Joint Event on

International Conference on

CELL AND GENE THERAPY

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CLINICAL AND MEDICAL MICROBIOLOGY

September 10-11, 2018 | Dublin, Ireland

DAY 1

Scientific Tracks & Abstracts

Day 1

SESSIONS

September 10, 2018

Clinical and Medical Microbiology | Clinical Immunology | Microbial Pathogenesis and Epidemiology

Session Introduction

Session Chair
Vipin K Rastogi
US ARMY, USA
Session Co-chair
James Mahony
McMaster University, Canada

Title: **Diagnostic assessment of immunological history by high-throughput TCR sequence**
Richard J Di Paolo, Saint Louis University, USA

Title: **Engineering extracellular vesicles for tumour targeted therapy**
Róisín M Dwyer, National University of Ireland Galway, Ireland

Title: **Development of a novel hand-held point-of-care test (poct) device for diagnosing infectious diseases.**
James Mahony, McMaster University, Canada

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Richard J DiPaolo et al., Biomed Res 2018, Volume 29 | DOI: 10.4066/biomedicalresearch-C3-007

DIAGNOSTIC ASSESSMENT OF IMMUNOLOGICAL HISTORY BY HIGH-THROUGHPUT TCR SEQUENCE ANALYSES

Richard J DiPaolo[1], Kyle Wolf[1], Tyler Hether[2], Pavlo Gilchuk[4,5], Amrendra Kumar[4,5], Julie Maybruck[3], Mark Buller[1] and **Sebastian Joyce[4,5]**

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[4]Tennessee Valley Healthcare System, USA
[5]Vanderbilt University, USA

During an immune response T-cells expressing unique T-cell receptor DNA rearrangements undergo clonal expansion. We hypothesized these unique TCR sequences can serve as diagnostic classifiers, providing information of immunological exposures. We used high-throughput sequencing to identify TCRβ sequences in separate cohorts of mice after smallpox vaccination and after Monkeypox virus (MPXV) infection. From millions of sequences in the peripheral blood we identified 315 TCR sequences associated with post-vaccinated samples. Vaccine-associated TCR sequences (VATS) were used as diagnostic classifiers and were used to correctly identify 100% of naive and post-vaccinated samples. The VATS were also 98% accurate at identifying samples from the independent cohort of samples infected with a highly related MPXV. The reproducibility of this method was verified repeating the analyses after identifying MPXV-associated TCRβ sequences (MATS). MATS distinguished infected/vaccinated samples from naïve (98% accuracy). The data show that computational identification of vaccine/pathogens expanded TCRs is a sensitive and specific method for determining exposure and can be used to track pathogen specific immune cells with unprecedented sensitivity.

BIOGRAPHY

Richard J DiPaolo is currently working as a Professor in Molecular Microbiology and Immunology at Saint Louis University, USA. He has pursued his Postdoctoral fellowship from NIAID, National Institutes of Health, PhD from Washington University in Saint Louis in 2002 and BA at University of Chicago in 1995. His research interest is in establishing mouse models of human diseases to develop strategies to suppress chronic inflammatory diseases. He currently has an on-going project to examine the T and B cell responses to vaccine and infections and his goal in this project is to understand which immune receptors are used to recognize different vaccines and infectious agents. He had several publications as well as he is a principal investigator in American Gastroenterological Association, American Cancer Society, Washington University, and Arthritis National Research Foundation.

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ENGINEERING EXTRACELLULAR VESICLES FOR TUMOUR TARGETED THERAPY

Róisín M Dwyer
National University of Ireland Galway, Ireland

Extracellular vesicles (EVs) shuttle genetic material including microRNA (miRNA) between cell populations and throughout the circulation, and hold immense potential as biomarkers of disease and vehicles for therapeutic drug delivery. Mesenchymal stem cells (MSCs) have the proven capacity to home to sites of metastatic tumours and to evade immune surveillance. MSC-tumour tropism and apparent immunosuppressive characteristics of the cells, has raised tremendous interest in their potential as tumour-targeted delivery vehicles for therapeutic agents. It has become clear that MSC-based therapy response does not correlate with the level of cell engraftment, but is paracrine in nature. MSCs are potent secretory cells, and release EVs in large quantities. These EVs are thought to target specific sites when systemically administered in a manner reflective of the parent cell. We recently engineered MSCs to secrete EVs loaded with a tumour-suppressor microRNA, miRNA-379. Systemic administration of miRNA-379-EVs was well tolerated and reduced breast cancer growth *in vivo*. This evidence strongly supports the hypothesis that systemic delivery of MSC-derived EV-encapsulated miRNAs may offer therapeutic promise in the treatment of metastatic breast cancer. Along with treatment of existing metastases, MSC-EVs have the potential to inhibit remodelling of pre-metastatic niches systemically, and reduce cancer progression and recurrence. EVs are also released into the circulation by cancer cells and may represent a fingerprint of the tumour, raising potential for the circulating EV-miRNA profile as a biomarker of response to therapy.

BIOGRAPHY

Róisín M Dwyer is a Lecturer in Translational Science in the discipline of surgery at National University of Ireland Galway. Following graduation from University College Dublin (UCD) with a degree in Science, she has completed her MSc in Biological Sciences at Dublin City University (DCU), and then was awarded her PhD in Medicine and Therapeutics from UCD. This led her to a postdoctoral research position at the Mayo Clinic, Rochester, Minnesota. She has established a research programme, in collaboration with both national and international research groups, focusing on novel approaches to breast cancer detection and therapy in Ireland.

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DEVELOPMENT OF A NOVEL HAND-HELD POINT-OF-CARE TEST (POCT) DEVICE FOR DIAGNOSING INFECTIOUS DISEASES

James Mahony
McMaster University, Canada

Nucleic acid amplification tests (NAATs) have become the cornerstone of clinical laboratories providing a same day diagnosis for a wide range of infections. Although polymerase chain reaction (PCR) has served laboratories well, PCR has significant disadvantages as it is labor intensive, requires a thermal cycler, and is relatively slow compared with newer isothermal amplification methods. Isothermal amplification methods such as loop-mediated isothermal amplification (LAMP) are rapid, have excellent sensitivity and can provide results in 20 minutes, which is required for next generation POC tests. Other requirements for next generation POC tests include low cost and ease-of-use for resource poor settings including developing countries. We have developed a hand-held next generation POCT device that employs microfluidics, a novel isothermal amplification method and on-plate nucleic acid detection to provide a rapid and visible test result without the need for any instrumentation. This fully integrated, hand-held POCT device performs pathogen lysis, specific pathogen target amplification and detection providing a swab-in, result-out answer in 20 minutes. The device can be used with a variety of clinical specimens including nasal, throat and vaginal swabs. The isothermal amplification method employs cleavable bivalent primers which provide excellent sensitivity with limit of detection of 100 copies and excellent specificity without primer-dimer amplification and false positive results. The POCT device includes both a positive and negative control channel and later versions will have up to 10 channels and the ability to detect multiple infectious agents on a single swab using a single test device. This low cost, one-time use, disposable test device is being manufactured for use in resource-poor settings in both developed and developing countries to provide a rapid test result for the detection of infectious agents in a range of clinical settings providing physicians with a rapid, actionable result leading to improved patient management.

BIOGRAPHY

James Mahony is currently working as a Professor Emeritus in Pathology and Molecular Medicine at University of Toronto, Canada. He is teaching within the faculty of health sciences includes medical microbiology/infectious diseases and pathology residency training programs, graduate course in clinical virology (MS763) and medical sciences. He completed his fellowship in Microbiology at American Academy of Microbiology as well as in Canadian College of Microbiology. He has decorated his carrier with several publication with local, international, industrial collaboration with Drs Mark Loeb, Jenny Johnstone, Marek Smieja, Peter Timms (Brisbane), Phil Hansbro (Newcastle, Australia), Lee Ann Campbell (Seattle), Theo Moraes (Toronto) and Luminex Molecular Diagnostics, Qiagen, Pro-L. The major focus area of his research is the pathophysiology of acute respiratory infections caused by specific viruses (influenza, RSV) and bacteria (*Chlamydia pneumoniae, P aeruginosa and C difficile*). One of the major focuses of his laboratory is the development of new antimicrobial agents for both respiratory viruses and bacteria. In addition to the development of novel therapeutics the other focus of his clinical research is in the areas of diagnostics.

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DAY 2

Scientific Tracks & Abstracts

Day 2

SESSIONS

September 11, 2018

Advances in Cell & Gene Therapy | Cell & Gene Therapy Innovation | Molecular Therapy Research

Session Introduction

Session Chair
Chonghe Jiang
The People's Hospital of Qingyuan City, China

Session Co-chair
James Mahony
McMaster University, Canada

Title: **Dopaminergic agonists improve obesity by its action on lipid profiles and leptin**

Ghada Mohammad Al-Ashmawy, Tanta University, Egypt

Title: **Enhanced anticancer effect and reduced toxicity of doxorubicin in combination with thymoquinone released from poly-N-acetyl glucosamine nanomatrix in mice bearing solid Ehrlish carcinoma**

Nahla E El-Ashmawy, Tanta University, Egypt

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DOPAMINERGIC AGONISTS IMPROVE OBESITY BY ITS ACTION ON LIPID PROFILES AND LEPTIN

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[2]Delta University, Egypt

Background: The efficacy of a non-prescription drug to support weight loss programs has yet to be compared. This clinical trial investigates the comparability of the lipase inhibitor orlistat and the dopaminergic agonist bromocriptine.

Methods: 75 obese females were randomized into three groups according to treatment received; obese control group (OC, n=25), orlistat group (OR, n=25, 120 mg capsules, three times a day) and bromocriptine group (OB, n=25, 20 mg tablet, once a day). This prospective observational study was conducted with norm caloric diet for eight weeks. Serum concentration of leptin and lipid profile were measured, along with Body Mass Index (BMI) at baseline and after the study.

Results: Bromocriptine treatment (OB) caused an increase in serum leptin concentration compared to OC and OR groups (ANOVA, $p<0.01$). Beneficial changes in anthropometric and BMI values were observed following orlistat and bromocriptine administration with the greatest advantage seen in the OB group.

Conclusions: Beneficial effects were observed on weight loss, and body composition in all examined groups, with the greatest advantage on serum leptin being associated with the bromocriptine treatment. We find these strategies more promising for the treatment of obesity and its related complications in obese women.

BIOGRAPHY

Ghada Al-Ashmawy is currently working in Tanta University, Egypt.

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ENHANCED ANTICANCER EFFECT AND REDUCED TOXICITY OF DOXORUBICIN IN COMBINATION WITH THYMOQUINONE RELEASED FROM POLY-N-ACETYL GLUCOSAMINE NANOMATRIX IN MICE BEARING SOLID EHRLISH CARCINOMA

Nahla E El-Ashmawy[1], Eman G Khedr[1], El-Zeiny M Ebeid[1], Mohamed L Salem[1], Abdel-Aziz A Zidan[2] and **Esraa M Mosalam[3]**
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[3]Menoufia University, Egypt

The incidence of breast cancer remarkably increases all over the world. Therefore, there is a great demand to introduce new approaches into cancer treatment field. The current study was designated to evaluate the role of doxorubicin (DOX) and/or thymoquinone (TQ) nano matrix in potentiating the cytotoxicity of either drug, and to investigate the ability of TQ to reduce cardiotoxicity of DOX in solid Ehrlich carcinoma (SEC)-bearing mice. DOX and TQ were loaded into F2 gel, which is a fully-acetylated poly-N-acetyl glucosamine nanofiber. SEC was induced in female albino mice as a model for experimentally induced breast cancer. Mice were randomly divided into eight groups (n=10): normal control, tumor control, F2 gel, free DOX, DOX+F2 gel, free TQ, TQ +F2 gel, and DOX+ TQ+ F2 gel. On day 28th from tumor inoculation, mice were sacrificed, and blood samples were collected for measurement of the cardiac markers; lactate dehydrogenase (LDH) and creatine kinase (CK-MB). In addition, cardiac tissue was utilized for determination of lipid peroxide, and tumor tissue was used for measurement of anti-apoptotic protein Bcl-2 as well as gene expression of the tumor suppressor gene P53. DOX and/or TQ showed a significant reduction in tumor volume, cardiac markers, tumor Bcl-2, and P53 upregulation compared to free conventional therapies. Co-treatment with DOX+ TQ+ F2 gel was superior to all other groups in exerting beneficial effects. Use of TQ as an adjuvant therapy with DOX could improve its cytotoxic effects and limit its cardiac toxicity. Furthermore, loading of DOX and/or TQ into F2 gel showed a remarkable anti-cancer activity.

BIOGRAPHY

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