research specimens.

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# CANCER THERAPY AND ONCOLOGY

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# NEUROLOGY AND BRAIN DISORDERS

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Alan Prem Kumar, Allied J Med Res 2018, Volume 2

## DEAD-BOX RNA HELICASE DP103 ENHANCES YAP SUMOYLATION FOR YAP-TEAD DEPENDENCE AND STATIN SENSITIVITY IN TRIPLE NEGATIVE BREAST CANCER

**Alan Prem Kumar**

Cancer Science Institute of Singapore - National University of Singapore, Singapore

**S**imvastatin, a lipophilic statin used for lowering cholesterol, inhibits 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR), the key enzyme of the mevalonate pathway. Studies have shown that cancer cells express deregulated level of HMGCR and statins exert anti-tumoral activities. We first assessed correlation between mevalonate pathway genes and DDX20 (DP103, Gemin-3) in 1325 breast cancer patients and observed a positive correlation between DDX20 and the mevalonate pathway genes. Having this data, we then proceeded to explore the effect of statins on DDX20 expression. We used various *in vitro* cell lines and *in vivo* statin clinical trial patients' specimens, mouse xenograft, mouse intravenous tail injection and *Drosophila* (wild-type vs Gemin-3 knockdown vs Gemin-3 overexpression flies) models. We show exposure to statin decreases the expression of DDX20. Through a series of add-back experiments, we show that the decrease in DDX20 expression by statins is via the mevalonate pathway and downstream of RhoA. In clinical specimens, we observed breast cancer patients with high baseline DDX20 positively correlates with high baseline YAP-TEAD expression. Having known that SUMOylation of YAP maintains its activity and that DDX20 is a critical enhancer of the SUMOylation machinery, we showed through a series of experiments that a physical interaction between DDX20 and YAP is crucial for maintaining SUMOylation of YAP; thereby decreasing its ubiquitination and degradation. Interestingly, we also identified for the first time that DDX20 is a direct target of YAP-TEAD complex and that maintenance of DDX20 expression is needed as a positive feedback forming an Achilles heel for sustained YAP-TEAD activity.

## BIOGRAPHY

Alan Prem Kumar has completed PhD from University of North Texas, USA. He is currently an Assistant Professor at the National University of Singapore. He has over 150 publications that and his publication H-index is 36 and has been serving as an editorial board member of reputed Journals and established several industry collaborations.

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## THERAPEUTIC TARGETING OF TFF3 INHIBITS ONCOGENESIS IN COLORECTAL CANCER

**Rumei Chen, Qingyun Chong, Vijay Pandey, Mengyi Zhang,  
Basappa Salundi, Alan Prem Kumar and Peter Edward Lobie**

National University of Singapore, Singapore

**T**refoil Factor 3 (TFF3) expression was observed to be upregulated in colorectal cancer (CRC) and correlated with distant metastasis and poor survival outcomes. The present study investigates the functional role of TFF3 and explores the potential of therapeutic inhibition of TFF3 in CRC alone and in combination with conventional chemotherapy. We demonstrated that the forced expression of TFF3 increased cell viability of CRC cells, being attributed to increased cell cycle S-phase entry and decreased apoptosis. Furthermore, the forced expression of TFF3 enhanced the capacity for foci formation and promoted the cancer stem cell-like behaviour of CRC cells. In contrast, the siRNA-mediated depletion of TFF3 decreased the oncogenicity of CRC cells as indicated by the above parameters. Furthermore, AMPC, a novel and selective small molecule inhibitor of TFF3, has been developed in our laboratory and is used to examine the functional implications of TFF3 inhibition in CRC cells. Consistently, AMPC inhibition of TFF3 in CRC cells resulted in reduction of oncogenic properties. Mechanistically, we demonstrate that the TFF3-stimulated oncogenic behavior of CRC cells is dependent on TFF3 activation of the MAPK/ERK pathway. Besides showing efficacy as a single agent, AMPC when used in combination with 5-fluorouracil (5-FU) exhibited a synergistic inhibitory effect, consistent with our observation that TFF3 depletion increased 5-FU sensitivity in CRC cells. In summary, our study highlights the potential of TFF3 as a therapeutic target in CRC and underscores the potential benefits of its pharmacological inhibition in this cancer using AMPC.

## BIOGRAPHY

Rumei Chen received her BSc with academic excellence scholarship from Nan Kai University, China. Upon graduation, she was conferred a full-time PhD research scholarship offered by the Yong Loo Lin School of Medicine in National University of Singapore, Singapore. Her research focus revolves around the profiling of an estrogen-regulated oncogene (TFF3) in CRC and the development of novel therapeutic strategies against it. Meanwhile she has been accredited by Experimental Therapeutics Centre & D3 in Singapore during a course that educates scientists about conducting translational R&D theory and practice. From which, she learnt many practical guidance to translate basic research findings into full-fledged R&D projects. Other than research, she has been active in promoting science-related events such as assisting to organize the International Union of Basic and Clinical Pharmacology world conference. She is a member of many international committees, such as European Association for Cancer Research, Pharmacological Society of Singapore.

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**DAY 2**

**Scientific Tracks & Abstracts**



# Day 2

# SESSIONS

June 22, 2018

Neuroimmunology | Neurological Disorders and Stroke | Central Nervous System | Psychiatric Disorders

## Session Introduction

**Session Chair**  
**Chan Kam Tim Michael**  
Hong Kong Academy of  
Medicine, Hong Kong

**Session Co-chair**  
**Sanjoy Mukerji**  
Kandivali Medical  
Association, India

- Title: Itch-scratch cycle is a chronic cognitive addictive behaviour in our mind**  
Chan Kam Tim Michael, Hong Kong Academy of Medicine, Hong Kong
- Title: Pharmacogenetics of extrapyramidal syndromes associated with coadministration of opioids and antidepressants**  
Helena Sarac, University Hospital Centre Zagreb, Croatia
- Title: Are inflammatory cytokines associated with mood symptoms among patients with bipolar disorder?**  
Esther Lin, National Cheng Kung University and Hospital, Taiwan
- Title: Effects of EEG-based active assisted neurofeedback therapy on hemiplegic upper extremity motor function**  
Joo-Hee, Park, Yonsei University, South Korea

# CANCER THERAPY AND ONCOLOGY

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# NEUROLOGY AND BRAIN DISORDERS

June 21 - 22, 2018 | Osaka, Japan

Chan Kam Tim Michael, Allied J Med Res 2018, Volume 2

## ITCH-SCRATCH CYCLE IS A CHRONIC COGNITIVE ADDICTIVE BEHAVIOUR IN OUR MIND

**Chan Kam Tim Michael**

Hong Kong Academy of Medicine, Hong Kong

Scratching is a distinguishing feature of many resistant dermatosis like Chronic atopic dermatitis. Recently, discovery in neuroendocrinology, immunology and MRI studies suggest itch – scratch cycle may be an addictive neuroendocrine mediated pathological movement pathway with an aberrant and imbalance of neurotransmitters in Central Nervous system (CNS). Mas-related G protein-coupled receptor A3 (MrgprA3) and MrgprC11 expressed afferent neurons penetrated in the epidermis together with Transient Receptor Potential (TRP) receptors like TRPV (vanilloid) 1, TRPV 3, TRPV4, TRPA (ankyrin) 1 together with Serotonin receptors relay itch signals from the periphery synapses to the dorsal horn of spinal cord. Pruritogenic signals via the afferent neurones synapse with gastrin -releasing peptide receptors (GRPR) in the spinal cord. GRPR activation released substance P, Calcitonin G Releasing Peptide, Vasoactive Intestinal Peptide including Pituitary adenylate cyclase activating peptides which was distributed in the CNS. Endothelin-1, tachykinin through neurogenic inflammation increased levels of Th2 cytokines and interleukin – 31 also mediate itch. The central station of itch transmission in our brain is the Thalamus. Hedonic scratch activated the primary somatosensory S1 areas gave the perception of comfort in the cingulate cortex decided the planned motor response of scratching. The midbrain, striatum, ventral tegmental area, caudate nucleus and ventromedial prefrontal cortex as shown by MRI studies are activated in this pleasant circuitry. If this endogenous neuroendocrine circuitry become uncontrolled; harmful cravings behaviour superseded. Insula cortex and Claustrum of the brain play a prominent role in interoception including addiction. They are highly activated when itch is intensified. The adverse pruritic experience is represented in amygdala, subcallosal gray matter and nucleus accumbens. The miswiring and imbalance of 5 Hydroxytryptamine and its multiple receptors are involved. Besides pharmacological intervention, cognitive behavioural therapy including education, refocusing attention strategy; virtual reality immersion; audio visual distraction techniques; habit reversal training; arousal reduction and cognitive restructuring are helpful.

## BIOGRAPHY

Chan Kam Tim Michael is a practicing private Dermatologist in Hong Kong. He received Dermatology Specialist Fellowship in Hong Kong Academy of Medicine in 1998. In the same year, he was granted a Government of Hong Kong scholarship for post graduate training in UCLA, USA. He is now the Vice President of the Association of Integrative Aesthetic Medicine in Hong Kong. He was editor of the Hong Kong Journal of Dermatology and Venerology from 2002 to 2007. He acts as Editorial Board Members of the following international journals since 2017: Research Journal of Nervous System; The Cognitive Neuroscience Journal, Medical Reports and Case Studies and Advances in Neurology and Neuroscience. He has been working in the University of Hong Kong as Honorary Clinical Assistant Professor from 2007 to 2009. He is now a part time lecturer in the Baptist University of Hong Kong for teaching Master Course in Public Health.

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## PHARMACOGENETICS OF EXTRAPYRAMIDAL SYNDROMES ASSOCIATED WITH COADMINISTRATION OF OPIOIDS AND ANTIDEPRESSANTS

Helena Sarac, Neven Henigsberg, Nada Božina and Ervina Bilić

University Hospital Centre Zagreb, Croatia

Opioid analgesics are widely used for the pain relief. More than 0.8% of the global population between 15 and 65 used opioid analgesics, in last years. The currently marketed alkaloid opiates are codeine, hydrocodone, oxycodone, methadone, tramadol, fentanyl, morphine, hydromorphone and oxymorphone. Opioids have a narrow therapeutic index, and can be associated with severe adverse reaction, addiction, dependance, tolerance and fatal overdose. Opioid's adverse effects have been shown to increase the risk of seizures and serotonin syndrome characterized as a triad of neuro-excitatory features; altered mental status (e.g. sedation or agitation), autonomic hyperactivity (e.g. diaphoresis, mydriasis, tachycardia, nausea, urinary retention, diarrhea) and neuromuscular hyperactivity (tremor, myoclonus, hyper-reflexia, pyramidal rigidity). Although the development of extrapyramidal symptoms is under-recognized in clinical practice, with the widespread use of opioid analgesics, increasing numbers of patients with movement disorders following exposure to these drugs have been reported. Chronic pain syndromes are commonly associated with depression and clinicians simultaneously treat both of these conditions prescribing opioids for pain while also administer a selective serotonin reuptake inhibitor (SSRI) for depression. Although there are much efforts has been directed to prevention of misuse, the importance of pharmacokinetic drug-drug interactions related to opioids has received little attention. Drug-drug-interactions-induced serotonin syndrome caused by treatment with oxycodone and SSRI antidepressants is widely known.<sup>2,3,4</sup> Herein, we report a cases of extrapyramidal syndromes induced by coadministration of antidepressants and opioids, caused by cytochrome 450 polymorphisms and drug-drug interactions.

## BIOGRAPHY

Helena Sarac was born in 1968 in Zagreb. She graduated from Medical School in 1992 and attained her PhD from Medical School University of Zagreb in 2013. She was a visiting research scientist at the Mount Sinai Hospital, New York. Since 1999 she had headed the Diagnostic Center Neuron at the Croatian Institute for Brain Research, Medical School University of Zagreb. She is neurologist at the Department of neurology, University Hospital Centre Zagreb, Croatia and scientist at the Centre of Research Excellence for Clinical and Translational Neuroscience. Her research topics are movement disorders, neurodegeneration, and pharmacogenetic of extrapyramidal syndromes. Her significant contribution to the development of science in the neuroimmunology. Dr Sarac has long been interested in how serotonergic system is influenced by autoimmune disorders. She authored multiple scientific publications that have been cited, and has been serving as an editorial board member of reputed Journals and has been serving as an editorial board member of reputed Journals. Dr Sarac has been guest speaker at the international conferences worldwide.

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## ARE INFLAMMATORY CYTOKINES ASSOCIATED WITH MOOD SYMPTOMS AMONG PATIENTS WITH BIPOLAR DISORDER?

**Esther Ching-Lan Lin**

National Cheng Kung University and Hospital, Taiwan

**B**ipolar disorder (BD) is a severe mental illness characterized by chronic course, pervasive instability, and higher recurrence and suicide rate. Evidence supports the associations of instable social rhythm and increased inflammatory cytokines and symptom severity in BD. This cross-sectional study examined the relationships among inflammatory cytokines and mood symptoms. One-hundred and twenty-one individuals with a DSM-IV diagnosis of BD were recruited from the psychiatric ward and outpatient department of a southern medical center in Taiwan. Most participants were female, unmarried, unemployed, diagnosed as bipolar II, and outpatients. There were no significant associations between inflammatory cytokines and mood symptoms. Relative lower level of inflammatory cytokines in these stabilized patients cannot reflect from different mood states. Future studies should compare the inflammatory cytokines of patients who were at different mood states.

## BIOGRAPHY

Esther Ching-Lan Lin is an Associate Professor in the Department of Nursing, College of Medicine, National Cheng Kung University, and adjunct Head Nurse of the Department of Psychiatry, National Cheng Kung University Hospital, Tainan, Taiwan. She has been a nurse, a manager, a teacher, and an advisor for 18 years. After completing her PhD at National Taiwan University. She continued her academic career in nursing education and has focused on improving the quality of care for patients with severe mental illness. She has published 30 papers in English-language and Chinese-language journals—most recently on developing and evaluating psychosocial treatments for patients with schizophrenia and bipolar disorder—and has been an editorial board member for the past 3 years of a national nursing journal in Taiwan.

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# Day 2

# SESSIONS

June 22, 2018

Stem Cells and Oncology | Organ Specific Cancer | Genetic Mutations & Cancer |  
Neuro-Oncology and Brain Tumour

## Session Introduction

### Session Chair

**Zongbing You**  
Tulane University School  
of Medicine, USA

Title: **Exploration of the therapeutic potential of semaphorin 5A in human glioblastomas**

Lee AY, Monash University, Malaysia

Title: **Are IDRFs good predictors of surgical outcomes for patients with abdominal neuroblastoma**

Ahmed Awad Salem, South Egypt Cancer Institute, Egypt

Title: **Alternative splicing of extended synaptotagmin-2 as a prognostic biomarker in renal cell carcinoma**

Dan Huang, The Chinese University of Hong Kong, Hong Kong

Title: **Pregnancy and breast cancer: Repercussions and complications**

Radhouane Achour, Tunis- El Manar University, Tunisia

## EXPLORATION OF THE THERAPEUTIC POTENTIAL OF SEMAPHORIN 5A IN HUMAN GLIOBLASTOMAS

**Lee AY, Menon A, Ann Mary B, Shah Jahan FR and Law JW**  
Monash University, Malaysia

**A**strocytomas are the most common form of brain tumor in human, among which glioblastoma multiforme is highly malignant and exhibits high invasiveness and resistance to radiotherapy, leading to high recurrence rate even after radical surgical resection of the tumor and short survival after initial diagnosis. This calls for development of novel effective treatment regimens, which apparently requires a more thorough understanding of the pathoetiology at both cellular and molecular levels. Recently, accumulating evidence points to the emerging role of axon guidance molecules such as semaphorins, neuropilins and plexins in glioma progression. We have previously demonstrated the effects of semaphorin 5A (Sema5A) and its receptor plexin-B3 in inhibiting glioma cell migration, invasion and proliferation. Notably, analysis of human glioblastoma specimens revealed a marked decline in Sema5A protein level from low to high grade, suggesting a correlation between its loss of function and tumor progression. Restoration of Sema5A level by forced expression or exogenous supply of Sema5A protein in advanced grade glioblastomas successfully counteracts tumorigenicity of cancer cells. These findings provide compelling evidence that Sema5A and plexin-B3 subserve anti-tumorigenic functions, which are compromised in glioblastomas due to a downregulation of Sema5A protein expression, hence contributing to high infiltration and malignancy. In this presentation, the mechanisms of tumor suppressor effect of Sema5A and the exploration of its therapeutic potential will be discussed.

## BIOGRAPHY

Lee AY obtained his PhD from the University of Hong Kong. He is currently a senior lecture at the School of Pharmacy, Monash University Malaysia. Current focus of his research is to understand the functions of axon guidance molecules semaphorins and plexins in cell migration and invasion, axon navigation, cellular differentiation, neuronal regeneration and brain tumor development. His research team has recently revealed the tumor suppressor functions of semaphorin 5A in human glioblastomas and is currently exploring its therapeutic potential. He has published his research findings in leading journals in neurosciences and cancer biology, and has served as editorial board member and reviewer in reputable journals.

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Note:

## ARE IDRFS GOOD PREDICTORS OF SURGICAL OUTCOMES FOR PATIENTS WITH ABDOMINAL NEUROBLASTOMA

### Ahmed Awad

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**Background:** Image defined risk factors IDRFs are risk factors, detected on images and make total tumor excision risky or difficult at time of diagnosis of pediatric abdominal neuroblastoma.

**Objectives:** To evaluate if the IDRFs detected by MDCT are good predictors of surgical outcomes in pediatric abdominal neuroblastoma.

**Material and Methods:** 40 cases with abdominal neuroblastoma were evaluated in a prospective study for the presence or absence of IDRFs using contrast enhanced multi-detector computed tomography (MDCT) and correlated with the surgical outcome.

**Results:** According to the pre-operative MDCT, patients classified into two groups; group I have no IDRFs included 18 patients (45%) while group II, had one or more of the IDRFs included 22 patients (55%). In group II when one or more of the IDRf were present, patients received neoadjuvant chemotherapy in the form of three courses of OPEC alternating with OJEC chemotherapy, complete excision of the mass was done in only 10 patients (45.5%), incomplete excision was done in 12 patients (54.5%). While group I who had none of the IDRFs in their pre-operative MDCT study, complete resection of the mass was feasible in all of the patients (100%).

## BIOGRAPHY

Ahmed Awad currently works as the Lecturer of Surgical Oncology and Director of Endoscopy unit at South Egypt Cancer Institute-Assiut University-Egypt. He earlier worked as a Visitor researcher at the Department of Gastroenterology at Aichi Cancer Centre Hospital Japan.

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## ALTERNATIVE SPLICING OF EXTENDED SYNAPTOTAGMIN-2 AS A PROGNOSTIC BIOMARKER IN RENAL CELL CARCINOMA

Dan Huang<sup>1</sup>, FY Hu<sup>1</sup> and Nelson Tang<sup>1,2</sup>

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<sup>2</sup>Li Ka Shing Institute of Health Sciences, Faculty of Medicine - The Chinese University of Hong Kong, Hong Kong, China

The protein of gene ESYT2 Extended synaptotagmin-2 has been demonstrated to be interacted with the Fibroblast Groth Factor Receptor and activated FGF receptor. It plays an important role in growth factor signaling. However, the expression and function of the transcript variants of this gene is unclear in cancer. In this study, we observed a significant isoform switch of ESYT2 based on the RNA-seq data of the renal cell carcinoma (KIRC) samples downloaded from the TCGA database. Although the expression level of gene ESYT2 is higher in KIRC tumor samples, the expression ratio of the long ESYT2 isoform (ESYT2-L) which includes a cassette exon between exons 13 and 14 to the short isoform (ESYT2-S) is higher in kidney normal samples. The Kaplan-Meier survival curves showed that samples with higher expression ratio of ESYT2-L are associated with better survival ( $p=2.04e-06$ ). Multivariate Cox proportional hazards regression revealed that the expression ratio of the ESYT2-L could be as an independent prognostic factor for patients with CRC (hazard ratio, 0.037; 95% confidence interval, 0.01-0.125;  $P=1.24e-07$ ). In addition, the Gene set enrichment analysis (GSEA) revealed that genes correlated with the expression ratio of ESYT2-L is enriched in hallmark of the EMT and invasiveness signature from cancer cell. In conclusion, our findings show that the alternative splicing of ESYT2 could be a potential prognostic biomarker in KIRC and samples with lower expression ratio of the ESYT2-L isoform may be more likely to have the potential to become metastatic.

## BIOGRAPHY

Dan Huang is a PhD candidate from The Chinese University of Hong Kong. She has been involved in the design, application, and evaluation of bioinformatics pipelines for transcriptome studies based on high throughput sequencing data. She mainly focus on the alternative splicing events that may be associated with cancer by studying large genetic and genomic datasets downloaded from The Cancer Genome Atlas (TCGA) database.

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# CANCER THERAPY AND ONCOLOGY

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Radhouane Achour, Allied J Med Res 2018, Volume 2

## PREGNANCY AND BREAST CANCER: REPERCUSSIONS AND COMPLICATIONS

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**B**reast cancer is common, and is currently considered the first cancer in women. In Tunisia, it accounts for about 30% of all female cancers. The term "pregnancy-associated breast cancer" is used if this cancer is diagnosed during pregnancy and up to one year after giving birth. This association was considered for a long time to be of rapid evolution and unfavorable prognosis. Breast surgery during pregnancy is complicated due to the hypervascularization of the gland during this period. Therefore, it imposes proper hemostasis and lymphostasis. The main effects of radiotherapy during the preimplantation period (from conception to 10 days) are represented by embryonic death and malformation risk during the embryonic phase (days 10-14 up to 8 weeks). When chemotherapy is administered in the first trimester, the rate of malformations is 14% to 19%, and the rate dropped to 1.3% when chemotherapy is introduced in the second or third trimester. The literature reported a 3.8% of fetal malformations in his study, However; A protocol based on Anthracyclins (up to 100 mg/m<sup>2</sup> but 50 mg/m<sup>2</sup> in most studies) appears to be prescribed without major materno-fetal consequences. Experience of maternity and neonatology center of tunis-tunisia; We report in this retrospective study a series of 25 patients with pregnancy-associated breast cancer (PABC) recorded over 10 years at the Tunis Maternity and Neonatal Center (TMNC). In conclusion; it seems that the prognosis of breast cancer is not much aggravated by pregnancy itself as by the delay in diagnosis and management. Treatment should be started promptly during pregnancy.

## BIOGRAPHY

Radhouane Achour is an Associate Professor at the Faculty of Medicine of Tunis-Tunisia. He has published many basic and clinical articles in relation to Gynecology and Obstetrics. His research interests include Rare Diseases in gynecology and prenatal diagnosis. He serves as associate professor, Emergency Department of Gynecology and Obstetrics in maternity and neonatology centre Tunis Tunisia. He also serves as the member of the editorial team for Asian Pacific Journal of Reproduction, the Global Journal of Rare Diseases, Journal of Neonatal Biology, Current pediatric research, Obstetrics and Gynecology: Open access, Pediatrics and Health Research and Member of the Science Advisory Board.

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