INFORMM's Second International Conference on

MOLECULAR DIAGNOSTICS & BIOMARKER DISCOVERY

Advances in Biomarker Discovery and Technologies for Better Diagnostics

3 - 4 May 2017

Hotel Equatorial Penang, Malaysia

Programme & Proceedings

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MOLECULAR DIAGNOSTICS & BIOMARKER DISCOVERY

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Prof Dr Rahmah Noordin
Dr Eugene Ong
Dr Mervyn Liew

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Welcoming Remarks

Greetings of Peace to All,

I am delighted and honoured to welcome you to the 2nd International Conference on Molecular Diagnostics and Biomarker Discovery (MDBD). The mission of our institute is "to strive to attain research and academic excellence via knowledge creation through training, research and innovation in molecular medicine". One of the ways to achieve this is through scientific discoveries that are translated into better diagnostics, leading to better treatment for patients and improve health. Since its inception, the core strength of INFORMM has been in the area of Diagnostics, especially those that provides solutions for infectious diseases and cater for the needs of populations in low resource settings. We have received national recognition from the Ministry of Higher Education Malaysia, under the HICoE program, as a centre of excellence in the niche area of Diagnostics Platform, with antibody engineering being the principal technology. We also have groups at INFORMM that delve into investigating new infection makers, and develop and evaluate nucleic acid and protein-based tests, some of which have been commercialised. Each of these phases of diagnostics research requires continuous updates in technology, methodology and approaches. Thus it is important that we bring together experts, scientists, postgraduate students and scientific companies to an event, such as MDBD, that is of mutual interest and benefit to all participants. Thus it is apt that the conference is themed "Advances in Biomarker Discovery and Technologies for Better Diagnostics"

This MDBD 2017 conference promises to be an exciting event with thirteen invited speakers from various parts of the world - Spain, Iran, USA, Saudi Arabia, Singapore, Australia, Brazil, Germany and Malaysia. Thus I hope everyone will take this golden opportunity to interact with these experts and get their insights into the research questions that you are tackling. Our participants are also from diverse backgrounds and countries, thus the opportunity for establishing new collaborations and networking, and strengthening existing ones are tremendous. The latest scientific supplies and services that can facilitate your research are also on display by our sponsors.

For those from outside Penang, we hope you will also take this opportunity to visit and sample the many tourist attractions that the 'Pearl of the Orient' has to offer. Again, I welcome all of you and hope that this conference will be a scientifically rewarding experience. Thank you.

Sincerely,

Rahmah Noordin, Ph.D., F.A.Sc.
Conference Chair

Conference Programme

Day 1	3 May 2017		
0800 - 0845	Registration		
0845 - 0900	Opening Remarks Director & Conference Chairperson		
0900 - 0935	**Plenary 1** **Diagnostic Technologies I** Approaches to development and commercialisation of POC Tests – Burnet Institute experience ***David Anderson*** *Chairperson: Norsyahida Arifin*		
0935 - 1000	**Technology Session 1** Biomarker discovery: Multiplexing with Luminex xMAP technology		
1000 - 1035	Tea Break, Poster Viewing, Exhibition and Networking Session		
1035 - 1100	**Technology Session 2** Going digital: In molecular dagnostics		
1100 - 1200	**Symposium 1** **Diagnostic Technologies II** ASSURED Molecular diagnostics: Drivers, barriers and reality ***Ionis Katakis*** Rapid and low-cost assays for pathogens detection ***Mohammed Zourob*** *Chairperson: Gurjeet Kaur*		
1200 - 1300	**Symposium 2** **Biomarker Discovery & Assay Development Using Proteomics Approach I** A genomic and immunoproteomic approach to identify diagnostic antigens for human paragonimiasis ***Peter U. Fischer*** Rational design and evaluation of a multi-epitope chimeric fusion protein for detection of Toxoplasma IgM antibodies ***Majid Golkar*** *Chairperson: Prof Rahmah Noordin*		
1300 - 1400	Lunch, Poster Viewing & Exhibition		
1400 - 1430	**Symposium 3** **Infectious Disease Diagnosis Using Genomics Approach** Molecular biology and the environmental monitoring of enteric viruses ***Fernando Spilki*** *Chairperson: Aziah Ismail*		
1430 - 1500	**Opening Ceremony** Vice Chancellor's Address Prof Datuk Dr Asma Ismail		
1500 - 1515	MOU Exchange		
1515 - 1615	**Keynote Address 1** Cost-effective point-of-need diagnostics – combining aptamers and advanced lateral flow devices' ***Ciara O'Sullivan*** *Chairperson: Aziah Ismail*		
1615 - 1630	Tea, Poster Viewing & Exhibition		
1630 - 1815	Oral Presentation Session 1A	Oral Presentation Session 1B	Oral Presentation Session 1C
1815	End of Day		

Conference Programme

Day 2	4 May 2017		
0900 - 1000	**Keynote Address 2** Advanced Nanosystems for Diagnostic Applications Jackie Ying Yi-Ru *Chairperson: Prof Rahmah Noordin*		
1000 - 1030	**Symposium 4** **Diagnostic Test Development & Translational Research** From bench to market: Challenges in the development and commercialization of diagnostic tools." ***Andreas Latz*** *Chairperson: Norsyahida Arifin*		
1030 - 1100	Tea Break		
1100 - 1130	**Symposium 5** **Diagnostic Technologies III** Use of lateral flow membranes for diagnostic rapid tests in the future ***Klaus Hochleitner*** *Chairperson: Tye Gee Jun*		
1130 - 1200	**Symposium 6** **Biomarker Discovery & Assay Development Using Proteomics Approach II** Proteomics and cancer diagnosis Discovery and validation of biomarkers for the early detection of ovarian cancer ***Peter Hoffmann*** *Chairperson: Gurjeet Kaur*		
1200 - 1300	**Symposium 7** **Cancer Diagnosis** Circulatory miRNA biomarkers as "liquid biopsy" in diseases ***Too Heng-Phon*** Identification and utilization of biomarkers of drug response for precision medicine ***Cheong Sok Ching*** *Chairperson: Noor Fatmawati Mokhtar*		
1300 - 1400	Lunch, Poster Viewing & Exhibition		
1400 - 1530	**Oral Presentation** Session 2A	**Oral Presentation** Session 2B	**Oral Presentation** Session 2C
1530 - 1550	Tea, Poster Viewing & Exhibition		
1550 - 1700	**Oral Presentation** Session 3A	**Oral Presentation** Session 3B	**Oral Presentation** Session 3C
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1730	END		

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3 May 2017
Time: 4.15pm – 5.30pm

Chairperson: Assoc. Prof. Dr. Aziah Ismail

Presentation time: 12 mins presentation + 3 mins Q&A

Code	Title	Speaker	Time
OP1	Identifying a diagnostic target for Group B Streptococcus	Hannah Swinburne	4.15 – 4.30pm
OP2	Reverse flow immunochromatography assay for early detecting autoimmune marker (autoantibody to GAD_{65}) on autoimmune diabetic patients	Aulanni'am Aulanni'am	4.30 – 4.45pm
OP3	Isolation and characterization of an anti-salbutamol scFv antibody from a chicken phage display library for immunodiagnostics	Warren Lee Xian Liang	4.45 – 5.00pm
OP4	Innovation challenge: the feasibility from lab scale to mass production. Can we bring good medical device for more people? Ex: Blood Glucose Monitoring System Industry	Sue, Jun Wei	5.00 – 5.30pm

FREE PAPERS SESSION 1B
3 May 2017
Time: 4.15pm – 5.30pm

Chairperson: Assoc. Prof. Dr. Venugopal Balakrishnan

Presentation time: 12 mins presentation + 3 mins Q&A

Code	Title	Speaker	Time
OP5	Influence of human immunodeficiency virus (HIV) and smear status, and host characteristics on seroimmunological biomarkers of pulmonary tuberculosis	Siti Khayriyyah Mohd Hanafiah	4.15 – 4.30pm
OP6	Association of Interleukin-13 gene (*IL13*) rs20541 single nucleotide polymorphism with obesity-related traits and allergies among UTAR Kampar students	Say Yee How	4.30 – 4.45pm
OP7	QTc interval prolongations in opioid dependent patients on methadone maintenance therapy (MMT)	Muslih Abdulkarim Ibrahim	4.45 – 5.00pm
OP8	*In silico* structure based functional annotation of putative conserved hypothetical proteins from *Streptococcus pneumoniae* R6 strain	Tinna Devi Armasamy	5.00 – 5.15pm
OP9	*COMT* methylation as a potential peripheral biomarker of schizophrenia	Nour El Huda binti Abd Rahim	5.15 – 5.30pm

FREE PAPERS SESSION 1C
3 May 2017
Time: 4.15pm – 5.30pm

Chairperson: Dr. Lai Ngit Shin

Presentation time: 12 mins presentation + 3 mins Q&A

Code	Title	Speaker	Time
OP10	Upregulation of metastatic markers MMP2 and N-cadherin in MCF-7 cells by TSA	Nur Sabrina Kamarulzaman	4.15 – 4.30pm
OP11	Effects of gold nanoparticles on dendritic cells in PBMC of asthmatic and healthy individual	Suhana Ahmad	4.30 – 4.45pm
OP12	*miR-21, miR-27b* and *ABCB1* expression implies new markers of chemoresistance in triple negative breast cancer	Ahmad Aizat bin Abdul Aziz	4.45 – 5.00pm
OP13	Identification of ibmr3 antigen in cancer cell lines using two dimensional gel electrophoresis coupled liquid chromatography-tandem mass spectrometry technique	Mohd Nazri Ismail	5.00 – 5.15pm
OP14	Investigating the growth and invasion phenotypes of the three-dimensional (3D) spheroids generated from cervical cancer cell lines	Kalaivani Muniandy	5.15 – 5.30pm

FREE PAPERS SESSION 2A
4 May 2017
Time: 2.00pm – 3.30pm

Chairperson: Dr. Lim Theam Soon

Presentation time: 12 mins presentation + 3 mins Q&A

Code	Title	Speaker	Time
OP15	*in vitro* selection of RNA aptamer against CD36 protein by Systematic Evolution of Ligand by Exponential Enrichment (SELEX)	Nik Abdul Aziz Nik Kamarudin	2.00 – 2.15pm
OP16	Construction of shark semi-synthetic VNAR library for malaria RDTs improvement	Cheong Wei Shien	2.15 – 2.30pm
OP17	Screening for cystic echinococcosis in migrant workers revealed significant discordant results among three immunoassays	Sam Khanbabaie	2.30 – 2.45 pm
OP18	Construction of semi-synthetic phage display library by randomization of CDR3 region of human single chain Fv for antibody generation targeted against Japanese Encephalitis Virus NS1	Chong Hui Ying	2.45 – 3.00pm
OP19	Lateral flow dipstick test using recombinant antigens TES-26, TES-30 and TES-120 for rapid detection of human toxocariasis	Muhammad Hafiznur Yunus	3.00 – 3.15pm
OP20	The value of a panel of autoantibodies and complement as biomarkers in Lupus Nephritis patients in HUSM	Siti Khadijah binti Syed Mohammed Nazri	3.15 – 3.30pm

FREE PAPERS SESSION 2B
4 May 2017
Time: 2.00pm – 3.15pm

Chairperson: Dr. Nurulhasanah Othman

Presentation time: 12 mins presentation + 3 mins Q&A

Code	Title	Speaker	Time
OP21	Detection and identification of microsporidia antigens in HIV/AIDS patients via serum proteomic approach	Nurul Shazalina Zainudin	2.00 – 2.15pm
OP22	Role of TolC in the invasiveness of *Salmonella enterica* serovar Typhi	Ashraf Hussain	2.15 – 2.30 pm
OP23	Detection of proteins as potential biomarkers in *Acanthamoeba* exposed to lead and zinc: *in vitro* study	Nakisah bt Mat Amin	2.30 – 2.45pm
OP24	Identification of novel immunogenic proteins of *Leptospira spp*. using ORFeome phage display	Siti Roszilawati Ramli	2.45 – 3.00pm
OP25	Simultaneous identification of *Salmonella* serovars causing enteric fever using a Multiplex PCR-Line Probe Assay (mPCR-LiPA)	Carlos Silvester	3.00 – 3.15pm

FREE PAPERS SESSION 2C
4 May 2017
Time: 2.00pm – 3.30pm

Chairperson: Dr. Lai Ngit Shin

Presentation time: 12 mins presentation + 3 mins Q&A

Code	Title	Speaker	Time
OP26	Identification of potential biomarkers in synovial fluid in monoiodoacetate induced osteoarthritis in rabbit model	Tan Wei Miao	2.00 – 2.15pm
OP27	Paternal lineage affinity of the earliest inhabitants in Peninsular Malaysia: evidence from Y-STRs analysis	Sharifah Nany Rahayu Karmilla binti Syed Hassan	2.15 – 2.30pm
OP28	Protumourigenic CTAG1B is a potential bladder cancer biomarker	Siti Farizan Mansor	2.30 – 2.45 pm
OP29	Expression profile of E2F genes in cervical carcinogenesis using human transcriptome array gene expression	Shandra Devi Balasubramaniam	2.45 – 3.00pm
OP30	Evaluating the efficacy of polysaccharide extract of basidiomycetes on MMP-1 mechanism: A skin rejuvenation approach	Nur Amira Syairah binti Abdul Halim	3.00 – 3.15pm
OP31	Targeting HIF-1α /CBP to combat Nav1.5-mediated breast cancer metastasis: Potential therapeutic biomarker	Hemaniswarri Dewi A/P Dewadas	3.15 – 3.30pm

FREE PAPERS SESSION 3A
4 May 2017
Time: 3.50pm – 5.05pm

Chairperson: Dr. Leow Chiuan Herng

Presentation time: 12 mins presentation + 3 mins Q&A

Code	Title	Speaker	Time
OP32	Development of a prototype rapid antigen detection test for acute leptospirosis in human	Chang Chiat Han	3.50 – 4.05pm
OP33	Development of carbon nanotube-based aptasensor for detection of *Salmonella* spp.	Thong Kwai Lin	4.05 – 4.20pm
OP34	Species specific recognition of bacterial pathogens using targeted antibody design	Christopher Johnson	4.20 – 4.35pm
OP35	Lateral flow rapid dipstick test for detection of *Entamoeba histolytica* antigen in stool	Syazwan Saidin	4.35 – 4.50pm
OP36	Production of recombinant monoclonal antibody against B*m*SXP filarial antigen	Anizah bt Rahumatullah	4.50 – 5.05pm

FREE PAPERS SESSION 3B
4 May 2017
Time: 3.50pm – 5.05pm

Chairperson: Dr. Leow Chiuan Yee

Presentation time: 12 mins presentation + 3 mins Q&A

Code	Title	Speaker	Time
OP37	Optimisation of dAbs against HSP16.3 from *Mycobacterium tuberculosis*: *in silico* approach	Soong Jia Xin	3.50 – 4.05pm
OP38	Optimisation of domain antibody against ac_2sgl from *Mycobacterium tuberculosis* in complex with CD1b, from the perspective of molecular modelling	Law Cheh Tat	4.05 – 4.20pm
OP39	Membrane proteome analysis of *Entamoeba histolytica*	Jorim Ujang	4.20 – 4.35pm
OP40	Elucidation of antigenic membrane proteins of virulent and avirulent variants of *Entamoeba histolytica* HM1:IMSS strain	Gaayathri d/o Kumarasamy	4.35 – 4.50pm
OP41	An investigation of differential protein expression of the membrane of virulent and avirulent variants of *Entamoeba histolytica* HM1:IMSS	Ng Yee Ling	4.50 – 5.05pm

FREE PAPERS SESSION 3C
4 May 2017
Time: 3.50pm – 5.05pm

Chairperson: Dr. Ong Ming Thong

Presentation time: 12 mins presentation + 3 mins Q&A

Code	Title	Speaker	Time
OP42	In-depth investigation on DNA-AgNCs designs for adenosine detection	Lee Shi Ting	3.50 – 4.05pm
OP43	Application of human neonatal Fc receptor in antibody immobilization	Ng Woei Kean	4.05 – 4.20pm
OP44	Functional role of Fringe in tumor angiogenesis	Cheng Wei Kang	4.20 – 4.35pm
OP45	Endogenous bioactive dynorphin 3-14 as a biomarker in chronic rhinosinusitis and its immunomodulatory effects	Siti Sarah Fazalul Rahiman	4.35 – 4.50pm
OP46	*Nepenthes gracilis* pitcher pot fluid fractions anti-proliferation effects on MDA-MB231 cell line via ER-α36 signalling pathway	Geethaa Sahgal	4.50 – 5.05pm

Keynote, Plenary and Symposium Speakers

Plenary 1-Diagnostic Technologies I

IL 01

David A. Anderson, PhD
Head, Diagnostics Development Laboratory
Macfarlane Burnet Institute for Medical Research and Public Health (Burnet Institute)
Adjunct Appointments:
Associate Professor, University of Melbourne
Visiting Associate Professor, Rush University, Chicago; Senior Lecturer, Monash University.
E mil: david.anderson@burnet.edu.au

Title :
Approaches to development and commercialisation of POC tests – Burnet Institute experience

CURRICULUM VITAE

Associate Professor Dr. Anderson completed a PhD in molecular virology in 1988, and has worked at the Burnet Institute as a full-time research scientist since that time, with a strong focus on translational research in diagnostics and vaccines for more than 25 years. His work in diagnostics has expanded from a focus on hepatitis viruses (hepatitis A, hepatitis E and hepatitis B) to include other infectious diseases including HIV, syphilis, tuberculosis and malaria.

Assoc. Prof. Anderson led the development of licensed diagnostic products for hepatitis E (Assure™ HEV IgM rapid point of care (RPOC) test, HEV IgM ELISA 3.0 and 4.0; MP Biomedicals, Singapore) and led the design and development of the Visitect CD4 T-cell test, now manufactured under license by Omega Diagnostics, UK, and co-inventor of new syphilis point of care test technology also licensed to Omega Diagnostics, with ongoing grant support from Saving Lives at Birth (Gates Foundation, USAID, Grand Challenges Canada, DFID) and the Thrasher Foundation for validation of this important tool for improved prevention of congenital syphilis.

Assoc. Prof. Anderson was Founder and serves as President and CEO for the Burnet Institute spinoff company, Nanjing BioPoint Diagnostics, established to facilitate accelerated translation, commercialisation, manufacture and impact of Burnet's diagnostic innovations, including the VL-Plasma device to support expanded access to HIV viral load testing, and the BioPoint liver disease (ALT) test to support expanded access to therapies for hepatitis C, hepatitis B and other forms of liver disease worldwide.

In the area of vaccine development, Assoc. Prof. Anderson was co-inventor and project leader for new technology platforms in vaccine development, including the Metavax™ VLP system (licensed by Burnet Institute to Artes Biotechnology, Germany, and sublicensed to Crucell and other companies).

RESEARCH INTEREST

i. Point of care tests for diagnosis of infectious diseases (HIV, viral hepatitis, syphilis, TB etc), with the aim of bringing validated and affordable diagnostics to populations of resource-poor countries worldwide
ii. Point of care tests in management of liver disease and other chronic conditions, as above.
iii. Vaccine development based on a virus-like particle (VLP) technology from my lab, now known as Metavax (Artes Biotechnology, Germany) with whom we are collaborating in malaria and HCV vaccine development.
iv. Commercialisation of academic biotechnology, especially in the areas of diagnostics including the establishment of Burnet spinoff company, Nanjing BioPoint Diagnostics (PR China).

RECENT KEY PUBLICATIONS AND PATENTS

- **Anderson, D**. A., Li, F., Riddell, M. A., Howard, T., Seow, H.-F., Torresi, J., Perry, G., Sumarsidi, D., Shrestha, S. M., and Shrestha, I. L. (1999). ELISA for IgG-class antibody to hepatitis E virus based on a highly conserved, conformational epitope expressed in Eschericia coli. Journal of Virological Methods **81**:131-142.
- Chen H. Y., Lu Y., Howard T., **Anderson D**., Fong P. Y., Hu W., Chia C. P., and Guan M. 2005. An immunochromatographic test and its comparison to enzyme-linked immunosorbent assay for rapid detection of immunoglobulin M antibodies to hepatitis E virus in human sera. Clinical and Diagnostic Laboratory Immunology 12:593-598.
- International Patent Application PCT/AU2007/001449, granted S. African patent, "A method of diagnosis and kit therefor": **D. Anderson**, S. Crowe, A. Landay, R. Lloyd, M. Garcia. Burnet Institute. (CD4 diagnostic test)
- PCT/AU2015/050715 Biological sample collection and storage assembly: **D. Anderson**, B. Haile, W. Hopper (Plasma separation device).
- Chinese Patent Application, "Point of Care Test" (liver disease test device): D. Anderson, M. Garcia, H. Van, Z. Zhang.

ABSTRACT

Diagnostic tests are essential for the management and control of both infectious and chronic, non-infectious diseases, but the vast majority of R&D expenditure worldwide is directed to expensive, complex tests for diseases prevalent in wealthy countries. The Burnet Institute's mission is to achieve better health for vulnerable communities by accelerating the translation of research, discovery and evidence into sustainable health solutions, and the development of improved diagnostic tools is one of our areas of focus. Over the past 15 years we have developed a number of point-of-care (POC) tests for infectious diseases including hepatitis E, HIV (CD4 T-cells), syphilis, liver disease etc. This presentation will provide a summary of the technologies that we have used in diagnostic test development, and will examine the different approaches that we have used in commercialization of tests in order for them to reach target populations worldwide, including the important role of academic institutions in validation of new diagnostics to be of benefit in global health.

Symposium 1-Diagnostic Technologies II

IL 02

Ioanis Katakis, PhD
Associate Professor, Departament d'Enginyeria Química
Universitat Rovira i Virgili
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Title :
ASSURED Molecular Diagnostics: Drivers, Barriers and Reality

CURRICULUM VITAE

Ioanis Katakis (B.Eng. Aristotelion University of Thessaloniki 1988, PhD The University of Texas at Austin, 1994) is associate professor of Chemical Engineering at the Universitat Rovira i Virgili in Tarragona, Spain since 1997. His research interests centre in the fields of Bioelectrochemistry and Bioengineering, with applications in biosensors, bioelectronics, and biorefineries. Innovation outcomes of his research target the human diagnostics, and food industries. He has co-authored more than 70 peer reviewed papers and is co-inventor of six patents in these fields. He has led the creation of two technological companies and has received awards for his innovation activities. He is teaching Chemical Process and Product Design and Bioprocess Engineering and Environmental Technologies. He has directed 13 doctoral theses. He has served as director of the Department of Chemical Engineering from 2005 to 2013.

RESEARCH INTEREST

i. Bio/electrochemical approaches for the development of field diagnostics
ii. Biofuel cells for algal biorefinery processes
iii. Nano/biotechnology for the development of the cell/electrode interface

RECENT KEY PUBLICATIONS AND PATENTS

- Mayboroda, O; Benito, AG; del Rio, JS; Svobodova, M; Julich, S; Tomaso, H; O'Sullivan, CK; Katakis, I, Isothermal solid-phase amplification system for detection of Yersinia pestis, Analytical and Bioanalytical Chemistry, 408(3): 671-676, (2016)
- Joda, H; Beni, V; Willems, A; Frank, R; Hoth, J; Lind, K; Strombom, I; Katakis, I; O'Sullivan, CK, Modified primers for rapid and direct electrochemical analysis of coeliac disease associated HLA alleles, Biosensors & Bioelectronics, 73:64-70 (2015)
- Washe, AP; Lozano, P; Bejarano, D; Katakis, I, Eletrochemically Actuated Stop-Go Valves for Capillary Force-Operated Diagnostic Microsystems, ChemPhysChem, 14(10):2164-2173, (2013)

ABSTRACT

ASSURED (Affordable, Sensitive, Specific, User-friendly, Rapid and robust, Equipment-free and Deliverable to end-users) diagnostics is not only a requirement for devices aimed specifically for the detection of infectious diseases in developing countries or environments with limited resources. We argue, that, all diagnostics ideally should be ASSURED, including the devices aimed to rationalize spending on healthcare in developed countries; in fact, development costs for products destined for life-changing detection and prevention in resource-limited environments could be met by advanced economies if the need for ASSURED diagnostic devices is realized. This is so, because less than 5% of public and private annual spending on health care is directed towards prevention, including diagnostics. This pattern is difficult to change since the more than 80% of the more than $ 5 trillion (1012) worldwide annual health care costs is spent on "last resort" efforts to reverse the outcomes of disease. This trend is sure to continue as longevity is increased and more humans escape poverty. We argue therefore, that scientists and engineers should adjust their development efforts so that diagnostic devices be affordable and disease prevention through early diagnosis can be realized within the existing budgetary distribution both for developed and developing economies.

Our thesis is that the widespread availability of cost effective diagnostic tools assisting prevention reliably is an important element that technology can provide for the public good: preventive, personalized medicine should not add to the cost of health care, it should provide more at the same cost if it is to be a catalyst of change in the current health care system. The ASSURED diagnostic device is already making strides in this direction and successful examples can be found in small analyte (e.g. the glucose sensor) and immunological target detection (e.g. a plethora of lateral flow devices, including the pregnancy test and numerous rapid tests for infectious diseases).

However, as our capacity to correlate molecular markers (such as DNA and RNA) to disease and disease progression and management (keys for the implementation of personalised medicine) the question arises if we can develop similar simple and low cost platforms for these (molecular) diagnostic targets. What are the main barriers to such development?

In our presentation we discuss others' and ours (probably Sisyphean) efforts to combine the steps (manipulation of sample and clinical operations, that we call "unit operations") that can be integrated to bring to the market ASSURED molecular diagnostics tools for personalized medicine. Our case studies include molecular (gene based) detection of biological warfare agents where field-based, real time detection has obvious advantages, real time toxic algae detection, and low resolution HLA typing. We show that multiplex isothermal amplification of genetic material permits the identification of these targets at relevant concentrations in less than one hour (and in some cases in 20 minutes). Isothermal amplification allows the independence from the molecular biology lab, and facilitates the field use of molecular diagnostics. Even so, reliable and robust detection methods should accompany such advances. We also show several methods for the electrochemical quantitative detection of amplicons on-line with the amplification techniques. Finally, we show a possible integration platform that can allow operation of the whole diagnostic device at a cost calculated (bill of materials) at less than € 1 and at power consumption of less than 100 mW, making it operable by power sources used in portable communication devices. We argue that the same concept can be applied for management of chronic liver disease and other conditions that require expensive hospitalization and medical personnel time, and certainly for the detection and identification of infectious agents.

Assuming that such efforts lead to solutions for ASSURED field diagnostics/theranostics/personalized medicine, we examine examples where they may be used to benefit society.
This work was made possible partially through support by the Ministry of Economy and Competitiveness of Spain (Project SEASENSING: Ref. BIO2014-56024-C2-1-R).

Symposium 1-Diagnostic Technologies II

IL 03

Mohammed Zourob, Ph.D.
Professor of Biosensors, Alfaisal University, Riyadh, KSA
E mail: mzourob@alfaisal.edu

Title :
Rapid and low-cost assays for pathogens detection

CURRICULUM VITAE

Mohammed Zourob obtained his Ph.D from the Department of Instrumentation and Analytical Science (DIAS) at the University of Manchester in 2003. He was a postdoctoral scientist at DIAS, working in chemical/biosensors and lab-on-a-chip for biomedical and environmental applications. Then he moved to the Department of Materials Science, University of Manchester, to work on developing high-throughput screening platforms for "Omics" applications. At the end of 2005, he moved to the Institute of Biotechnology, University of Cambridge, where his research focused on optical sensing and biomemetic materials. Dr. Zourob headed the biosensors division at Biophage Inc, a biotech company based in Montreal. In 2009 he joined GDG Environment Ltd as Director of R&D. In 2010 he joint INRS-University of Quebec as associate professor and then he moved to Cranfield University-UK. Now Dr Zourob is holding professor of Biosensors at Alfaisal University-KSA. Prof. Zourob is now leading the Biosensors BioMEMS and Bionanotechnology Lab (BBBL). The BBBL has more than 20 researchers working in various projects related to food, biomedical, security and environmental applications. Dr. Zourob has published many scientific papers in peer-reviewed journals, more than thirteen book chapters, and thirteen patents. He edited six books in chemical/biosensors, microarrays and lab-on-a-chip.

RESEARCH INTEREST

i. Novel diagnostic tools
ii. Highly specific recognition receptors for diagnostic and imaging applications
iii. Lab-on-a-chip systems for sample processing

RECENT KEY PUBLICATIONS AND PATENTS

- Rapid and low-cost biosensor for the detection of *Staphylococcus aureus*, G. Suaifan, S Alhogail, M Zourob, Biosensors and Bioelectronics *90, 2017, 230-237*
- Development of magnetic nanoparticle based calorimetric assay for the detection of bovine mastitis in cow milk, R. Chinnappan, S. Al Attas, W. E. Kaman, F. J. Bikker, M. Zourob, *Analytical* Biochemistry 523, 2017, 58–64.
- Paper-based magnetic nanoparticle-peptide probe for rapid and quantitative colorimetric detection of *Escherichia coli*O157:H7, G. Suaifan, S Alhogail, M Zourob, Biosensors and Bioelectronics 92, 2017, 702–708
- Rapid colorimetric sensing platform for the detection of Listeria monocytogenes foodborne pathogen, S Alhogail, G. Suaifan, M Zourob, Biosensors and Bioelectronics 86, 2016, 1061-1066.
- Emerging Loop-Mediated Isothermal Amplification-Based Microchip and Microdevice Technologies for Nucleic Acid Detection, M Safavieh, MK Kanakasabapathy, F Tarlan, MU Ahmed, M Zourob, W. Asghar, H. Shafiee ACS Biomaterials Science & Engineering 2 (3), 2016, 278-294.
- 'Method and kit for the detection of microorganisms, US PATENT APPLICATION NUMBER: 14852526, 2015.
- 'A novel assay for early detection of a disease using a magnetic nanoparticple biosensor ' US PATENT APPLICATION NUMBER: 14819195, 2015.
- 'Biosensor using magnetic particles for pathogen detection', M. Zourob, US PATENT APPLICATION NUMBER: 14867353, 2015.
- "Device for pathogens detection", M. Safavieh, M. Uddin Ahmed M. Zourob (US patent, application No. 13/987,392)

ABSTRACT

The challenges for today's biosensing platforms are numerous: they have to work with real samples, poor detection limit which is far from the infectious dose, suffer from the long analysis time, and use of washing steps and liquids which defeat the purpose of field applications. Another challenge is the stability and availability of highly specific recognition receptors to be integrated with the sensing platform to have a functional device.

The presentation will highlights our recent developments to overcome such challenges for various biomedical, food and security related analytes. We developed various optical, electrochemical, colorimetric sensing platforms and integrate it with various natural and synthetic recognition receptors. We integrated a number of techniques with the various transducers to concentrate and enrich the analyte onto the immobilized recognition receptors on the sensor surface. This technique enhanced and improved the detection limit, shortened the analysis time and reduced the non-specific binding, to reduce the false positive results.

Symposium 2 -Biomarker Discovery & Assay Development Using Proteomics Approach I

IL 04

Peter U. Fischer, PhD, MS
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Division of Infectious Disease,
School of Medicine
Washington University
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Title :
A Genomic and Immunoproteomic Approach to Identify Diagnostic Antigens for Human Paragonimiasis

CURRICULUM VITAE

Dr. Fischer got his master's degree in Biology from the Free University of Berlin, Germany and a PhD in Zoology from the University of Hamburg, Germany. He did postdoctoral research at Smith College in Northampton MA, USA and was a laboratory leader at the Bernhard Nocht Institute for Tropical Medicine in Hamburg. Following his habilitation in parasitology he joined the Infectious Diseases Division at Washington University School of Medicine in St. Louis MO, USA, as a Visiting Associate Professor in 2005 and became an Associate Professor in 2011. His primary research interest involves medical helminthology, especially filariasis and other neglected tropical diseases caused by parasitic worms. He has performed extensive field research on the diagnosis, epidemiology and control of filarial parasites in Uganda, Indonesia and many other countries and conducted basic laboratory research on filarial nematodes and their *Wolbachia* endosymbionts. He is co-investigator on the Bill and Melinda Gates Foundation funded DOLF project which studies alternative filariasis treatment strategies in large scale community trials in Asia and Africa. In addition Dr. Fischer studies North American paragonimiasis in Missouri to improve diagnostics for paragonimiasis globally and he investigates digenean trematodes as hosts for intracellular *Neorickettsia* bacteria.

RESEARCH INTEREST

i. Control and elimination of Neglected Tropical Diseases, especially helminthiasis.
ii. Diagnosis of helminth infections.
iii. Interaction of helminth parasites with bacteria (endosymbionts, metagenomics)

RECENT KEY PUBLICATIONS AND PATENTS

- McNulty SN, Rosa BA, Fischer PU, Rumsey JM, Erdman-Gilmore P, Curtis KC, Specht S, Townsend RR, Weil GJ, Mitreva M (2015). An integrated multi-omics approach to identify candidate antigens for serodiagnosis of human onchocerciasis. Molecular and Cellular Proteomics, 14:497-503.
- McNulty SN, Fischer PU, Townsend RR, Curtis KC, Weil GJ, Mitreva M (2014) Systems biology studies of adult Paragonimus lung flukes facilitate the identification of immunodominant parasite antigens. PLoS Neglected Tropical Diseases, 8:e3242.
- Fischer PU, Curtis KC, Folk SM, Wilkins PP, Marcos LA, Weil GJ (2013) Serological diagnosis of North American paragonimiasis by Western blot using Paragonimus kellicotti adult worm antigen. American Journal of Tropical Medicine and Hygiene, 88:1035-1040.
- Supali T, Djuardi Y, Bradley M, Noordin R, Ruckert P, Fischer PU (2013) Impact of six rounds of mass drug administration on brugian filariasis and soil-transmitted helminth infections in eastern Indonesia. PLoS Neglected Tropical Diseases, 7:e2586.
- McNulty SN, Foster J, Mitreva M, Hotopp-Dunning JC Martin J, Fischer K, Wu B, Davis PJ, Kumar S, Hotopp-Dunning JC, Brattig NW, Slatko BE, Weil GJ, Fischer PU (2010) Endosymbiont DNA in endobacteria-free filarial nematodes indicates ancient horizontal genetic transfer. PLoS One, 5:e11029.

ABSTRACT

Paragonimus lung fluke infection affects about 23 million people mainly in South-East Asia, but also in Africa and the Americas. *Paragonimus kellicotti* is the only *Paragonimus* species in North America and is prevalent in its animal reservoirs, but only rarely infects humans. While effective treatment strategies exist, diagnosis of paragonimiasis is often difficult, because parasitological or DNA detection of worm eggs in sputum or stool is insensitive. Clinically, paragomimiasis is often misdiagnosed as tuberculosis or lung cancer. We identified several *P. kellicotti* adult worm antigens by immunoprecipitation using patients' sera and proteomics as highly immunoreactive antigens with serodiagnostic potential. A full-length cysteine protease (Pkcp-6) of 35 kDa was expressed in *E. coli*, purified and its diagnostic potential was compared to crude total *P. kellicotti* extract. In a Western Blot assay Pkcp-6 was specific for the detection of IgG4 subclass antibodies in 27 subjects with either proven *P. kellicotti* or *P. westermani* infection. The recombinant antigen did not cross-react with sera of 30 subjects with other trematode or with cestode infections or with sera from healthy volunteers. Results showed a similar sensitivity of Pkcp-6 as the crude worm extract, but decreased background. The assay was also used to screen 157 serum samples from a paragonimiasis focus in western Cameroon, and detected 10.8% positive subjects while microscopic detection of eggs in sputum or stool identified fewer positive individuals (2.5% and 3.2%, respectively). The novel, specific and sensitive antigen for the detection of parasite-specific IgG4 antibodies may greatly improve the serodiagnosis of human paragonimiasis and may help to evaluate paragonimiasis control programs globally.

Symposium 2 -Biomarker Discovery & Assay Development Using Proteomics Approach I

IL 05

Majid Golkar, PhD
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Pasteur Institute of Iran,
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Title :
Rational Design and Evaluation of a Multi-epitope Chimeric Fusion Protein for Detection of Toxoplasma IgM antibodies

CURRICULUM VITAE

Dr. Majid Golkar received a Pharm.D from Shahid Beheshti University of Medical Science, Tehran, Iran (1992-1998). He got his PhD in Medical Biotechnology from Pasteur Institute of Iran (1999-2004) working on development of DNA and protein vaccine against *Toxoplasma gondii* infection. He worked for one year in the lab of Dr. Cesbron Delauw, Grenoble, France, to complete his PhD. He continued his career as a faculty member in department of Parasitology, Pasteur Institute of Iran. His research has been mainly focused on development of recombinant diagnostic tests for parasitic infections, mainly *Toxoplasma* infection. He developed, in collaboration with international collaborators, *Toxoplasma* IgG, IgM and IgG avidity ELISA tests for human use. The IgG test kit was approved by Iranian ministry of health for human use. The IgM and IgG avidity tests are to be approved by ministry of health. He has established a spin-off company to commercialize the diagnostic tests. Apart from diagnostic field, He is also actively focused on production and commercialization of recombinant pharmaceutical proteins i.e. active pharmaceutical ingredients such as human Epidermal Growth Factor (hEGF). Dr. Golkar is currently an associate professor in department of Parasitology, Pasteur Institute of Iran

RESEARCH INTEREST

i. Production and Evaluation of Toxoplasma Protein and DNA Vaccines using different adjuvant systems, for prevention against acute and chronic infection
ii. Assessment of Toxoplasma Recombinant Proteins in serological tests for detection of Toxoplasma infection,
and discriminating acute from chronic infection.
iii. Development of Molecular and Serological Tools for Accurate diagnosis of T. gondii infection
iv. Recombinant Production, Process Development and formulation of Recombinant therapeutic proteins

RECENT KEY PUBLICATIONS AND PATENTS

- 2015: Allahyari M, Mohabati R, Babaie J, Amiri S, Siavashani ZJ, Zare M, Sadeghiani G, Golkar M. Production of in-vitro refolded and highly antigenic SAG1 for development of a sensitive and specific Toxoplasma IgG ELISA. J Immunol Methods. 416:157-66.
- 2014: Havakhah Y, Esmaeili Rastaghi AR, Amiri S, Babaie J, Aghighi Z, Golkar M. Prevalence of Toxoplasma gondii in Sheep and Goats in Three Counties of Gilan Province, North of Iran; the More Humid Climate the Higher Prevalence. J Med Microbiol Infec Dis. 2 (2): 80-83
- 2014: Talebzadeh M, Mohabati R, Babaie J, Amiri S, Allahyari M , Golkar M. Production of MAG1 Antigen of Toxoplasma gondii in Escherichia coli. J Med Microbiol Infec Dis. 2(1): 40-44.
- 2013: Amerizadeh A, Khoo BY, Teh AY, Golkar M, Abdul Karim IZ, Osman S, Yunus MH, Noordin R. Identification and real-time expression analysis of selected Toxoplasma gondii in-vivo induced antigens recognized by IgG and IgM in sera of acute toxoplasmosis patients. BMC Infect Dis. 24:13-287.
- 2013: Mohabati R, Babaie J, Amiri S, Talebzadeh M, Fard-Esfahani P, Darbouy M, Golkar M. Expression and Purification of Recombinant ROP1 of Toxoplasma gondii in Bacteria. Avicenna J Med Biotechnol. 5(4):227-33.

ABSTRACT

Recombinant antigens present advantages such as ease of production and higher specificity for development of diagnostic tests. Instead of using a combination of antigens, a multi-epitope chimeric antigen can be designed by fusing epitopes/antigenic part(s) of several target antigens. In order to develop a chimeric antigen for detection of Toxoplasma IgM antibodies, linear antibody epitopes from protein sequences of dense granule protein 6 (GRA6), GRA8 and rhoptry protein 1 (ROP1) were predicted using Bepipred B-cell epitope prediction tool. The predicted epitopes/antigenic parts were fused together by triglycyl linkers. The recombinant Toxoplasma chimeric protein was expressed in Escherichia coli and purified in a single step by immobilized metal ion affinity chromatography. Western blot analysis showed serum from a rabbit immunized with the chimeric antigen was capable of recognizing individual antigens, indicating correct folding of individual antigenic parts within the chimeric antigen. An enzyme-linked immunosorbent assay (ELISA) was developed using the chimeric antigen to detect Toxoplasma IgM antibodies in a seroconversion panel of 98 patient sera. The test showed sensitivity and specificity of 77.7 and 95.5 %, respectively, for detection of IgM antibodies and performed better than a commercial recombinant IgM ELISA kit. Interestingly, the sensitivity for sera collected between 1 to 4 month after infection was higher than for IgM positive sera collected between 5 to 11 month after infection.

Symposium 3-Infectious disease diagnosis using genomics approach

IL 06

Fernando Spilki, PhD
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Title :
Molecular biology and the environmental monitoring of enteric viruses

CURRICULUM VITAE

Holds a Veterinary degree (DVM , 2001) and Master's in Veterinary Sciences (2004) from the Federal University of RioGrande do Sul, Brazil. He earned his PhD in Genetics and Molecular Biology from State University of Campinas (2006), Brazil. Dr. Spilki is now Professor at Feevale University, Novo Hamburgo, Brazil and his main research focus is on the detection and characterization of enteric viruses from human beings and domestic animals in environmental matrices and food samples. Another current research line is in the biology and epidemiology of arboviruses.

RESEARCH INTEREST

i. New methods for detection and monitoring of viruses in water and food
ii. Next-generation sequencing and metagenomics use in environmental and veterinary virology
iii. Emerging and re-emerging arboviruses in humans and non-human primates
iv. Antivirals and vaccines for viral diseases

RECENT KEY PUBLICATIONS AND PATENTS

- Staggemeier R, Heck TM, Demoliner M, Ritzel RG, Röhnelt NM, Girardi V, Venker CA, Spilki FR. Enteric viruses and adenovirus diversity in waters from 2016 Olympic venues. Sci Total Environ. 2017 May 15;586:304-312. doi: 10.1016/j.scitotenv.2017.01.223.
- Scheffer CM, Varela AP, Cibulski SP, Schmidt C, Campos FS, Paim WP, Dos Santos RN, Teixeira TF, Loiko MR, Tochetto C, Dos Santos HF, de Lima DA, Cerva C, Mayer FQ, Petzhold SA, Franco AC, George TS, Spilki FR, Roehe PM. Genome sequence of bubaline alphaherpesvirus 1 (BuHV1) isolated in Australia in 1972. Arch Virol. 2017 Jan 6. doi: 10.1007/s00705-016-3218-8.
- Heldt FH, Staggmeier R, Gularte JS, Demoliner M, Henzel A, Spilki FR. Hepatitis E Virus in Surface Water, Sediments, and Pork Products Marketed in Southern Brazil. Food Environ Virol. 2016 Sep;8(3):200-5. doi: 10.1007/s12560-016-9243-7.

ABSTRACT

Enteric viruses are widely recognized as a major threat to human health, being most often transmitted by water and/or contaminated food. However, due the lack of cost-effective and trained personnel, the monitoring of these pathogens in environmental matrices is neglected in many countries. Adenovirus, enterovirus, rotavirus and norovirus infections are associated to diarrhea, and the most susceptible are children, elderly and immunosuppressed individuals. People living under poor sanitary conditions are heavily impacted, and lack of sewage and/or water treatment is a major risk factor for transmission of these viruses. Despite the burden of water- and foodborne, the advancement of the molecular based protocols which occurred in the last 3 decades, detection of viral contaminants of water and food remains a matter of research rather than routine in health surveillance laboratories around the globe, especially in developing countries. The presentation will show situation of enteric viruses' prevalence in environmental samples, drinking water, and point-of-sale products, using Brazil and Latin America as an example. After, it will be discussed how the development of innovative, cost-effective and robust detection methods could solve the problem of adoption of a proper monitoring of these microbial contaminants by public health authorities.

Keynote Address 1

IL 07

Ciara O' Sullivan, PhD
ICREA Research Professor,
Engineering Sciences Universitat Rovira i Virgili (URV).
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Title :
Cost-effective point-of-need diagnostics – combining aptamers and advanced lateral flow devices

CURRICULUM VITAE

Ciara O' Sullivan, is an ICREA (Catalan Institute for Research and Advanced Studies) Research Professor. She received a BSc in Analytical Chemistry from Dublin City University in 1992, a PhD. in Biotechnology from Cranfield University in 1996 and then went on to lead the sensors group at University College Cork from 1996-99. She then took up a Marie Curie Candidateship at the Universitat Rovira i Virgili (1999-2001) and was then awarded a "Ramon y Cajal Candidateship" which she pursued for 1 year prior to taking up her current position as ICREA Research Professor and establishing the Nanobiotechnology and Bioanalysis Group at the Universitat Rovira i Virgili. Prof. Ciara K. O' Sullivan has published/presented over 180 articles in diverse areas ranging from biosensors to liposomes to aptamers. Her research interests have focused on the development of electrochemical biosensors exploiting advances in tailored biocomponents and integrating these sensors with microsystem technology. Presently, her work focuses on reducing to practise ultrasensitive immuno- apta- and geno- sensors exploiting isothermal amplification, labelled dNTPs and paper diagnostics and she is currently expanding into the area of next generation molecular tools for personalised medicine and advanced forensics. She is currently visiting professor at Newcastle University, UK and University of the Western Cape, South Africa. She has a H-index of 34.

RESEARCH INTEREST

i. Aptamers and their application in analytical devices
ii. Low cost molecular diagnostics
iii. Biosensors and biosensor arrays
iv. Paper analytical diagnostics

RECENT KEY PUBLICATIONS AND PATENTS

- Jauset Rubio, M., Sabaté del Río, J., Mairal, T., Svobodová, M., Saeed, A., Nooredeen Abbas, M., El-Shahawi, M., Bashammakh, A.S.,. Alyoubi, A.O. and O 'Sullivan, CK, Ultrasensitive, rapid and inexpensive detection of DNA using paper based lateral flow assay, 2016, Scientific Reports, DOI: 10.1038/srep37732
- Jauset Rubio, M., Sabaté del Río, J., Mairal, T., Svobodová, M., Keegan, N., McNeil, C., El-Shahawi, M., Bashammakh, A.S.,. Alyoubi, A.O. and O 'Sullivan, CK,, Aptamer lateral flow assays for ultrasensitive detection of β-conglutin combining recombinase polymerase amplification and tailed primers, 2016, Analytical Chemistry, 88 (21), pp 10701–10709
- Sabaté del Rio, J., Conejeras, P., and O' Sullivan, C.K., Electrochemical detection of *Piscirickettsia salmonis* genomic DNA from salmon samples using solid-phase recombinase polymerase amplification, 2016, Anal Bioanal Chemistry, DOI: 10.1007/s00216-016-9639-0
- Acero Sanchez, J. L., Henry, O. Y. F., Joda, H., Werne Solnestam, B., Kvastad, L., Johansson, E., Akan, P., Lundeberg, J., Lladach, N., Ramakrishnan, D., Riley, I. and O'Sullivan, C. K., Multiplex PCB-based electrochemical detection of cancer biomarkers using MLPA-barcode approach, 2016, Biosensors & Bioelectronics, 15; 82: 224-32
- Debela, A.M., Beni, V., Thorimbert, S., Hasenknopf, B., O' Sullivan, C.K.* and Ortiz, M.*, Electrochemical primer extension for detection of single nucleotide polymorphisms in the cardiomyopathy associated MYH7 gene, 2016, Chemical Communications, 252, 757-759

ABSTRACT

Trichomonas vaginalis infection is the most prevalent non-viral sexually transmitted disease worldwide with an estimated prevalence of at least 170 million each year. Despite its widespread threats to public health, the available diagnostic methods today remain insufficient because of several limitations. We report on the use of an aptamer against the Ap65 adhesion protein, a cell surface marker for *Trichomonas vaginalis*. Aptamers are oligonucleotides, either single-stranded deoxyribonucleic acids (ssDNAs) or ribonucleic acids (RNAs) that can bind to target molecules with high affinity, and, possess several properties that may become more desirable than the use of standard antibodies in molecular detection. The DNA aptamer was selected in a process of systematic evolution of ligands by exponential enrichment (SELEX) and demonstrated to have a Kd of ca. 1nM. The specificity of the aptamer has been demonstrated with *T. vaginalis* cells, and no cross-reactivity observed with *Bacillus subtilis, Escherichia coli, Enterococcus faecalis, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus vulgaris, Staphylococcus aureus, Salmonella enterica* or *Candida albicans*. The aptamer was exploited in a lateral flow easy for the rapid and inexpensive detection of *T. vaginalis* in vaginal swabs. The sensitivity of competition and sandwich lateral flow assays were compared and a lateral flow combining isothermal amplification, tailed primers and the selected aptamer was demonstrated to achieve ultrasensitive detection limits, with the assay being completed in less than 15 minutes. Work is ongoing to test and validate the lateral flow device with real samples. The talk will give an overview of this generic platform that can be applied to a multiplicity of infectious diseases.

Keynote Address 2

IL 08

YING Jackie Yi-Ru, PhD
IExecutive Director
Institute of Bioengineering and Nanotechnology, Singapore, 2003-Present
Professor, Department of Chemical Engineering, Massachusetts Institute of Technology (USA), 2001-2005
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Title :
Advanced Nanosystems for Diagnostic Applications

CURRICULUM VITAE

Jackie Y. Ying received her B.E. and Ph.D. from The Cooper Union and Princeton University, respectively. She joined the faculty at Massachusetts Institute of Technology in 1992, where she was Professor of Chemical Engineering until 2005. She has been the Founding Executive Director of the Institute of Bioengineering and Nanotechnology in Singapore since 2003. For her research on nanostructured materials, Prof. Ying has been recognized with the American Ceramic Society Ross C. Purdy Award, David and Lucile Packard Fellowship, Office of Naval Research Young Investigator Award, National Science Foundation Young Investigator Award, Camille Dreyfus Teacher-Scholar Award, American Chemical Society Faculty Fellowship Award in Solid-State Chemistry, Technology Review's Inaugural TR100 Young Innovator Award, American Institute of Chemical Engineers (AIChE) Allan P. Colburn Award, Singapore National Institute of Chemistry-BASF Award in Materials Chemistry, Wall Street Journal Asia's Asian Innovation Silver Award, International Union of Biochemistry and Molecular Biology Jubilee Medal, Materials Research Society Fellowship, Royal Society of Chemistry Fellowship, Crown Prince Grand Prize in the Brunei Creative, Innovative Product and Technological Advancement (CIPTA) Award, American Institute for Medical and Biological Engineering Fellowship, Academy of Sciences of Iran Medal of Honor, American Association for the Advancement of Science Fellowship, Islamic World Academy of Sciences-COMSTECH Ibrahim Memorial Award, Singapore National Academy of Science Fellowship, and The Cooper Union Alumni Association Gano Dunn Award.

Prof. Ying was elected a World Economic Forum Young Global Leader, and a member of the German National Academy of Sciences, Leopoldina. She was named one of the "One Hundred Engineers of the Modern Era" by AIChE in its Centennial Celebration. She was selected by The Muslim 500 in 2012, 2013, 2014, 2015 and 2016 to be one of the world's 500 most influential Muslims. She was selected as an Inaugural Inductee for the Singapore Women's Hall of Fame in 2014. She was the inaugural winner of the Mustafa Prize "Top Scientific Achievement Award" in 2015 for her research in bio-nanotechnology. The laureate of this science and technology award receives a certificate, an engraved medal and US$500,000 in prize money. She is the Editor-in-Chief of Nano Today, which has an impact factor of 13.157.

RESEARCH INTEREST

i. Bio-Nanotechnology
ii. Nanosystems for diagnostic applications
iii. Lab-on-a-cartridge
iv. Paper-based-assays

RECENT KEY PUBLICATIONS AND PATENTS

- G. Xu, T.-M. Hsieh, D. Y. S. Lee, E. Mohamed Ali, H. Xie, X. L. Looi, E. S.-C. Koay, M.-H. Li, and J. Y. Ying, "A Self-Contained All-in-One Cartridge for Sample Preparation and Real-Time PCR in Rapid Influenza Diagnosis," Lab Chip, 10 (2010) 3103-3111.
- Y. Zu, M.-H. Tan, B. Chowbay, S. C. Lee, H. Yap, M. T. M. Lee, L.-S. Lu, C.-P. Chang, and J. Y. Ying, "Nanoprobe-Based Genetic Testing," Nano Today, 9 (2014) 166-171.
- Y. Zhang, J. Bai, and J. Y. Ying, "A Stacking Flow Immunoassay for the Detection of Dengue-Specific Immunoglobulins in Salivary Fluid," Lab Chip, 15 (2015) 1465-1471.
- I. Cima, S. L. Kong, I. B. Tan, W. M. Phyo, D. Lee, M. Hu, D. Sengupta, C. Iliescu, J. H. Vo, W. L. Goh, M. Rahmani, N. A. Mohamed Suhaimi, J. A. Tai, J. H. Tan, C. Chua, R. Ten, I. Alexander, R. M. van Dam, W. Y. Lim, S. Prabhakar, B. Lim, P. K. Koh, P. Robson, J. Y. Ying, A. M. Hillmer, and M. H. Tan, "Tumor-Derived Circulating Endothelial Cell Clusters Detect Colorectal Cancer," Science Translational Medicine, 8 (2016) 345ra89.
- Y. Zu, M. H. Tan, E. C. Ren and J. Y. Ying, "Facile and Phase-Defined Determination of HLA Alleles with Morpholino-Functionalized Nanoparticle Probes," Nanomedicine, (2016) DOI: 10.1016/j.nano.2016.09. 009.

ABSTRACT

Our laboratory has been developing various nanosystems for diagnostic applications. These include designing plasmonic nanocrystals for single nucleotide polymorphism (SNP) genotyping. The platform involves polymerase chain reaction (PCR) for target sequence amplification and colorimetric detection for pharmacogenomics applications. We have also established polymer-based lab-on-a-cartridge for automated sample preparation and PCR detection. The integrated all-in-one system, termed MicroKit, allows for the rapid and accurate typing and subtyping of influenza and other viral infections within 2 hours. We have created the silicon-based Microsieve system for rapid and selective isolation of circulating tumor cells (CTCs) from peripheral blood. This non-invasive, near real-time, inexpensive liquid biopsy approach allows for the enumeration and biomarker analysis of CTCs for cancer diagnosis, prognosis and monitoring. Recently, we have also developed paper-based assays for the rapid detection of various diseases. For example, we have created a novel stacking flow immunoassay platform, and demonstrated successful detection of dengue-specific IgG in salivary fluid.

Symposium 4-Diagnostic Test Development & Translational Research

IL 09

Andreas Latz, Dr. rer. nat.
NovaTec Immundiagnostica GmbH, Dietzenbach, Germany.
Project Leader of the genetic engineering department;
Principal investigator of antigen development and veterinary ELISA;
Group leader of human diagnostic development
E mail: a.latz@novatec-id.com

Title :
From bench to market: Challenges in the development and commercialization of diagnostic tools.

CURRICULUM VITAE

Dr. Latz is a Project Leader of the Genetic Engineering Department at NovaTec Immundiagnostica GmbH, Dietzenbach, Germany since 2010. He is also the principal investigator of antigen development and veterinary ELISA and group leader of human diagnostic development at NovaTec. He received his undergraduate (1996-2002) and doctoral education (2003-2007) at the Julius Maximilian University Wuerzburg, Germany and was a postdoc and group leader at the Department of Microbiology at Eberhard Karls University Tuebingen, Germany (2007-2010).

RESEARCH INTEREST

i. One health: Development of diagnostic tools for the application in the human as well as veterinary field
ii. Diagnostic tools for Zoonotic diseases
iii. Diagnostics on tropical diseases with an special emphasis on parasites and worms

RECENT KEY PUBLICATIONS AND PATENTS

• Epidemiological and clinical profile of paediatric malaria: A prospective study performed in five epidemiological strata of malaria in Cameroon Tebit Emmanuel Kwenti, MSc; Tayong Dizzle Bita Kwenti, MSc; Andreas Latz, PhD; Longdoh Anna Njunda, PhD; Theresa Nkuo-Akenji, PhD BMC Infectious Diseases INFD-D-17-00363 (submitted)

ABSTRACT

Every year, many publications in scientific journals are focusing on the discovery of biomarkers and the development and evaluation of diagnostic tools. Only very few of these innovations ever reach the market and are accessible to the end users. There is a gap in applying that knowledge into products to reduce the burdens of illness and disability. This discrepancy between scientific innovation and commercial product is mostly due to the fundamental challenge of applying research and development advances into operations. In this talk, I will discuss strategies on how to bridge this valley of death in order to overcome barriers to more effectively translate research findings into health care practice.

It is crucial that a translational cooperation between scientific institutions and the industry is established right at the beginning of a new development. This may start with a joint application for funding and has to be intensively continued during the development and commercialization process. Even after launching a product into market, the continuation of the cooperation will be essential for the commercial success of the diagnostic product.

During the initial stages of research and development, many points have to be considered; like the assessment that a discovery has commercial value or an important impact on the health care industry. After choosing the appropriate platform for a new diagnostic tool, many different points; like product design, usability, reproducibility, precision, stability, constant evaluation, quality control, quality management or risk assessment have to be addressed.
For the period of the validation/verification process, interferences, cross reactivity, clinical evidence, sample material (serum/plasma/liquor/milk/urine etc…), sample population and statistical significance or high dose hook effect have to be considered.
To be able to produce the final product, production flow charts and operation protocols have to be established.

Most of the diagnostic tools, for veterinary or human use, have to be registered by local authorities prior of use. The requirements differ from parameter to parameter and from country to country. Furthermore, they are one of the most crucial and time consuming steps during the commercialization process.
Finally, the product will need marketing and external validation data. OEM businesses and/or dealers' network have to be established. As well as systems for post market surveillance.
These points will be discussed with practical examples from our company.

Globalization, demographic shifts, urbanization, climate change and internet proliferation are the macroeconomic megatrends that will shape the 21st century and will have an influence on future development in biomarker discovery and development of new diagnostic tools.

Symposium 5-Diagnostic Technologies III

IL 10

Klaus Hochleitner, Dr. rer. nat.
Global Lead Technology
Product Specialist bei GE Healthcare
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Title :
Use of lateral flow membranes for diagnostic rapid tests in the future

CURRICULUM VITAE

Dr. Klaus obtained his Dr. rer. nat. (PhD) from the University of Essen Medical School in 1992. He has many years of experience in diagnostics, particularly in the development of lateral flow tests. He has previously worked at Schleicher & Schuell GmbH as a Laboratory Manager of Life Science (1993-1997), Business Development Diagnostic Components (1997-2001) and Application Manager Life Science and Diagnostics (2001-2005). After that he led the R&D manager at Whatman GmbH (2005-2011) in design development and design control of cellulosic and polymeric membranes in ISO 9001/ISO 13485 QM system. Since 2011, he is the Global Lead Technology Product Specialist at GE Healthcare. This role sees him applying his vast experience to provide clinical, technical and professional guidance to the global field in developing applications in immuno- and molecular diagnostics. He holds several diagnostics-related patents.

RECENT KEY PUBLICATIONS AND PATENTS

- Improvements in and relating to lateral flow testing. United Kingdom WO2015150067. Filed March 31, 2014. A.Schenk, S.Kiel, Klaus Hochleitner, M.Thieme
- Membrane filter including bile acid and method manufacturing same. Europe EP2819772 Filed February 29, 2012. Klaus Hochleitner, , S.Kiel
- Membrane filter including bile acid and method manufacturing same. China CN104379242. Filed February 29, 2012. Klaus Hochleitner, S.Kiel
- Medical diagnostic systems and a matrix therefor United Kingdom WO2014122094. Filed February 8, 2013. Klaus Hochleitner, A.Schenk, S.Kiel, W. Sun
- Method for detecting concentration of antibody or fusion protein. China CN103376327. Filed April 28, 2012. L.Chen, R.Hou, Klaus Hochleitner, L.Lu
- Method and apparatus for isolating nucleic acids. Europe EP2794631. Filed December 22, 2011. L.Chen, Klaus Hochleitner, B.Zhang, R.Hou
- Method and apparatus for isolating nucleic acids. Japan JP2015503324. Filed December 22, 2011. L.Chen, Klaus Hochleitner, B.Zhang, R.Hou
- Method and apparatus for isolating nucleic acids. United States US9441220 B2. Issued September 13, 2016. L. Chen, Klaus Hochleitner, B.Zhang, R.Hou
- Improvements in and relating to polymeric membranes. United Kingdom WO2016156250. Filed March 30, 2015. Dr. Marcel Thieme, Suzana Kiel, Klaus Hochleitner, Dr. Alexander Schenk

ABSTRACT

Introduction: Since their invention in the middle of the 1980s, lateral flow rapid tests have become a widespread and versatile tool for the detection of analytes in sample liquids ranging from water over urine and blood to resolubilized solid materials.
A key component of lateral flow tests is the membrane part on which the detection of the analyte is performed. Recent developments to improve test sensitivity, permit quantitation of analytes, reduce reagent usage, and improve multi-parameter analysis will be discussed.

Methods: Optimization of membrane manufacturing conditions, surface activation, and improved dispensing technologies were used to achieve improved test performance.

Results and Discussion: Compared to standard materials, it is possible to achieve an up to 6-fold higher sensitivity, and tests CVs far below 10 % for selected test systems with a concomitant reduction of reagent use of up to 50 %.
Multiplexing can be achieved by the creation of lateral flow arrays.

Symposium 6-Biomarker Discovery and Assay using Proteomics Approach II

IL 11

Prof Peter Hoffmann, PhD
Strand Leader and Lloyd Sansom Chair
Biomaterials Engineering and Nanomedicine
Future Industries Institute
University of South Australia
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Title :
Proteomics and cancer diagnosis
Discovery and validation of biomarkers for the early detection of ovarian cancer.

CURRICULUM VITAE

Prof Hoffmann received his PhD in Analytical Chemistry at University of the Saarland, Germany in 1999. He spent four years in Melbourne working with Prof Richard Simpson and Prof Bruce Kemp where he specialised in the use of free-flow electrophoresis in proteomics and the detection of protein phosphorylation by mass spectrometry. He moved back to Germany in 2003 and played an integral role in establishing a proteomics facility at the University Leipzig, Germany. In 2005, he was recruited back to Australia to establish a Proteomics Centre at the University of Adelaide and held a Chair in Proteomics and was Director of the Adelaide Proteomics Centre at the University of Adelaide. His research is focused on biomarker discovery in cancer, detection of protein phosphorylation and Tissue Imaging Mass Spectrometry. The Adelaide Proteomics Centre houses the national facility for Tissue Imaging Mass Spectrometry for Australia. Prof Hoffmann was also Deputy Director of Institute of Photonics and Advanced Sensing one of the five research institutes at the University of Adelaide. Prof Hoffmann is currently the Strand Leader and Lloyd Sansom Chair of Biomaterials Engineering and Nanomedicine at Future Industries Institute at the University of South Australia. Prof Hoffmann is also an elected member of the HUPO Council and Treasurer of the HUPO executive committee.

RESEARCH INTEREST

i. Imaging Mass Spectrometry using FFPE gynecological cancer tissue
ii. Discovery of Biomarkers for the early detection of ovarian and gastric cancer
iii. Identification and characterization of beer and food related spoilage and production specific microorganisms
iv. The use of label free mass spectrometry technology for the quantification of disease specific changes in protein expression

RECENT KEY PUBLICATIONS AND PATENTS

- A.V. Everest-Dass, M.T. Briggs, K. Gurjeet, M.K. Oehler, P. Hoffmann*, N.H. Packer*. N-glycan MALDI imaging mass spectrometry on formalin-fixed paraffin-embedded tissues enables the delineation of ovarian cancer tissues. Mol Cell Proteomics, 2016, 15(9): 3003-3016. * equal contribution
- M.T. Briggs, J.S. Kuliwaba, D. Muratovic, A.V. Everest-Dass, N.H. Packer, D.M. Findlay, Peter Hoffmann. MALDI mass spectrometry imaging of N-glycans on tibial cartilage and subchondral bone proteins in knee osteoarthritis. Proteomics, 2016 Jun;16(11-12):1736-41.
- Winderbaum LJ, Koch, I., Mittal, P., Hoffmann, P. Classification of MALDI-MS imaging data of tissue microarrays using canonical correlation analysis based varible selection. Proteomics. 2016 Jun;16(11-12):1731-5.

- Gustafsson OJ, Briggs MT, Condina MR, Winderbaum LJ, Pelzing M, McColl SR, Everest-Dass AV, Packer NH, Hoffmann P. MALDI imaging mass spectrometry of N-linked glycans released from formalin-fixed murine kidney. Analytical and Bioanalytical Chemistry, 2015, 407, 2127-2139
- Humphries JM, Penno MA, Weiland F, Klingler-Hoffmann M, Zuber A, Boussioutas A, Ernst M, Hoffmann P. Identification and validation of novel candidate protein biomarkers for the detection of human gastric cancer. Biochim Biophys Acta. 2014, May;1844(5):1051-8.

ABSTRACT

In this presentation, potential autoantibody biomarkers for ovarian cancer were discovered, verified and validated as an early detection test. A new immunoproteomic strategy was developed to identify novel autoantibodies that were elevated in serous ovarian cancer patients. Lysate extracted from the ovarian tissue of a patient was applied to an immunoaffinity column generated with autologous antibodies and a paired control immunoaffinity column. Relative quantification of captured autoantigens was performed using isotope coded protein label (ICPL) technology coupled with high resolution LC-MS. At a protein ratio cutoff of 1.45-fold, 148 autoantibodies were found to be enriched in ovarian cancer patients compared to the corresponding controls. Upon bioinformatic prioritisation 50 autoantibody candidates were selected for verification. Protein microarray analysis of 98 samples revealed 9 autoantibody candidates to be significantly different in early stage cancer patients compared to healthy and benign controls. Biomarker candidates anti-ANXA1, anti-SAHH and anti ARP3 showed the greatest potential where each marker achieved greater than 90% specificity at 83.3% sensitivity. As a 4 biomarker panel with the 'gold standard' for ovarian cancer detection, cancer antigen (CA)125, a sensitivity of 76.5% at 100% specificity was attained. These values of sensitivity and specificity for early stage ovarian cancer surpassed the minimum requirements for an implementable screening test and showed great promise as a diagnostic tool.

Symposium 7- Cancer diagnosis

IL 12

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Title :
Circulatory miRNA biomarkers as "liquid biopsy" in diseases

CURRICULUM VITAE

Dr Too Heng Phon received his undergraduate training in Biochemistry, Imperial College of Science & Technology, UK. He then continued with his PhD training in a joint research project in Imperial College, Institute of Ophthalmology and West Minister Hospital, London. Thereafter, he received further training in the Medical Research Council, Cambridge (UK), where he was a Procter & Gamble Fellow. He then moved to the Department of Anesthesiology and Department of Biological Chemistry & Molecular Pharmacology, Harvard Medical School where he was a recipient of the Merck Sharpe Dohme Academic Development Fellowship. Currently, he is a faculty in the Department of Biochemistry, National University Singapore, a Principal Scientist in the Bioprocess Technological Institute and was a Fellow of the Singapore Massachusetts Institute of Technology Alliance (Molecular Engineering of Biological & Chemical Systems program; Chemical & Pharmaceutical Engineering program). Dr Too is a molecular biologist focusing on biotechnology and neuroscience. In recent years, Roche Diagnostics (USA & Asia Pacific) and National Institute of Health (USA) funded him to develop qPCR assays for infectious diseases. He is an awardee of a number of Commercialization of Technology grants from A*STAR and Singapore-Massachusetts Research & Technology (SMART). Dr Too has recently been awarded a KHIDI-A*STAR grant with a Korean company to co-develop IVD for prognostic/ diagnostic of breast cancer. He is the founder of MiRXES and the lead principal investigator of the miRNA profiling facility (μRSIC), A*STAR. He has intellectual property protections on specific diagnostic platforms with various research departments and with Massachusetts Institute of Technology, USA.

RESEARCH INTEREST

i. Molecular tools for the detection of microRNAs & replicating viruses.
ii. Non-viral gene delivery.
iii. *in vivo* & *in vitro* Metabolic Engineering of the DXP pathway.
iv. Glial-derived neurotrophic growth factor (GDNF) and related factors.

RECENT KEY PUBLICATIONS AND PATENTS

- Zhang C, Zou R, Chen X, Stephanopoulos G, Too HP. Experimental design-aided systematic pathway optimization of glucose uptake and deoxyxylulose phosphate pathway for improved amorphadiene production. Appl Microbiol Biotechnol. 2015. 99(9):3825-37.
- Low SY, Ho YK, Too HP, Yap CT, Ng WH. MicroRNA as potential modulators in chemoresistant high-grade gliomas. J Clin Neurosci. 2014; (3):395-400.
- Zhou L & HPToo. Mitochondrial localized STAT3 is involved in NGF induced neurite outgrowth. PLoS ONE 6(6): e21680, 2011.
- Zhou L, Too, H. P. GDNF family ligand dependent STAT3 activation is mediated by specific alternatively spliced isoforms of GFRα2 and RET. Biochim. Biophys. Acta. 2013;1833(12):2789-802.

- Lim QE, Wan G, Ho YK and Too, H. P. Multiplexed, Direct miRNA Quantification from Cell Lysates without RNA Isolation. Nat. Protoc. Exchange (2011) doi:10.1038/protex.2011.202.
- Wan G, Lim QE, Too HP. High-performance quantification of mature microRNAs by real-time RT-PCR using deoxyuridine-incorporated oligonucleotides and hemi-nested primers. RNA (2010) 16(7):1436-45.
- Ajikumar PK, Xiao WH, Tyo KE, Wang Y, Simeon F, Leonard E, Mucha O, Too HP, Pfeifer B, Stephanopoulos G. Isoprenoid pathway optimization for Taxol precursor overproduction in Escherichia coli. Science (2010) 330 (6000):70-4.

ABSTRACT

MicroRNAs (miRNAs) belong to a class of small noncoding RNAs (ncRNAs). These miRNAs are short single-stranded RNA (~ 22 nt) in length and the number of publications has escalated exponentially, impacting on almost all fields of medical and basic sciences. miRNA are now known to regulate gene expression at the post-transcriptional level and to control protein expression noise in the cell. Considering this wide involvement in gene control, aberrant miRNA expression is strongly associated with the presence and progression of a disease, hence it is not a surprise that miRNAs may serve as biomarkers for the diagnosis and prognosis of human disorders including cancers, cardiovascular and others. The majority of miRNAs are intracellular, but recently they have been reported in numerous bodily fluids at low levels. Here we describe the use of real time qPCR and the design of discovery workflows with extensive quality control system to avoid pre-analytical and analytical variables as well as the quantitative determination of expression levels to enable the rapid identification of panels of useful biomarkers. Using these validated sequence-independent qPCR platform with unparalleled sensitivity and robustness, we found a large number of circulating miRNA that can detect the emergence of diseases at early stages and to stratify patients in many disorders. The next step is to adapt the panels of biomarkers onto dPCR platform. This presentation will discuss the value of circulating miRNAs as biomarkers.

Symposium 7- Cancer diagnosis

IL 13

Cheong Sok Ching, Prof. Dr.
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Title :
Identification and utilization of biomarkers of drug response for precision medicine

CURRICULUM VITAE

Prof. Cheong currently leads the Head and Neck Cancer Research Team at Cancer Research Malaysia. She received her first class honors degree in Biochemistry from the National University of Malaysia (UKM). She continued to pursue her PhD in UKM under the mentorship of Prof Sheila Nathan (UKM) and Prof Dorothy Bennett (St Georges Hospital Medical School, London). Her work focuses on identifying genetic changes that drive head and neck cancer development with the goal of using this understanding to improve clinical management of cancer patients. Her research has resulted in the development of an immunotherapy that is currently in preclinical testing. Further, her team has conducted extensive research into building and validating tools to that could accelerate cancer research and drug development. To do this, she works with scientists from different areas of expertise to leverage on their experiences and to translate laboratory findings into the clinic. Her work has received a number of awards including the Norman-Rowe Educational Trust (United Kingdom), L'Oreal for Women in Science Award, American Association for Cancer Research (AACR) Scholar-In-Training Award and several UICC fellowships. She has published in international peer-reviewed journals, delivered keynote and plenary lectures in international and national conferences. She is a regular reviewer of many cancer and molecular biology related journals and review grants from international bodies including those from the Union for International Cancer Control (UICC), The World Academy of Sciences (TWAS) and the African Medical Council amongst others. Professor Dr. Cheong serves as an Adjunct Professor at University of Malaya, Kuala Lumpur and Visiting Professor at the University of Khon Kaen, Thailand. She is currently the Co-Chair of The World Academy of Sciences (TWAS) Young Affiliate Network (TYAN), an Associate of the Malaysian Academy of Sciences (ASM), an honorary member of the Young Scientist Network (YSN) of the ASM, and a Fellow of the International Academy of Oral Oncology (IAOO) and the UICC.

RESEARCH INTEREST

i. Cancer immunotherapy
ii. Drug repurposing for cancer
iii. Models for cancer research

RECENT KEY PUBLICATIONS AND PATENTS

- B.K.B. Lee, K.H. Tiong, J.K. Chang, C.S. Liew, Z.A.A. Rahman, A.C. Tan, T.F. Khang & S.C. Cheong. DeSigN: connecting gene expression with therapeutics for drug repurposing and development. BMC Genomics. Accepted- Aug 2016.
- M.Z.H. Fadlullah, I.K-N. Chiang, K.R. Dionne, P.S. Yee, C.P. Gan, K.K. Sam, K.H. Tiong, A.K.W. Ng, D. Martin, K.P. Lim, T.G. Kallarakkal, W.M. Wan Mustafa, S.H. Lau, M.T. Abraham, R.B. Zain, ZA.A. Rahman5, A. Molinolo, V. Patel, J. S. Gutkind, A.C. Tan & S.C. Cheong. Genetically-defined novel oral squamous cell carcinoma cell lines for the development of molecular therapies. Oncotarget. 2016 Apr 1. doi: 10.18632/oncotarget.8533. [PMID: 27050151]

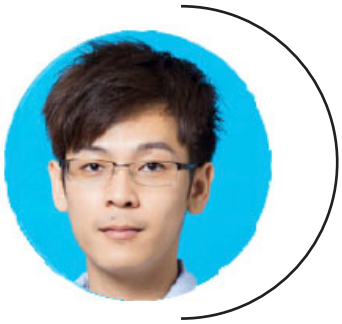
- C.P. Gan, V. Patel, C.M. Mikelis, R.B. Zain, A.A. Molinolo, M.T. Abraham, S.-H. Teo, Z.A.A. Rahman, J. S. Gutkind & S.C. Cheong. Heterotrimeric G-protein alpha-12 (Gα12) subunit promotes oral cancer metastasis. Oncotarget 2014 Oct 30;5(20):9626-40. [PMID: 25275299]
- K.P. Lim, N.A.L. Chun, C.P. Gan, S.H. Teo, Z. A. Abdul Rahman, M.T. Abraham, R.B. Zain, S. Ponniah & S.C. Cheong. Identification of immunogenic MAGED4B peptides for vaccine development in oral cancer immunotherapy. Hum Vaccin Immunother 2014;10 (11):3214-23. [PMID: 25000177]
- C.E. Chong, K.P. Lim, C.P. Gan, C. A. Marsh, R.B. Zain, M.T. Abraham, S.S. Prime, S-H Teo, J.S. Gutkind, V. Patel & S.C. Cheong. Over-expression of MAGED4B increases cell migration and growth in oral squamous cell carcinoma and is associated with poor disease outcome. Cancer Letters 321 (2012): 18–26. [PMID: 22459352]
- Ajikumar PK, Xiao WH, Tyo KE, Wang Y, Simeon F, Leonard E, Mucha O, Too HP, Pfeifer B, Stephanopoulos G. Isoprenoid pathway optimization for Taxol precursor overproduction in Escherichia coli. Science (2010) 330 (6000):70-4.

ABSTRACT

Precision medicine is about matching the patient with the right drug to achieve the most desirable outcome for the patient. In cancer treatment, several companion diagnostic markers indicative of response are currently used clinically such as the V600E in BRAF for the use of Vemurafenib or KRAS mutations for the use of EGFR inhibitors. In this lecture, I will be focusing on our work in identification of novel therapies for head and neck cancer, and in parallel describe approaches to identify biomarkers of response for these drugs.

Technology Session 1

TS01



Chong Mun Keat, PhD,
Regional Head of Research Marketing,
Flow Cytometry and Multiplexing,
Merck Emerging Asia

Title :
Biomarker Discovery: Multiplexing with Luminex xMAP Technology

CURRICULUM VITAE

Chong Mun Keat is the regional head of research marketing in flow cytometry and multiplexing technologies, Merck Emerging Asia. His role is to give presentations, training and marketing materials to the team on flow cytometry and multiplexing. He received his B.Sc. and Ph.D. degrees from the National University of Singapore, under the supervision of Professor Mary Ng. He has 7 years of research experience in molecular virology with vast knowledge on protein expression and purification, cellular analyses, molecular cloning and high-throughput screening. He has presented more than 20 conference papers in international and local conferences with 2 best oral presentation awards and 1 young investigator award.

ABSTRACT

Biomarker is becoming an essential evaluative tool in drug discovery and development. Various high-throughput and high-content platforms have been developed to identify potential biomarkers for cancer, infectious diseases, diabetes, neurodegenerative diseases and other diseases. Luminex xMAP technology is one of the widely used multiplexing platform to boost biomarker discovery studies. In this seminar, the principles of Luminex xMAP technology will be elucidated and the roles of Milliplex biomarker kits in infectious diseases and immunology studies will be explored.

Technology Session 2

TS02

Hoe Li Nah, PhD
Technical support manager,
Canvio

Title :
Going Digital: In Molecular Diagnostics

CURRICULUM VITAE

Hoe Li Nah received her PhD for Biochemistry from Universiti Kebangsaan Malaysia. She has over 13 years of experience in the Life Science industry and have performed various functions including technical consultancy, support, marketing, and management. In her line of profession, she has had the opportunity to acquaint herself with current and upcoming technologies that provide solutions to the research community. During this period of time, she has given numerous seminars and workshops to both local and overseas researchers.

ABSTRACT

Quantitative real-time PCR is widely used for several applications across life science research, applied testing and molecular diagnostics. This 20-year old technology is facing increasing challenges with today's demands for more data with less samples and the need for higher precision, sensitivity and reproducibility. Therefore it is important to look into new technologies that can improve research data and come out with better methods for diagnostics and ultimately treatment strategies. One of these exciting new technologies is Droplet Digital PCR (ddPCR). We will be highlighting the key applications of ddPCR and how it can address some of your research questions.

Oral Presentations

OP01: Identifying a diagnostic target for Group B Streptococcus

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Abstract

One in four pregnant women carry the bacterium *Streptococcus agalactiae*, which, when passed from mother to infant during childbirth, can cause sepsis, pneumonia, meningitis and ultimately death. Current microbiological culture diagnosis takes between 36 and 72 hours. Due to inaccurate due dates, mothers are tested at 35-37 weeks to ensure results are available prior to labour. Levels of *S. agalactiae* rapidly fluctuate in the body, therefore premature testing results in antibiotic prescribing being informed by outdated information. With the rise of antibiotic resistance, accurate diagnosis and appropriate drug prescription becomes increasingly important. This project aims to develop a sensitive, specific, point of care diagnostic test able to detect the 10 serotypes of *S. agalactiae*, which could be performed at the onset of labour. A novel computer programme has been developed to identify peptide sequences distinctive to a group of bacteria. The programme captures the protein sequences from all complete bacterial genomes in the RefSeq database and splits them into tokens of 15 amino acids in length. Currently this dataset comprises of 1.77 billion tokens from 4,791 organisms. Tokens are then assessed for their conservation within, and uniqueness to, a group of bacterial strains. Three peptides from a surface exposed protein have been identified bioinformatically as being present in all *S. agalactiae* serotypes, and verified using reverse transcription PCR. Murine monoclonal antibodies were generated in house against these peptides. Binding affinity to the peptide, recombinant protein and bacterial cells is being determined prior to lateral flow assay development.

Keywords: Antibodies; Biomarkers; S. agalactiae

OP02: Reverse flow immunochromatography assay for early detecting autoimmune marker (autoantibody to GAD_{65}) on autoimmune diabetic patients

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and [1,2]Wuragil, Dyah Kinasih

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Abstract

Autoantibody profiles are gaining widespread interest as a way to diagnose, predict, and monitor a variety of diseases. Insulin-dependent diabetes mellitus (IDDM is an organ-specific autoimmune disease resulting from the destruction of pancreatic islet beta cells and consequent insulin deficiency. Glutamic acid Decarboxylse (GAD_{65}) autoantibodies can be found in human islets and have been detected in recent onset diabetic children, so in this long studies we developed reliable clinical screening methods based on biomolecular interactions to predict, a patient's risk of developing an autoimmune disease such as type 1 diabetes. Several autoimmune abnormalities are detectable in type 1 diabetic sera at the time of diagnosis, although they are observed in the sera of subjects who are at increased risk for progression to the disease. The aim of this study was to constructs a rapid test for early detection of autoimmune marker as an autoantibody to GAD_{65} on autoimmune diabetic patients. Human Recombinant GAD_{65} that produced in *E. coli* BL21 as competent cell used as antigen for detecting autoantibody GAD_{65} that release in early phase in beta pancreas cell destruction on autoimmune diabetic patients. The design of Rapid Test use material such as membrane of nitrocellulose and polyester, adsorbent paper, Human Recombinant GAD_{65}, goat anti-mouse IgG as control line, and signal reagent contained Nano gold particle and Protein A. The Rapid test based on reverse flow immunochromatography assay has been tested with sera of diabetic patients and have a sensitivity of 100% and specificity up to 96 %.

Keywords: autoantibody-GAD_{65}; Type 1 diabetic patients; reverse flow immunochromatogrpahy assay

OP03: Isolation and characterization of an anti-salbutamol scFv antibody from a chicken phage display library for immunodiagnostics

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Abstract

To date, salbutamol is a preferred β2-agonist drug of abuse in athletics and as a livestock growth promoter due to its inexpensiveness. For the detection and isolation of β2-agonists, antibodies remain as the key biomolecules to fulfil such purposes. In this study, the use of the chicken (*Gallus gallus domesticus*) as an immunization host for the generation of a monoclonal anti-salbutamol antibody by phage display is investigated. A single chicken immunized against SAL-KLH conjugate was used to construct the phage display library. Colony PCR and *Bst*NI fingerprinting revealed ~84% of the library had full-length scFvs and ~80% of distinct clones respectively. Biopanning from this library isolated six scFv clones which were reactive to salbutamol. Following single-point competitive ELISA, one clone with highest apparent affinity was selected for soluble scFv expression in *Escherichia coli* T7 SHuffle Express B (DE3). The functionality of the expressed scFv was tested by multi-point competitive ELISA by inhibition with free salbutamol (IC_{50} salbutamol = ~0.310 µg/ml (scFv). The affinity of the antibody was deemed potentially suitable for use as an immunosorbent for immunochromatographic-capture solid phase extraction (SPE) for the isolation of salbutamol and its detection by more sensitive methods such as LC-MS or GC-MS.

Keywords: beta-2-agonist; salbutamol; chicken scFv; phage display; ELISA

OP04: Innovation challenge: the feasibility from lab scale to mass production.

Can we bring good medical device for more people? Ex: Blood Glucose Monitoring System Industry

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Abstract

The development of biosensor in the IVD industry is always the important topic for each one who want to introduce their technical aspect change the patient behaviours. Especially, batch to batch variety, quality assurance, regulatory of medical device, quality assurance, & user need in the market are serious points during lab scale to mass production if scientist want to improve the patient outcome effectively. Each research topic should bring new concept for treatment become more effective & also bring the new niche milestone to the team who create this biosensor. It is always popular to have the discussion for chronic disease like diabetes. According to the report from international diabetes forum (IDF) & WHO, they mentioned almost 10% of prevalence in diabetes. It is not only related the budget of health care but also crowded the budget of the other field out because the prevalence of diabetes is still going up now. It really impact the social economic status in each territory if the policy of health care want to reduce the cost of hospitalization. And blood glucose monitoring system (BGMS) is the necessary key point for diabetes care to control glucose level well & prevent too much cost used in the hospital. This presentation wants to share the successful example of diabetes care & service. It was started from the electrochemical analysis lab in the national university & bring new unique platform of biosensor in IVD industry. The performance was also better than major competitor, reduces the cost at the beginning stage and provides affordable product to patient.

Keywords: IVD Industry; Diabetes; Blood Glucose; Biosensor; Electrochemical Analysis

OP05: Influence of human immunodeficiency virus (HIV) and smear status, and host characteristics on seroimmunological biomarkers of pulmonary tuberculosis

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Abstract

Globally, pulmonary tuberculosis (PTB) causes disease and death in millions. Early detection and treatment is limited by lack of point-of-care (POC) diagnostics. Efforts to develop accurate seroimmunological POC diagnostics is hampered by a heterogeneous patient immune response, which are compounded in paucibacillary/smear-negative and human immunodeficiency (HIV)-positive PTB patients. To understand the variation of common seroimmunological biomarkers across PTB subpopulations, we screened anti-antigen 60 (A60) IgG and IgA, and C-reactive protein by ELISA in Vietnamese and South African PTB and non-TB patient sera (n=404) (including HIV-positive/negative and smear-positive/negative). Statistical analysis for biomarker distribution, diagnostic value and host variables across PTB subpopulations were conducted. Combined biomarkers had the highest diagnostic value in smear-positive HIV-negative (AUC:0.830), HIV-negative (AUC:0.754), and total population (AUC:0.739). CRP had higher accuracy across subpopulations (AUC: 0.614-0.828), with lowest accuracy in smear-negative and HIV-positive subpopulations. Anti-A60 IgA combined with CRP had highest accuracy in HIV-positive (AUC:0.687) and smear-positive HIV-positive subpopulations (0.774). Two-way ANOVA indicates significant HIV-status and diagnostic group interaction for anti-A60 IgA ($p=0.003$) and CRP ($p=0.005$), but not anti-A60 IgG. Anti-A60 IgG and IgA positively correlates in all subgroups except smear-negative HIV-positive patients while CRP is not correlated with either anti-A60 IgG or IgA. In non-TB, wasting predicted CRP; in smear-positive, weightloss, disease severity, BCG vaccination, and HIV status predicted CRP; while in smear-negative, BCG vaccination and smoking predicted anti-A60 IgA, while hemoptysis predicted CRP. In conclusion, diagnostic values of biomarkers vary by PTB subpopulation and relate to several host characteristics including clinical symptoms and vaccination status.

Keywords: tuberculosis; biomarkers; serodiagnosis; HIV; host factors

OP06: Association of Interleukin-13 gene (*IL13*) rs20541 single nucleotide polymorphism with obesity-related traits and allergies among UTAR Kampar students

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Abstract

Obesity and allergies are complex disorders caused by genetic and environmental factors. IL-13 is a Th2 immunoregulatory cytokine which stimulates B cell secretion of IgE and inhibits pro-inflammatory cytokine production. The *IL13* rs20541 (R130Q) single nucleotide polymorphism (SNP) has been associated with increased risk of allergies such as allergic rhinitis (AR), atopic dermatitis (AD) and asthma, but its association with obesity-related traits is still elusive. Therefore, this study investigated the association of rs20541 SNP with obesity-related traits and allergies among 440 UTAR Kampar students (M/F: 207/233; Chinese/Indians: 416/24). Anthropometric measurements were taken, allergy questionnaire and skin-prick test were conducted, and genotyping was performed by Taqman® SNP Genotyping Assay using DNA extracted from mouthwash samples. The prevalence of obesity, AR, AD and asthma was 19.5%, 24.7%, 13.1% and 14.3%, respectively. The rs20541 Q allele frequency for Chinese/Indians was 0.50/0.54. *IL13* rs20541 genotypes were significantly associated with waist circumference (WC) and total body fat (TBF) classes (both p=0.02). Logistic regression analysis further revealed that subjects with QQ genotype had increased risk of having high TBF (OR=2.60; 95% CI=1.27, 5.32; p=0.01 and OR=2.35; 95% CI=1.14, 4.85; p=0.02 in unadjusted and adjusted for ethnicity analysis, respectively). AD was associated with body mass index (BMI) and WC classes (both p=0.01), while its co-existence with asthma was associated with BMI class (p<0.001). However, *IL13* rs20541 was not associated with AR, AD and asthma, or their combinations. In conclusion, *IL13* rs20541 is associated with adiposity, but not allergies among UTAR Kampar students.

Keywords: Interleukin-13; single nucleotide polymorphism; allergic conditions; anthropometric measurements; adiposity

OP07: QTc interval prolongations in opioid dependent patients on methadone maintenance therapy (MMT)

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Abstract

Methadone inhibits the cardiac potassium channel hERG and can be associated with a corrected QT (QTc) interval prolongation and torsade de pointes (TdP). We conducted a cross-sectional study to investigate QTc interval among opioid dependent patients on methadone maintenance therapy (MMT). The sample comprised opioid naive individuals and opioid dependent patients from MMT clinics between March and October 2013. All participants underwent 12-lead electrocardiogram (ECG). Of the 145 patients who had satisfactory ECG recordings, 29 (20%) had QTc interval prolongation > 450 msec. Four (2.8%) opioid naive individuals had a prolonged QTc interval. No participant had QTc interval > 500 msec. Patients had significantly longer QT and QTc interval compared to opioid naive individuals ($p < 0.001$). Number of patients with QTc interval prolongation > 450 msec was significantly higher compared to opioid naive individuals ($p < 0.001$). The results demonstrate clinical evidence of significant longer QTc interval in opioid dependent patients on MMT compared to opioid naive individuals. QTc interval prolongations also occured in a significant proportion of patients. Methadone therapy may cause QTc interval prolongations and appropriate clinical management measures should be considered to address this challenge.

Keywords: methadone maintenance therapy (MMT); opioid dependence; electrocardiogram; corrected QT (QTc) interval; QTc prolongation

OP08: *In silico* structure-based functional annotation of putative conserved hypothetical proteins from *Streptococcus pneumoniae* R6 strain

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Abstract

Streptococcus pneumoniae (pneumococcus) is a major human respiratory pathogen that causes several serious diseases, including pneumonia, otitis media (ear infection), sinusitis, meningitis, and septicaemia. Despite the introduction of antimicrobial drugs over the past few decades it remains a significant threat to health due to antibiotic resistance developed. Hypothetical proteins are the protein which has been identified its existence but the function in vivo remains unpredictable. The aim of the study is to identify novel potential drug target by structural and functional annotation of hypothetical proteins. In our study, we analysed 484 hypothetical proteins available in *Streptococcus pneumoniae* R6 strain genome using various functional and structural annotation bioinformatics tools. We used functional annotation tools like Pfam, CDD, Inteproscan and SMART tools. We classified successfully out 484 hypothetical proteins, 138 proteins as enzymes, 39 proteins as binding proteins, 11 proteins as factor, regulator & hormones, 17 proteins as transporters, 8 proteins as cell cycle related, 3 protein cellular process regulatory, 2 proteins as ion channels, 1 protein-lipid binding protein, 184 proteins related to DUF domain with 100% confidence in which all the four tools were consistent with prediction. Through sub-cellular localization prediction, 297 were identified as cytoplasmic protein. We structurally characterized proteins which are cytoplasmic, functionally characterized and virulent predicted through homology modelling by using the Phyre2 server. Through subtractive genomics approach, we identified 14 potential drug targets. This present study will facilitate a better understanding of the mechanism of virulence, drug resistance, and pathogenesis and for identification drug targets in *Streptococcus pneumoniae*, which emphasizes future perspective to design rational drugs and vaccines.

Keywords: Pneumoniae; drug target; hypothetical protein; bioinformatics

OP09: *COMT* methylation as a potential peripheral biomarker of schizophrenia

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Abstract

Schizophrenia is a common debilitating neuropsychiatry disorder. Currently, absolute clinical criteria (DSM-V) are used for the diagnosis. Identification of prediction and therapeutic markers of schizophrenia could expedite the disease diagnosis and management. Catechol-O-methyltransferase (*COMT*) which regulates catecholamine and cognitive function in the developing neurons has long been considered as one of the candidate genes of schizophrenia. Recent studies have discovered hypomethylation of the *COMT* gene in the brain of schizophrenia patients. Our study aims to assess the *COMT* DNA methylation in the peripheral blood, on the premises that there are global epigenetic changes and the changes in the peripheral blood mirrors the methylation changes of the brain in the schizophrenia patients and the healthy controls. 138 schizophrenia patients from the Psychiatry Clinic, Hospital Kuantan Ampuan Afzan, Kuantan Pahang and 132 matched healthy controls from Kuantan district were recruited. Genomic DNA from the peripheral blood was bisulfite converted and quantitatively measured for the *COMT* DNA methylation using the MethyLight Taqman® assay and normalized with the *ALU* reference control to give the percentage methylation ratio. We found a significant hypomethylation of *COMT* in schizophrenia as compared to the control group (p=0.000). The hypomethylation was also significant in males (p=0.002) and females (p=0.032). This study suggests that DNA methylation analysis of *COMT* can be a potential peripheral biomarker in schizophrenia.

Keywords: COMT; DNA methylation; schizophrenia

OP10: Upregulation of metastatic markers MMP2 and N-cadherin in MCF-7 cells by TSA

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Abstract

Histone deacetylase inhibitors (HDACis) have now appeared as a new therapeutic agent in cancer management. Application of HDACis has been reported to be effective in treating haematological malignancies. However, clinical trials on HDACis have shown some disappointment in patients with solid tumours. The underlying molecular reasoning for this problem is yet to be determined but previous *in vitro* studies showed that HDACis induced epithelial-to-mesenchymal transition in cancer cells and importantly, evidences revealed that HDACis caused cardiac toxicity in patients. We have previously reported that HDACi, Trichostatin A (TSA) inhibits the mRNA expression of histone deacetylases, hence promotes motility and migration in the weakly metastatic human breast cancer cells, MCF-7. Here, we aimed to evaluate the mRNA expression level of two metastatic markers, Matrix Metalloproteinase 2 (MMP2) and N-cadherin in MCF-7 cells after TSA treatment. MCF-7 cells were treated with several concentrations of TSA (100-10 000 ng/ml) for 24 hours. The mRNA expression of MMP2 and N-cadherin was determined by quantitative real-time PCR. Our findings showed that TSA significantly upregulate the mRNA expression of both of MMP2 and N-cadherin in dose-dependent manner. Therefore, this study supports our previous data that treatment with TSA enhances metastatic behaviour of breast cancer cells via upregulation of metastatic markers MMP2 and N-cadherin. We conclude that HDACis such as TSA should be carefully evaluated as a potential therapy for patients with solid tumours as application of HDACi could induce metastasis.

Keywords: metastatic markers; TSA; breast cancer; MMP2; N-cadherin

OP11: Effects of gold nanoparticles on dendritic cells in PBMC of asthmatic and healthy individual

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Abstract

Asthmatic condition involves the exposure of various environmental stimuli including allergen that resulted in an activation of effector T cells by antigen-presenting dendritic cells (DCs), secreting various pro-inflammatory cytokines. Nanoparticles (NPs) have been shown to have anti-inflammatory properties and reduce the symptoms such as hypersecretion of mucus in asthmatic individuals. However, the precise mechanisms of NPs exert these effects on DCs, the sentinels of immune system, are still vague. Gold NPs have been chosen as NPs of interest due to its advantageous properties including customizable size and shapes, surface functionality, low cytotoxicity and biocompatibility. This study have reported that upon exposure to PBMCs of healthy donor and asthmatic, we found that gold NPs were taken up by DCs, which were revealed by SEM images. Further analyses with flow cytometry and confocal microscopy showed that gold NPs were preferentially internalized by DCs of both study cohorts. The uptake of gold NPs induced low cytoxicity and immune response associated with a DCs maturation state. This study suggests the potential manipulation of DCs with gold NPs, specifically, as targeted delivery for immunotherapies.

Keywords: dendritic cells; gold nanoparticles; asthma

OP12: ***miR-21, miR-27b and ABCB1 expression implies new markers of chemoresistance in triple negative breast cancer***

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Abstract

Triple negative breast cancer (TNBC), characterized by absence of ER, PR and lack of overexpression of HER2, is typically associated with poor prognosis, aggressive tumour phenotype(s), partial response to chemotherapy and lack of clinically established therapies. TNBC patients receive standard chemotherapy with Taxane/Adriamycin/Cyclophosphamide (TAC) regimen but still early relapse is very common in TNBC patients. This highlight the urgent need for identification of novel biomarkers for TNBC subtyping and prediction of prognosis. The expression of drug efflux transporter gene ABCB1 is associated with altered treatment response. microRNAs (miRNAs) are widely recognized as key player in cancer progression and drug resistance. This study investigated the expression profile of ABCB1 and 6 miRNAs (miR-21, miR-27b, miR-34a, miR-182, miR-200c and miR-451) in FFPE samples of 41 TNBC patients. Total RNA was isolated, transcribed and preamplified. The expression of ABCB1 and miRNAs were quantified using quantitative real time PCR (qRT-PCR) and normalized by normal adjacent tissues. The disease outcome of the patients was evaluated after chemotherapy completion. When analyzed to the risk of recurrence, expression of ABCB1 mRNA was upregulated (2.833) whereas miR-21 and miR-27b were significantly down regulated (0.354 and 0.388 respectively) in recurrent group compared to non-recurrent group with p-value 0.041 and 0.036 respectively. The results suggest that expression levels of ABCB1 together with miR-21 and miR-27b signatures may serve as biomarkers for prediction of recurrent risk in TNBC patients. Identification of such prognostic biomarkers for TNBC patients would allow an optimized treatment selection of regimens that could eventually benefit to the patients.

Keywords: Triple negative breast cancer; chemotherapy; recurrence risk; ABCB1; microRNAs

OP13: Identification of IBMR3 antigen in cancer cell lines using two dimensional gel electrophoresis coupled liquid chromatography-tandem mass spectrometry technique

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Abstract

IBMR3 is a monoclonal antibody (MAb) which was raised against synthetic peptides that were based on the sequence of human interleukin-4 receptors. IBMR3 has been previously shown to be able to inhibit the proliferation of cell lines and thus has the potential in cancer treatment. This study aimed to identify the expression of IBMR3 antigen in carcinoma (HEp-2 and HT-29), T-leukemic (Jurkat cell line) and normal peripheral blood mononuclear cells (PBMC). Immunostaining revealed that IBMR3 MAb can recognize antigen in a variety of cell types, including epithelial and haematopoietic cancers and normal cells. Interestingly, IBMR3 Ag was found to be expressed in the cytoplasm but was absent on the cell surface except for normal lymphocytes. Protein extracts were separated via one dimensional electrophoresis and immunoblotting and the results showed 2 bands with molecular weights (MWs) of 45 and 25 kDa in HT-29 and one band with MWs of 25 kDa in HEp-2. IBMR3 antigen was then identified by combining techniques consisting of two-dimensional gel electrophoresis (2-DE), immunoblotting and liquid chromatography tandem mass spectrometry (LC-MS/MS). The results revealed eight candidate proteins, seven of which are common molecules associated with cancer. The protein with the highest significance score in this study was 14-3-3 zeta. Differently expressed 14-3-3 proteins have been correlated with the prognosis of several cancers. The findings from this study exhibited a significant relationship between IBMR3 antigen expression and different types of cancer cells. IBMR3 Ag could be a molecule that participates in tumorigenesis through involvement in cell proliferation.

Keywords: immunoblotting; monoclonal antibody; cancer; liquid chromatography tandem mass spectrometry

OP14: Investigating the growth and invasion phenotypes of the three-dimensional (3D) spheroids generated from cervical cancer cell lines

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Abstract

Spheroids are self-assembled mass of cells that produce their own extra cellular matrix encompassing the complex cell-matrix and cell-cell interactions that mimics the functional properties of the corresponding tissue *in vivo.* The aim of this study is to establish a three-dimensional (3D) spheroid model using the cervical cancer cell lines, HeLa (HPV18), CaSki (HPV16) and C33A (non-HPV) as well as to determine its growth and invasion phenotype. The liquid overlay method was employed to generate the spheroids which were then embedded in bovine collagen I matrix. The HeLa and CaSki cells formed compact spheroids within 72 hours while C33A formed loose aggregates. The data obtained showed a remarkable difference in growth and invasion phenotype between the HeLa and CaSki spheroids. HeLa spheroids grew and invaded into the collagen matrix gradually. CaSki spheroids however, exhibited aggressive invasion phenotype into the collagen and the spheroids disintegrated over 10 days. The aggressive invasion phenotype by CaSki prompted us to compare the spheroid phenotype with another HPV 16 cell line (SiHa). Contrary to CaSki, SiHa spheroids grew and invaded more steadily into the collagen matrix. We also compared the phenotypes between two non HPV cell lines (C33A and HT3). Our results showed that both C33A and HT3 cells only formed loose aggregates. In conclusion, this study gave an insight into the different growth and invasion phenotypes between different cervical cancer cell lines and would be a stepping stone to test existing drugs or to design new treatment options for treating cervical cancer according to their HPV infection.

Keywords: 3-dimensional Spheroid; Cervical Cancer; HPV 16; HPV 18; non HPV cervical cancer cells

OP15: *in vitro* selection of RNA aptamer against CD36 protein by Systematic Evolution of Ligand by Exponential Enrichment (SELEX)

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Abstract

Post-mortem studies on patients died after hospital administration with malaria displayed cytoadherence of Plasmodium falciparum infected erythrocytes (IEs) on embedded endothelial cells in vital organs such as lung and brain. Cytoadherence of the malaria parasite in the organ is mainly mediated by endothelial surface receptor CD36 ligand protein that contributed to blockage microcirculatory blood flow. Therefore, it is needed to discover a new adjunct therapy to be used as reversal and blocking agent of parasite cytoadherence. Aptamer which is single stranded nucleotide (DNA or RNA) or peptide is a new therapeutic and diagnostic platform which also known as rival of mAb. In this study, we firstly reported on isolation and characterisation of RNA aptamers that specifically bind to CD36 protein. The *in vitro* SELEX selection was carried out using nitrocellulose membrane filter immobilisation method. After 13 rounds of selection, the final product of bound RNA pool to CD36 was cloned and sent for DNA sequencing. The sequencing results were aligned and clustered using ClusterW software. The RNA aptamer clusters were then analysed for it structures using Mfold program followed by evaluating the binding ability using semi-quantitative reverse transcription polymerase chain reaction (RT-PCR). Through the binding ability assay there are six RNA aptamer clusters were identified; RAC60, RAC25 and RAC46 ($p<0.0002$). This potential RNA aptamer candidates will be further investigated on its kinetic binding affinity through determination of the dissociation constant (Kd) value. As conclusion, this study successfully isolated RNA aptamers that can be served as potential candidates for development of malaria adjunct-therapy.

Keywords: Malaria; Cytoadherence; RNA aptamer; SELEX technology; CD36 protein

OP16: Construction of shark semi-synthetic VNAR library for malaria RDTs improvement

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Abstract

Malaria is a mosquito-borne infectious disease caused by 5 species of *Plasmodium* parasites. Species infection with *P. falciparum* is the most prevalent and lethal, causing significant morbidity and mortality worldwide. Early and accurate diagnosis of *P. falciparum* infection is crucial for providing appropriate treatment to patients. For this reason, rapid diagnostic tests (RDTs) are increasingly used for malaria diagnosis by detection of parasite biomarkers as they offer result in a short period. However, technical limitations of currently available RDTs have limited their use in malaria diagnosis. One possible reason is that the current antibodies used in RDTs have the propensity to degrade at high ambient temperatures. Therefore, novel antibodies with better thermal stability represent important objectives in enhancing the performance of RDTs. In this study, a shark semi-synthetic variable new antigen receptor (VNAR) library was constructed to target the malaria PfHRP2 protein. The resulting PCR products were ligated into M13 filamentous phagemid vector, and inserted into *E. coli* TG1 cells for the transformation and phage library construction. The result indicated that the primary library had a titre of 1×10^7 CFU/ml. DNA sequence analysis showed that 75% of VNAR fragments contained an in-frame sequence. In conclusion, VNAR may represent the novel antibody for malaria RDTs.

Keywords: Malaria; P. falciparum; RDTs; VNAR; PfHRP2

OP17: Screening for cystic echinococcosis in migrant workers revealed significant discordant results among three immunoassays

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Abstract

Cystic echinococcosis (CE) is a neglected zoonotic disease which infects both humans and animals worldwide. The disease has a big impact on the economy due to complications in treatment and can lead to disabilities. The objective of this study was to screen CE in 136 individuals serum samples from migrant workers in Malaysia from Bangladesh (n = 50), India (n = 52), Nepal (n = 23) and Myanmar (n = 11) using three different immunoassays. The serum samples were screened with two commercial ELISA kits ie. Anti-Echinococcus ELISA IgG (EUROIMMUN, Germany), NovaLisa Echinoccocus IgG-ELISA (NovaTec Immundiagnostica, Germany) and an In-house IgG4-lateral flow dipstick test using recombinant Ag B (Hyd Rapid). The results showed that 57, 10 and 69 sera were positive and 67, 116 and 67 sera were negative with NovaLisa, EUROIMMUN and Hyd Rapid respectively. Among the three assays, concordant positive results were seen in 5 samples, concordant negative results in 33 sample; and non-concordant results in 97 samples. Meanwhile, among the two commercial tests, concordant positive results were seen in 10 samples, concordant negative results in 67 sample; and non-concordant results in 58 samples. This study showed a surprising extent of discordant results among that the immunoassays. There may be several reasons for the discordant results such as the kind of antigen used, cut-off values in the ELISAs and the antibody detected (IgG vs IgG4). Thus it is recommended that an assay should be evaluated using a panel of local serum samples before adopting it as a diagnostic immunoassay.

Keywords: Cystic echinococcosis; commercial ELISAs; rapid test; discordant results

OP18: Construction of semi-synthetic phage display library by randomization of CDR3 region of human single chain Fv for antibody generation targeted against Japanese Encephalitis Virus NS1

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Abstract

Japanese Encephalitis virus (JEV) is known to be serologically similar with other flavivirus such as Dengue virus, Zika virus, Yellow Fever virus and others. Co-existence of these viruses with highly homologous antigenic epitopes results in antibody-based serodiagnosis being inefficient at detecting and distinguishing JEV efficiently from other flaviviruses. This often causes misdiagnosis and inaccurate treatments of flavivirus infection. Co-localization of the JEV NS1 protein with the membrane of JEV-infected cells renders the protein a potential target. For this reason, the NS1 viral replication protein that reported to confer specificity against JEV is used as antigenic marker in this study to generate human antibody fragment against JEV. To improve the JEV diagnostic test, we have constructed a human semi-synthetic library displaying single chain antibody fragment. Complementary determining region 3 (CDR3) of heavy chain (V_H) and light chain (V_L) are synthetically randomized using degenerate codons. V_H and V_L were then linked via glycine-serine linker by splice overlap extension PCR strategy in respect to construct a highly diverse scFv phage display antibody library. DNA sequencing revealed that the quality of library constructed was good with approximately 60% of in-frame scFv repertoires identified and all the sequenced clones confer distinct and unique sequences at the CDR3 region. Presently, this library is ready to be deployed for specific clones selection against our in-house synthetic recombinant JEV NS1 protein by undertaking repetitive biopanning.

Keywords: phage display; semi-synthetic library; scFv; CDR3 randomization

OP19: Lateral flow dipstick test using recombinant antigens TES-26, TES-30 and TES-120 for rapid detection of human toxocariasis

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Abstract

Toxocariasis is an important soil-transmitted and zoonotic infection in humans, especially children. Laboratory diagnosis of toxocariasis is still a challenge especially in developing countries with polyparasitism. Serodiagnosis of human infection is usually performed with commercial IgG-ELISA coated with native *Toxocara* excretory-secretory antigens (TES), however cross-reaction with antibodies to other parasitic nematodes is a limiting factor. Therefore, the use of defined recombinant antigens could address this problem. Three purified recombinant proteins to *Toxocara canis* excretory-secretory proteins were produced in this study i.e. rTES-26, rTES-30 and rTES-120. The three recombinant antigens were expressed, purified and analyzed by Western blot and MALDI TOF/TOF. A rapid test (TcRapid) using the antigens and anti-human IgG4 conjugated to colloidal gold was developed and evaluated for serodiagnosis of toxocariasis. Comparison of the diagnostic sensitivity and specificity was performed against Bordier's kit (Bordier Affinity Products SA), an IgG ELISA which uses toxocara lysate antigen; and against NovaLisa *Toxocara canis* IgG ELISA (Novatec Immundiagnostica Gmbh) which is an IgG-ELISA that uses a synthetic antigen. When compared to the commercial IgG-ELISA, TcRapid showed 93.1% sensitivity, and 100% specificity. IgG4 detection of tissue nematodes is associated with active infection, thus this can explain the lower sensitivity of TcRapid as compared to the IgG-based commercial test, the latter likely detects both active and 'old' infections. Thus, the laboratory prototype of TcRapid showed good potential for prompt and accurate diagnosis of toxocariasis and merits further multicentre validation studies.

Keywords: toxocariasis; recombinant TES proteins; lateral flow rapid test

OP20: The value of a panel of autoantibodies and complement as biomarkers in Lupus Nephritis patients in HUSM

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Abstract

Lupus nephritis (LN) is characterized by renal deposition of immune complexes and it is a serious complication in Systemic Lupus Erythematosus (SLE). Normally, serum levels of antinuclear antibodies (ANA), anti double stranded (dsDNA) antibodies, and complement levels are used to identify patients with high disease activity and at risk for developing LN. The aim of the study was to determine the role of autoantibodies (ANA, Anti-dsDNA) and complement (C3 and C4) in active and inactive LN patients. A total of 56 LN patients were enrolled in this study, 18 of which were diagnosed as having active LN, 18 with inactive LN and 20 healthy controls. The serums of each study groups were measured using indirect immunofluorescence assay (IIF) for ANA and anti-dsDNA and immunonephelometry for C3 and C4. Statistical analyses were performed using SPSS software, version 22.0 and values were expressed as mean ± standard deviation (SD). The results were analysed by One-Way ANOVA, independent t-test and chi-square test. ANA was detected in all LN patients with *p*-value <0.001. Anti-dsDNA antibodies were found in less than one-third of both LN patients (22.22%). Active LN patients presented a higher frequency of anti-dsDNA as compared to inactive LN patients (27.78% vs.16.67%). However, no significant difference was found in anti-dsDNA and C4 for both LN groups. Meanwhile, C3 levels were decreased in active LN patients as compared to inactive LN patients (active LN; 0.76 g/l (0.44 g/l), inactive LN; 1.04 g/l (0.22 g/l) *p*=0.010). To conclude, ANA and C3 may have a great potential as diagnostics factor for LN.

Keywords: lupus nephritis; ANA. anti-dsDNA; complement 3; complement 4

OP21: Detection and identification of microsporidia antigens in HIV/AIDS patients via serum proteomic approach

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Abstract

Microsporidia infections in human have been reported from all over the world, mostly involved immunocompromised patients. *Enterocytozoon bieneusi* (*E. bieneusi*) is one of the most common microsporidian species infecting HIV/AIDS patients. To date, routine diagnosis of microsporidiosis is limited to stool examination which unable to rule out systemic or disseminated infection. This study was conducted to detect circulating *E. bieneusi* DNA and proteins in blood specimen, which were not previously used for the diagnosis of disseminated microsporidiosis. Blood samples from HIV/AIDS-positive patients were collected from Sungai Buloh Hospital and Universiti Kebangsaan Malaysia Medical Centre (UKMMC). These samples were subjected to PCR assay using species-specific primer EBIEF1/EBIER1. The samples were sent for sequencing and phylogeny analysis was performed in MEGA 7 using neighbor-joining algorithms. Out of 100 patients, seven were confirmed positive for *E. bieneusi* by PCR. A fragment of 607 bp was successfully amplified. A gel-free shotgun proteomics analysis using Orbitrap Fusion (Thermo Fischer Scientific) was performed towards 7 positive serum samples to detect the circulating proteins of *E. bieneusi*. The analysis identified a few significant *E. bieneusi* proteins i.e. uncharacterized protein (B7XJ00), DNA topoisomerase 2 (B7XIW3), and actin (B7XHF2) which above protein scores cut-off level. Bioinformatic tools were used to analyse the protein sequences. Identification of circulating *E. bieneusi* DNA and proteins in blood samples may aid in early diagnosis, and can increase the awareness among the clinician that the disseminated cases of *E. bieneusi* did occur in our setting.

Keywords: E. bieneusi; HIV; serum; shotgun proteomic; circulating antigen

OP22: Role of TolC in the invasiveness of *Salmonella enterica* serovar Typhi

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Abstract

S. Typhi is a causative agent of typhoid fever in human. Several outer membrane proteins (OMPs) of the *S*. Typhi have been functionally characterized, but their involvement in pathogenicity and virulence are not fully known. The aim of this study was to investigate the function of TolC, outer membrane channel protein of *S*. Typhi, in the invasion of human cells and particularly in relation to the expression of the type III secretion system-1 (TTSS-1) that is needed for *Salmonella* invasion. Deletion of *tolC* resulted in a lower transcription of the *Salmonella* pathogenicity island-1 genes *invF*, *sipA*, *sipC,* and *sipD*, showing that all genes required for TTSS-1 biosynthesis are down-regulated in the *tolC* mutant. Consequently, the invasion experiments performed with the *tolC* mutant demonstrated that it was significantly less competent to invade HT-29 epithelial and THP-1 macrophages cells than its parental strain. Invasion and SPI-1 expression were restored and increased as compared to their wild-type parent by complementation of the *tolC* mutant with the wild-type allele of the *tolC* gene. These data suggest that TolC mediates the entry of *S*. Typhi into host cells. These results explain that the *tolC* mutants are attenuated and have reduced expression of TTSS-1 effectors that involved in pathogenicity. Recognition of common pathways that regulate the expression of the *tolC* and the type III secretion system-1 will give convincing evidence for its role in invasion of host cells.

Keywords: S. Typhi; TolC; type III secretion system-1 (TTSS-1); invasion

OP23: Detection of proteins as potential biomarkers in *Acanthamoeba* exposed to lead and zinc: *in vitro* study

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Abstract

Nowadays quality of water is at risk due to increasing disposals of toxic chemicals from agricultural, industrial, domestic wastewater, mine runoff and atmospheric pollution. The common metals found to pollute water include lead and zinc. Some metals like zinc is essential trace metal to living organisms, but become toxic at higher concentrations. Lead has no known biological function but it is toxic especially to aquatic organisms. Protozoa communities including free-living amoebae could provide valuable information on the health status of aquatic ecosystem since they are abundant and widely distributed in the ecosystem. Being single-celled eukaryotic organisms and have relatively short generation times and react rapidly to the changing of the environmental conditions to suggest these microbes are better indicator organisms for toxicity analysis of lead and zinc. A proteomic approach was employed to analyse the toxicity of both metals on *Acanthamoeba sp*, an environmental isolate, *in vitro*. The amoeba was exposed to the IC_{50} concentration of both metals in 24-well plates for 72 h at 30^{o}C before 2DE was carried out. Protein spots on 2D gels were captured using ImageMaster 2D Platinum 6.0 for analysis and identification the protein spots in control and treated gels. Proteins spots observed on the gels of heavy metals-treated amoeba are categorised as over exposed, under exposed and newly synthesized proteins as responses of the amoebae to avoid the metal toxicity. These proteins therefore, have potential as biomarkers for lead and zinc toxicity in amoeba.

Keywords: *Acanthamoeba*; protein spots; lead; zinc; biomarker

OP24: Identification of novel immunogenic proteins of *Leptospira spp*. using ORFeome phage display

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Abstract

Leptospirosis is the most widely spread zoonotic disease worldwide. It is also one of the Neglected Tropical Diseases (NTD). World Health Organization (WHO) estimates the annual incidence is 10 per 100 000 per year in the humid tropics with case fatality rate of 5-30%. Currently, commercially available ELISA assays are based on antibody detection of general WHO serovars. This study aims to identify novel immunogenic proteins for *Leptospira spp.* Subsequently, these would be used as candidates for novel pathogen biomarker and could potentially be developed into ELISA based diagnostic assays. Two ORFeome phage display libraries of the entire *Leptospira spp*. genomes from Malaysian local strains and WHO *Leptospira spp.* reference strains were constructed. Subsequently, 18 immunogenic oligopeptides were selected from these libraries using pooled sera from leptospirosis patients. The immunogenic character of these oligopeptides was validated using oligopeptide phage, analyzed by titration ELISA using sera from leptospirosis patients and control sera. Six immunogenic oligopeptides were validated. Currently, these potential biomarkers are being cloned for recombinant protein production for further confirmation. In conclusion, we identified six candidates of novel immunogenic proteins of *Leptospira spp.* and these will be validated using a panel of positive and negative sera for prospective applications in diagnostics of leptospirosis.

Keywords: Biomarker; Leptospira spp.; ORFeome

OP25: Simultaneous identification of *Salmonella* serovars causing enteric fever using a Multiplex PCR-Line Probe Assay (mPCR-LiPA)

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Abstract

Enteric fever is a systemic infection of humans caused by 4 *Salmonella* serovars, namely *S*. Typhi, *S*. Paratyphi A, *S*. Paratyphi B, and *S*. Paratyphi C. The inefficient detection method for these serovars due to its large diversity urges more serious attempts to find a rapid differential diagnostics method of the disease. In this study, a multiplex PCR-Line Probe Assay (mPCR-LiPA), a combination of PCR and reverse hybridization blotting technique that permits molecular detection of multiple DNA targets was developed and evaluated for the diagnosis of enteric fever. Reference strains ATCC7251, ATCC9150, ATCC8759, and ATCC9068 served as positive control to validate the mPCR-LiPA, and agarose gel electrophoresis (AGE) as the comparative method. The limit-of-detection (LoD) of the number of PCR cycle and the amount of genomic DNA needed for both platform was evaluated. The analytical specificity of the mPCR-LiPA was screened using 153 pure clinical isolates from INFORMM Biobank. There were no cross-reactions between the probes. The LoD for mPCR-LiPA was 15 PCR cycles and 1×10^{-5} ng/μL genomic DNA, thus demonstrating higher sensitivity than AGE which requires 20 PCR cycles and 1×10^{-3} ng/μL genomic DNA. All 83 strains of *S*. Typhi, 23 strains of *S*. Paratyphi A, 7 strains of *S*. Paratyphi B, and 1 strain of *S*. *paratyphi* C were tested positive, 29 strains of other *Salmonella* serovars and 10 strains of non-*Salmonella* bacteria were tested negative. In conclusion, a highly sensitive and specific mPCR-LiPA was developed and ready for further clinical trials.

Keywords: Salmonella; enteric fever; diagnostic assay; multiplex PCR; line probe assay

OP26: Identification of potential biomarkers in synovial fluid in monoiodoacetate induced osteoarthritis in rabbit model

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Abstract

Osteoarthritis is a disease of high economic burden and there is still no definitive method to diagnose early osteoarthritis. Biomarkers had proven to be useful in disease diagnosis. The objective of this study is to identify potential biomarkers from synovial fluid in early osteoarthritis. Twenty adult New Zealand white rabbits (n=20) were divided into two groups, Control group (n=5) and experimental group (n=15) which is subdivided into Week 4 (n=5), Week 8 (n=5), and Week 12 (n=5) groups. Rabbits from experimental group were induced using monoiodoacetate into right stifle joint. At the end of Week 4, Week 8 and Week 12 post induction, the rabbits were euthanized. Synovial fluid from the right stifle joint was collected for proteomic analysis via two dimensional gel electrophoresis and MALDI TOF/TOF. The right stifle joint were harvested and subjected to micro-CT and histology analysis as gold standard to stage osteoarthritis. Statistical analysis from micro-CT data was performed using ANOVA and the histology slides will be qualitatively graded via OARSI Cartilage Histopathology Grading/Staging System. Eleven proteins (ceruloplasmin, fibrinogen, serotransferrin, serum albumin precursor, serpin peptidase inhibitor, α-1-antiproteinase F precursor, haptoglobin precursor, complement 3a, apolipoprotein-IV precursor, immunoglobulin lambda chain C region, immunoglobulin gamma heavy chain) had significantly different expression (>2.0 fold) between synovial fluid obtained from control group and experimental groups. Changes in parameters of subchondral bone micro-architecture and articular cartilage demonstrated early onset of osteoarthritis and showed subtle variations across these time-points. The development of a panel of biomarkers could be useful in diagnosing early osteoarthritis.

Keywords: osteoarthritis; biomarkers; proteomics; subchondral bone; articular cartilage

OP27: Paternal lineage affinity of the earliest inhabitants in Peninsular Malaysia: evidence from Y-STRs analysis

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Abstract

Peninsular Malaysia is populated by the Malays (majority), Chinese, Indians and Orang Asli (OA) – Semang, Senoi and Proto Malays (~0.5%). The objective is to demonstrate the ancestral lineage of OA populations in Peninsular Malaysia using Y-STR haplotype data. This information may be useful in understanding the human dispersal in mainland and island of Southeast Asia, besides for forensic application. We have analysed 17 Y-STRs loci for 90 randomly unrelated OA males from selected settlements in Peninsular Malaysia using the AmpFlSTR Yfiler™ kit (Applied Biosystems™). The samples consist of 54 Semang (16 Kensiu, 13 Lanoh, 25 Bateq); 30 Senoi (21 Semai, 9 Che Wong) and 6 Proto-Malay (6 Orang Kanaq). A total of 52 different haplotypes were identified and 34 were individually unique. The discrimination capacity of OA calculated was 0.61333, which may suggest there were potentially only few common paternal ancestors. The PD, PIC, p-value and pairwise Rst analysis was calculated to show the genetic structure of the OA subgroups with the Malays and other world populations (from YHRD website). Y-STR data showed Lanoh and Kensiu (Semang) are very strongly related. Based on the MDS plot, the Orang Asli are genetically closer to the Negritos from Central African (Biaka Pygmy), South African (Xhosa); Australia Aborigines; Indian and Austronesian populations rather than to China and Taiwan populations. This study presents data for a very precious relict group, whom are the earliest inhabitants of Peninsular Malaysia. These OA groups are now very scanty and not showing any population growth for the past 10 years.

Keywords: Y-STR; Migration; Orang Asli; Peninsular Malaysia

OP28: Protumourigenic CTAG1B is a potential bladder cancer biomarker

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Abstract

Bladder cancer (BC) is the most expensive cancer to manage due to the high risk of recurrence and progression that requires life-long routine invasive monitoring. The development of non-invasive biomarkers of recurrence and progression can thus increase survival, decrease treatment costs and improve patient quality of life. However, to date, no biomarker(s) are routinely used in the clinical management of BC patients, especially in predicting risk of progression and recurrence. CTAG1B was previously found to be highly expressed in advanced BCs, albeit in Caucasian cohorts. Despite its potential as a target for cancer immunotherapy, the effect of expression modulation on cellular phenotypes is poorly understood. In this study, the pattern of CTAG1B expression in a cohort of Malaysian BC paraffin-embedded tissues was determined using immunohistochemistry. In addition, CTAG1B was overexpressed in EJ28, a minimally-expressing cell line through the transfection of CTAG1B-pcDNA3.1(-). At 72h post-transfection, the over-expressing transfected cells were subjected to cell-cycle and proliferation analyses. CTAG1B was expressed in a greater subset of advanced stage and grade BC tissues obtained from Malaysian patients. CTAG1B was successfully overexpressed in the transfected cells. The CTAG1B-overexpressing cells had a significantly higher proliferation rate at 72-96h post-transfection (p-value <0.05). The findings from this study indicate that CTAG1B overexpression has a protumourigenic effect in BC. Further functional studies are needed to clarify the potentially oncogenic role of CTAG1B and determine the potential utility as a biomarker in a subset of BCs.

Keywords: bladder cancer; cancer testis antigen; CTAG1B; biomarker; progression

OP29: Expression profile of E2F genes in cervical carcinogenesis using human transcriptome array gene expression

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Abstract

Infection by high risk human papillomavirus (HPV) and integration of HPV genome into host chromosome is a key event in neoplastic progression of cervical lesions. The viral oncoproteins E6 and E7 affect gene expressions involved in cell cycle, p53 pathway and retinoblastoma gene. Gene expression is mainly controlled through transcription regulation, which is mediated through transcription factors, E2F. E2F family is mainly involved in the G1/S transition in cell cycle. Increasing expression of these genes is linked to carcinogenesis. The study aimed to profile E2F genes expression in HPV-related precancerous cervical intraepithelial neoplasia (CIN) lesions and cancer lesions, using formalin fixed paraffin embedded (FFPE) tissues. Total RNA was extracted from 12 FFPE samples, consisting of 3 normal cervical tissues as control, 3 low grade CIN (CIN 1), 3 high grade CIN (CIN 2/3) and 3 squamous cell carcinoma (SCC). The extracted RNA was hybridized to human transcriptome array (HTA) 2.0 Affymetrix. Gene expression analysis was evaluated using Affymetrix transcriptome analysis console software. Normal tissue was used as control and analysed against CIN1, CIN 2/3 and SCC. The results showed a differential expression of E2F genes, whereby it was most up-regulated in SCC. Only E2F1 gene showed a significant difference, $p<0.05$, with -1.09-fold for CIN 1 vs normal, 1.21-fold for CIN 2/3 vs normal and 1.82-fold for SCC vs normal. The hypothesis is HPV oncoproteins inactivate pRb gene, leading to activation of E2F genes which mediate cell cycle proliferation and p53-dependent/independent apoptosis. E2F1 plays an important role in the regulation of genes involved in cervical carcinogenesis.

Keywords: Cervical cancer; high risk HPV; oncoprotein; gene expression; E2F

OP30: Evaluating the efficacy of polysaccharide extract of basidiomycetes on MMP-1 mechanism: A skin rejuvenation approach

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Abstract

Basidiomycetes, especially mushrooms have been regarded as one of the famous delicacies among Asian country and well known for their health promoting benefits. Due to their promising medicinal values and rich in bioactive compounds, it has extensively gained the attention of medical researchers and aestheticians to explore the efficacy of mushroom extract towards the biomarker MMP-1 synthesis in aging process. This work is going to demonstrate the biological activities of polysaccharides of three edible mushrooms after undergone hot water extraction and purification including antioxidant (1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging and Ferric Reducing Antioxidant Power (FRAP) assay), antibacterial and toxicity test (Brine shrimp lethality test). Additionally, understanding the correlation of collagen and MMP-1 biosynthesis were done on human dermal fibroblast cells in conjunction with the determination of wound healing. Of all extracts, *Pleurotus sajor caju* contains highest antioxidant capacities which showed IC_{50} at *1*.8771± 0.0120 mg/ml. Studies using human dermal fibroblast (HDF) cells showed that the extract has relatively low cytotoxicity effect and it even stimulated cell proliferation. *Tramella fuciformis* showed the highest increased in procollagen (PICP) stimulation using ELISA test kit and this will be further studied using gene expression level using Real Time PCR method. Studies using the MMP-1 will also be done by same method as procollagen test. In conclusion, the data indicated in this work show the crude polysaccharides of these mushrooms might potentially be deployed as functional element in dermatological industry.

Keywords: edible mushrooms; biomarkers; anti-aging; collagen biosynthesis; MMP-1

OP31: Targeting HIF-1α /CBP to combat Nav1.5-mediated breast cancer metastasis: Potential therapeutic biomarker

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Abstract

HIF-1α signaling is the crucial pathway for cancer cells in keeping its oncogenic drive and progression. In general, stabilize HIF-1α binds to hypoxia-response element (HRE) in the promoter region of target gene to start transcription. In addition to enhance its binding ability to the DNA of target gene, HIF-1α recruits co-activators such as CBP and p300. High expression of stabilize HIF-1α parallels to elevated voltage-gated sodium channels (VGSCs) expression in various types of aggressive human cancers. However, the role of HIF-1α/CBP/p300 in the regulation of VGSCs particularly the isoform Nav1.5 which is highly expressed in aggressive breast cancer cells has yet to be explored. Thus, this study was designed to investigate the role of HIF-1α/CBP/p300 in the regulation of Nav1.5 in aggressive breast cancer. HIF-1α was silenced in MDA-MB-231 cells using siRNA and the mRNA expression of CBP, p300 and Nav1.5 expression was measured using real time-PCR. Metastasis of the cells was investigated using transwell migration assay. Results indicate that only the expression of CBP and Nav1.5 was significantly down-regulated when HIF-1α was silenced, followed by 40% reduction in metastasis - represented by reduced number of migrated cells. As a conclusion, our study revealed the role of HIF-1α/CBP in regulating the expression of Nav1.5 in breast cancer in which interruption of the HIF-1α/CBP lead to suppression of metastasis of breast cancer cells. Ultimately, information gain from HIF-1α/CBP/Nav1.5 could be useful as potential biomarker target for breast cancer metastasis.

Keywords: HIF-1α; CBP; p300; Nav1.5; breast cancer metastasis

OP32: Development of a prototype rapid antigen detection test for acute leptospirosis in human

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Abstract

Diagnosis of leptospirosis based on clinical presentations is challenging since they mimic other acute febrile illnesses. In acute phase infection (<10 days), *Leptospira* bacteria and antigen circulate in a patient's peripheral blood. This study was aimed at developing a lateral flow rapid antigen detection dipstick test to complement the existing commercial antibody test for detection of acute leptospirosis. Several kinds of rabbit antiserum with high titers (≥ 1:128000) were raised against leptospiral recombinant proteins with reported diagnostic value (LipL32, LipL41, OmpL1 and LigA), as well as against a leptospiral lysate cocktail. Colloidal gold nanoparticle was used to conjugate IgG fraction of each antiserum and used for development of a lateral flow dipstick test. The results showed that the use of anti-leptospiral lysate (LL) IgG as both capture and gold-conjugated antibody was the best assay format. The test showed good sensitivity of ~10^5 cells, high specificity with clinically important pathogen panel, and broad reactivity with common *Leptospira spp.* serovars in Malaysia. Evaluation with a panel of patient serum from acute leptospirosis (n=54) and control serum (n=39) demonstrated diagnostic sensitivity and specificity of 57.4% and 87.2%, respectively. When the results of the antigen detection dipstick and a commercial antibody detection kit were combined, the sensitivity and specificity for detection of acute leptospirosis was approximately 70% and 84% respectively. In addition, an antigen detection dipstick test for human urine was developed. Further development and evaluation of the rapid test prototypes are needed to enable their potential application for patient diagnosis.

Keywords: leptospirosis; recombinant protein; leptospiral lysate; antigen detection; lateral flow dipstick

OP33: Development of carbon nanotube-based aptasensor for detection of *Salmonella* spp.

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Abstract

Foodborne disease is a major public health problem in both developed and developing countries. Rapid and accurate detection and identification of microbial pathogens in food is an essential component of food safety tool. The conventional microbiological approach is time-consuming, labour intensive and involves multiple steps and reagents costs. Hence, there is an increasing interest in the improvement of analytical methods in terms of speed, specificity and sensitivity and ease of operation. We have developed an amino-modified aptasensor using CNT-deposited ITO substrates for the detection of *Salmonella* species. Covalent coupling immobilization of aptamers was carried out on carboxy-rich multiwalled carbon nanotubes. The morphology of the aptamer-CNT substrate was characterized by table top scanning electron microscopy. The sensor conductivity behaviour and resistance values were checked by cyclic voltammetry and electrochemical impedance spectroscopy. The increased resistance values after exposing to the *Salmonella* samples indicated a covalent approach of bonding between the *Salmonella* and the anti-*Salmonella* aptamer. The linearity analysis showed the developed aptasensor was stable and maintains linearity with the increase of scan rate. Sensitivity testing revealed the limit of detection for *S. enteritidis* was 55.0 cfu/ml. This study shows the potential use of aptasensor-based carbon nanotubes for rapid and effective detection of the S. enteritidis through an electrochemical approach.

Keywords: Aptasensor; CNT; Electrochemical impedance spectroscopy; Salmonella

OP34: Species specific recognition of bacterial pathogens using targeted antibody design

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Abstract

A major hurdle in the development of bacterial diagnostics is the availability of an antigen in the target group of interest (Goi), which is ubiquitously expressed and conserved in all members. When considering diagnostic devices, the capture reagents must ideally recognise all members of the Goi, with minimal cross-reactivity to other bacteria in order to maximise the sensitivity and specificity of the device. In order to overcome this hurdle an *in house* biomarker discovery tool (IDRIS) has been developed. IDRIS allows the rapid integration and processing of complete genomic sequence data to identify conserved epitopes - stretches of amino acids present on the surface of a given Goi. IDRIS allows the user to ascertain if the epitope is common, for example, to a given species or genus of bacteria and critically allows the user to validate if the epitope occurs in other non-target bacteria in order to negate any cross-reactivity which may occur. IDRIS was used to identify unique species-specific epitopes in a *Clostridium difficile* surface associated protein. Monoclonal antibodies generated against these epitopes were found to recognise all *Clostridium difficile* species tested, with no cross-reactivity to closely related bacteria. Purification of the native protein target and probing antibody-target binding by SPR revealed one antibody (Ab521) bound with a K_D of 36.5 nM. IDRIS has been shown to be a useful tool to guide the production of antibodies suitable for diagnostic tests and has now been applied to other bacterial targets including Group B *Streptococcus*.

Keywords: biomarkers; Clostridium difficile; antibodies

OP35: Lateral flow rapid dipstick test for detection of *Entamoeba histolytica* antigen in stool

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Abstract

Amoebiasis, caused by *Entamoeba histolytica* is a public health problem in many developing countries, causing up to 100 000 fatal cases annually. The biggest challenge in the management of amoebiasis is its laboratory diagnosis. The available commercial antigen detection assays for intestinal infection vary in their sensitivities and specificities. Therefore, this study aimed at developing a test that can rapidly detect the parasite antigens in stool samples. Pyruvate phosphate dikinase (PPDK), one of the excretory-secretory proteins of *E. histolytica* (EhESA), has been shown to be of diagnostic importance. Thus polyclonal antibodies against rPPDK and EhESA were produced; and a rapid dipstick test developed using anti-rPPDK PAb lined on the dipstick as the capture reagent and anti-EhESA PAb conjugated to colloidal gold as the detector reagent. The performances of the dipstick, commercial Techlab *E. histolytica* II ELISA and real-time PCR were compared using 70 stool samples from patients infected with *Entamoeba* species (n=45) and other intestinal pathogens (n=25). When compared to real-time PCR, the diagnostic sensitivity of the dipstick for detection of *E. histolytica* was 65.4% (n=17/26); while the diagnostic specificity when tested with stool samples containing other intestinal pathogens was 92% (23/25). In contrast, Techlab *E. histolytica* II ELISA detected 19.2% (5/26) of the *E. histolytica*-positive samples as compared to real-time PCR. Therefore the lateral flow dipstick test produced in this study enabled rapid detection of *E. histolytica*, and showed good potential to be further developed into a diagnostic tool for intestinal amoebiasis.

Keywords: Entamoeba histolytica; stool antigen detection; pyruvate phosphate dikinase; excretory-secretory antigens; lateral flow rapid test

OP36: Production of recombinant monoclonal antibody against B*m*SXP filarial antigen

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Abstract

PanLF Rapid is a rapid diagnostic test that can detect infections caused by lymphatic filarial parasites. The test is being used by the Malaysian Ministry of Health in the lymphatic filariasis elimination programme. It is based on the detection of recombinant proteins B*m*R1 and B*m*SXP. The availability of recombinant monoclonal antibodies to the recombinant proteins would be very useful for various applications. In this study a human lymphatic filariasis scFv library was constructed using phage display technology. In total, six unique monoclonal antibodies (2F, 5B, 3A, 4F, 6D and E3) to B*m*SXP were successfully isolated. These clones represented the IgHV5KV1, IgHV2KV3, IgHV3KV1, IgHV3LV3, IgHV5LV8 and IgHV5LV2 V-gene family. Cross-reactivity, antibody concentration and assessment of the binding performance of the monoclonal antibodies were determined by ELISA. Out of six clones, two potential recombinant monoclonal antibodies (5B and 3A) were successfully identified, produced and tested in two applications. The first application was for making affinity column whereby single and mixture antibody columns were produced; and the results showed better performance with the latter. The second application was for preparation of colloidal gold conjugate, whereby monoclonal antibody 5B was successfully conjugated with gold nanoparticles, and the results showed positive reaction when tested with dipsticks lined with B*m*SXP and with the commercial PanLF Rapid cassette test. Thus this study has produced a novel lymphatic filariasis scFv library that can be used to screen target against filarial antigens. In addition, the isolated monoclonal antibodies were successfully utilized in two applications.

Keywords: filariasis; phage display; scFv library; BmSXP; recombinant monoclonal antibody

OP37: Optimisation of dAbs against HSP16.3 from *Mycobacterium tuberculosis*:

***in silico* approach**

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Abstract

Despite the continuous global battle against tuberculosis (TB), this deadliest disease had ailed a staggering number of 10.4 million people in estimation and claimed 1.8 million lives in year 2015 alone. It emerged next in line to HIV/ AIDS which has been known as the deadliest disease worldwide. Heat shock protein 16.3 had been identified as immunodominant antigen present in latent TB infected individuals. Thus, it serves as a promising diagnostic biomarker and therapeutic target for latent TB infection. This study highlights on *in silico* optimisation of two novel single domain antibodies, namely E3 and F1, from phage display library with specificity against HSP16.3. The models of antigen and dAbs were first predicted using comparative modelling. The dAbs were then docked against the predicted epitopes of HSP16.3. The docking complexes were refined using molecular dynamics (MD) simulations. Computational alanine scanning and per residue free energy decompositions were performed in order to identify the hot spot residues of dAbs. The effects of mutations on targeted hot spots were investigated using MM-GB/PBSA calculation. An improved binding free energy in mutated protein complex over the wild type is regarded as successful optimisation. The best candidate for E3 mutant had exhibited 68.8% improvement in binding free energy whereas 44.2% improvement was observed for F1 mutant. The findings provide guidelines for designing dAbs with affinity enhancement against HSP16.3 for future testing at *in vitro* level.

Keywords: HSP16.3; comparative modelling; free energy decomposition; antibody optimisation

OP38: Optimisation of domain antibody against ac_2sgl from *Mycobacterium tuberculosis* in complex with CD1b, from the perspective of molecular modelling

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Abstract

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis* (MTB) with 1.5 million of deaths annually. Thus, early diagnosis of TB is important for efficient management. In an earlier study, a light chain variable domain antibody clone D11 showed high relative binding to MTB lipid diacylated sulfoglycolipids (Ac_2SGL), presented on transmembrane glycoproteins cluster of differential 1 class b (CD1b), which is important marker for TB infected patient. The aim of the study was to predict the binding conformation of the D11 with Ac_2SGL-CD1b protein and optimise its binding. The conformations of D11 and Ac_2SGL-CD1b were modelled with MODELLER, docked using ZDOCK along with RosettaDock and further refined using molecular dynamics simulation to study the interactions. The study of the affinity changes upon mutating hot-spot residues was performed using mCSM-AB webserver and the binding free energy of the complex was calculated with MMPBSA/MMGBSA approximation. Results indicated that Tyr32 on CDR1 of D11 has hydrogen bonding with Ac_2SGL, while CDR2 and CDR3 formed significant hydrophobic interactions with the methyl branches of Ac_2SGL (-65.76 kcal/mol van der Waal force). This showed hydrophobic interaction is favourable in the immunogenic interaction and important for recognition. The screening single residue mutation screening on Ser28Arg showed an improvement in binding with difference of 15.5 kcal/mol energy whereas Tyr32Trp improved slightly of four kcal/mol. The changes of serine to arginine showed improvement in vdW interactions, which support stability of domain antibody D11 on CD1b during interaction with Ac_2SGL. This study provided some insights into D11 optimisation for future *in-vitro* testing.

Keywords: Ac_2SGL of Mycobacterium tuberculosis; single domain antibody D11; docking simulation; molecular dynamics simulation; MMPBSA/GBSA free energy calculation

OP39: Membrane proteome analysis of *Entamoeba histolytica*

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Abstract

Entamoeba histolytica causes amoebiasis, which leads to amoebic dysentery and amoebic liver abscess, of which is fatal if untreated. The membrane proteins of *E. histolytica* are key molecules in the development of the disease and are crucial to the discovery of biomarkers for drug therapy, vaccine development and diagnostic markers. In this study, two commercial membrane proteins extraction methods, ProteoExtract® Native Membrane Protein Extraction Kit (Calbiochem) and ProteoPrep® Membrane Extraction Kit (Sigma), and a conventional method were compared. The amount of proteins yielded for Calbiochem extracts were significantly higher than Sigma and conventional method. A total number of 171 proteins were identified using a combination of the three extraction methods by LC-MALDI-TOF/TOF; in which 56, 30 and 127 proteins were identified from Calbiochem, Sigma and conventional method, respectively. Furthermore, 35, 7 and 95 proteins were unique to Calbiochem, Sigma and conventional method. However, only 10 proteins were found to be common among the three methods. Functional classification of protein classes using PantherDB software revealed that the proteins are involved as oxidoreductase (23.9%), cell adhesion molecule (0.9%), membrane traffic protein (4.4%), receptor (3.5%), signalling molecule (1.8%) and transfer/carrier protein (0.9%). Overall, the Calbiochem kit gave the highest yield of membrane protein extract, while, the conventional method gave the best hits of protein identification. In conclusion, the methods compared in this study were complementary to each other based on mass spectrometry analyses and its combination improved membrane proteome coverage.

Keywords: Entamoeba histolytica; membrane proteins; LC-MALDI-TOF/TOF

OP40: Elucidation of antigenic membrane proteins of virulent and avirulent variants of *Entamoeba histolytica* HM1:IMSS strain

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Abstract

Entamoeba histolytica is a causative agent for amoebiasis, a disease of significant mortality in human in endemic areas, mainly in developing countries. To date there is no vaccine that prevents the infection of this parasite. Antigenic protein plays an important role in inducing immune response by triggering B-cells and T-cells, which may be potential biomarker in vaccine development. To date, there is no study on the antigenic membrane proteins of virulent and avirulent variants of *E. histolytica*. Thus, we compared two different variants of *E. histolytica* membrane proteins known as virulent and avirulent variants by western blot, then followed by MALDI-TOF/TOF and database search analyses. We identified eight antigenic protein bands from the virulent variant, i.e., 250kDa, 150kDa, 100kDa, 60kDa, 50kDa, 30kDa, 28kDa and 25kDa, and eight antigenic protein bands from the avirulent variant, i.e., 280kDa, 250kDa, 150kDa, 74kDa, 45kDa, 35kDa, 25kDa and 20kDa. From the MALDI-TOF/TOF analysis, four well-annotated proteins, one uncharacterized protein and five putative proteins were identified from the virulent variant. Whereas, two well-annotated proteins and seven putative proteins were identified from the avirulent variant. Furthermore, Calreticulin, putative protein was identified in both variants. Thus, this potential protein could be explored as a vaccine candidate in the future study.

Keywords: Entamoeba histolytica; vaccine; antigenic; putative

OP41: An investigation of differential protein expression of the membrane of virulent and avirulent variants of *Entamoeba histolytica* HM1:IMSS

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Abstract

Entamoeba histolytica is an enteric protozoan parasite that causes amoebiasis in humans as well as non-human primates. The invasive trophozoites of *E. histolytica* can inhabit in the host tissues and provoke diseases such as intestinal colitis and induce liver abscess formation. Membrane proteins of *E. histolytica* play a significant role in the expression of the virulence factor, as well as colonization and dissemination in their host. To deepen the understanding on the molecular mechanisms of the disease, we compared the membrane proteins from virulent and avirulent variants trophozoites of *E. histolytica* by a quantitative proteomics approach using isobaric tag labelling (iTRAQ), analysed with liquid chromatography (nano-LC) and MALDI-TOF/TOF to identify the differentially expressed proteins. Our analysis resulted in identification of 127 proteins in total. Differentially expressed proteins (fold change >2) were confidently quantified ($P < 0.05$) and we found 5 proteins were significantly up-regulated while 6 proteins were down-regulated, respectively. Significant differentially expressed proteins were further investigated by assessing their integration and prediction of protein-protein interactions network via STRING database (http://string-db.org). STRING predicted 14 associations among differentially expressed proteins in functional enrichment, whereby 3 proteins were involved in amoebiasis, 2 proteins were associated with phagosome and 3 proteins were closely associated with protein processing in endoplasmic reticulum (enrichment *P* value: 0.011). The identification of differentially expressed proteins in this study may contribute to better understanding on the mechanism of *E. histolytica* virulence.

Keywords: Entamoeba histolytica; virulence; iTRAQ; quantitative proteomics

OP42: In-depth investigation on DNA-AgNCs designs for adenosine detection

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Abstract

Discovery on DNA-templated silver nanocluster (DNA-AgNCs) has seen as an alternative to the conventional fluorescent probes (*i.e.* organic fluorophores and quantum dots). This is because DNA-AgNCs offer low cost of synthesis and good biocompatibility. Currently, DNA-AgNCs has shown its effectiveness in bioimaging and biosensing. The designs of these DNA-AgNCs can be as simple as a single DNA chimeric conjugate, or can be more complex with two or more individual DNA strands needed. Hitherto, the impact of DNA sequence formulation on the sensing performance of AgNCs remains ambiguous. In this work, we formulate three different designs of DNA-AgNCs and study their sensing performance towards adenosine. We systematically position AgNCs nucleation sequences and adenosine aptamer at different location of a single chimeric DNA template. We name these chimeric conjugates as Apta5, Apta3 and AptaM, with the last letter implies the position of AgNCs nucleation sequence at 5'-end, 3'-end and in the middle of DNA template. Among these designs, only Apta5 gives selective result against adenosine, with linear range of detection from 1 to 2500 μM. We deduced that the selectivity and emission behaviour are highly dependent on the relative position of AgNCs nucleation sequences and aptamer, as well as the sequences used to encapsulate AgNCs.

Keywords: DNA; silver nanocluster; aptasensor; adenosine

OP43: Application of human neonatal Fc receptor in antibody immobilisation

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Abstract

Antibody immobilisation is the key factor in the development of highly sensitive and reproducible antibody-based assay in diagnostic platform. The complexity of pinning antibodies is important in interfering the antigen binding as the antibody may have undergone structural changes upon immobilisation on solid phase. Consequently, the result of the diagnostic assay may be vary based on different strategy of immobilisation used. In this study, we sought to discover a new candidate of antibody binding protein – the human neonatal Fc receptor, for application of antibody immobilisation in diagnostic assay. Protein expression was carried out to produce the active form of human neonatal Fc receptor. The recombinant protein formed was tested on its efficiency in immobilising rabbit IgG against hepatitis B virus surface antigen. Study was extended further to develop a sandwich assay for detection of hepatitis B virus surface antigen. The result was compared to the conventional immobilisation approach through physical adsorption. The findings demonstrated that human neonatal Fc receptor was efficient in capturing antibody and generated higher signals compare to physical adsorption method.

Keywords: antibody immobilisation; human neonatal Fc receptor; physical adsorption; antibody binding protein; ELISA

OP44: Functional role of Fringe in tumor angiogenesis

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Abstract

Notch signaling pathway is implicated in angiogenesis. Clear Cell Renal Cell Carcinoma (CCRCC) is the most common type of kidney cancer which have abnormally high abundance of blood vessels. Current treatment for CCRCC are available however some patients may acquire resistance to current treatment. Fringe is a regulator of Notch Signalling however very little is known about the roles of Fringe in tumour angiogenesis. The aim of this project is to study the role of Fringe in tumour angiogenesis. Fringe gene knockdown was performed on Ea hy926 endothelial cell line using lentiviral transduction. These cells were then subjected to MTT assay and scratch assay to determine if Fringe can affect cell proliferation and cell migration. Fringe knockdown resulted in decreased proliferation and migration compared to Ea hy926 empty vector control (EV). Down regulation of Notch-related genes HEYL and HEY2 were found in Fringe knockdown when compared to Ea hy926 EV. In addition, Ve-cadherin and Thrombospondin-1 were downregulated in Ea hy926 shFringe cells, suggesting that Fringe plays a role in angiogenesis. The p21 gene was also downregulated which indicate that Fringe may be involved in cell senescence. This project is expected to shed light on the role of Fringe in tumour angiogenesis which may provide a novel strategy for cancer treatment. Future work includes co culture assay with renal cancer cell line to determine the effect of fringe in tumour angiogenesis.

Keywords: Clear cell renal cell carcinoma; ea hy926; HEYL; HEY2; p21

OP45: Endogenous bioactive dynorphin 3-14 as a biomarker in chronic rhinosinusitis and its immunomodulatory effects

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Abstract

Upon its release in rodent inflamed tissues, dynorphin 1-17 (DYN 1-17) is rapidly biotransformed into a range of fragments, with dynorphin 3-14 (DYN 3-14) being the most stable and prevalent fragment. DYN 1-17 has been shown previously to regulate the inflammatory response following tissue injury; biotransformation fragments of DYN 1-17 may also be involved in mediating these effects. This study aims to investigate the presence of DYN 3-14 following biotransformation of DYN 1-17 in human chronic rhinosinusitis (CRS) tissue and to determine its effects on the LPS-activated toll-like receptor 4 (TLR4) signalling pathway. DYN 1-17 was incubated with human inflamed nasal tissue explants and its biotransformation examined using liquid-chromatography mass spectrometry. The translocation of nuclear factor-kappaB/p65 (NF-κB/p65) and the release of pro-inflammatory cytokines interleukin-1beta (IL-1β) and tumor necrosis factor-alpha (TNF-α) were assessed in differentiated THP-1 cells. DYN 3-14 was identified as one of the major fragments produced following the metabolism of DYN 1-17 with human inflamed nasal tissues. Furthermore, DYN 3-14 (10 nM) inhibited (35%) of LPS-induced NF-κB/p65 nuclear translocation and modulated both IL-1β and TNF-α, inhibiting IL-1β and paradoxically augmenting TNF-α release. LPS-induced HEK-Blue™−hTLR4 cells were treated with DYN 3-14; DYN 3-14 (10 μM) inhibited TLR4 activation with approximately 300-fold lower potency than the potent TLR4 antagonist LPS-RS. These findings indicate that DYN 3-14 is a potential TLR4 antagonist, affecting cellular signalling in response to LPS and cytokine release, and thereby suggesting that this endogenous opioid peptide may be a useful biomarker for CRS and other inflammatory-related disease.

Keywords: Dynorphin; interleukin-1beta; tumor necrosis factor-alpha; toll-like receptor 4

OP46: *Nepenthes gracilis* pitcher pot fluid fractions anti-proliferation effects on MDA-MB231 cell line via ER-α36 signalling pathway

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Abstract

Breast cancer is remaining the second highly notorious killer among women in the age of 40-59. *Nepenthes gracilis* (N.G) is a carnivorous plant and well known for their digestive enzymes. The pitcher fluid of N.G. (N.G-pf) was collect and subjected to pH and protease inhibitors assays. The proteolytic activity test of N.G-pf showed a pH optimum at 3.0 and high aspartic protease activity compared to cysteine, metalloproteinase and serine protease. Besides, the crude N.G-pf was fractionated and cell detachment effect on selected breast cancer cell lines was determined. Cells were detached by the crude and fractionated N.G-pf but the effect was not significantly strong when compared with that of trypsin-EDTA. Nonetheless, the crude and fractionated N.G-pf has shown anti-proliferation effects on MDA-MB231 at a concentration 5 times lower than standard National Cancer Institute (NCI) criteria for cytotoxicity (IC50 < 30 µg/ml). Cell proliferation of MCF-10A (non-cancer origin breast cell line was affected by crude N.G-pf, but this was not observed when sub-fractions of N.G-pf was applied. Epidermal growth factor receptor (EGFR) highly effects on breast cancer's cell growth. The MDA-MB231 cells were treated with EGFR inhibitor (ICI 180 782), N.G-pf fractions and with the combination of EGFR-N.G-pf fractions. The cells treated with N.G-pf fraction and N.G-pf-EGFR inhibitor combination group successfully inhibited the growth up to 65 %. The EGFR inhibitor alone treated cells does not kills the MDA-MB231. This elucidate that, the N.G-pf fractions might involve in ER-α36-EGFR complex signaling pathway to inhibit the proliferation of MDA-MB231 cells.

Keywords: *Breast cancer; MDA-MB231; pitcher pot fluid; anti-proliferation activity; signaling pathway*

Poster Presentations

PP01: The anti-proliferative effect of crude protein extract from *Ximenia americana* roots on human breast cancer cell lines

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Abstract

Over centuries plants have been a rich source of natural therapeutic agents for the treatment of various types of cancer including breast cancer. *Ximenia americana* roots are widely used in many African countries as a traditional medicine to treat different types of cancer including breast cancer. However, the anti-cancer properties of *Ximenia americana* roots have not been investigated yet. This study aims to investigate the anti-proliferative effect of water, 50%ethanol and protein crude extracts of *X. americana* roots on MCF7 and MDA-MB-231 breast cancer cell lines and to assess the morphological changes induced by the active extract on these cell lines. Water, 50% ethanol extracts were prepared using maceration technique and protein extract was prepared using Tris-HCl (ph 7) buffer. The three extracts were screened for their anti-cancer activity using MTT assay. The morphological changes that induced by the active extract were assessed using hematoxylin and eosin staining and inverted light microscope. The results showed that, the crude protein extract exhibited dose and time-dependent anti-proliferative effect in MCF7 and MDA-MB-231 with the IC_{50} values of 1.57± 0.107 and 2.33 ± 0.161 µg/ml, respectively. Extract-treated MCF7 and MDA-MB-231 cell lines showed some apoptotic features when observed under light microscope. Thus, the *Ximenia americana* roots have cytotoxic proteins that could be further investigated as anti-breast cancer therapy. Further studies are ongoing to fractionate and identify the bioactive protein (s) that present in *Ximenia americana* roots and to investigate the therapeutic potentials.

Keywords: Ximenia americana; MTT assay; MCF7; MDA-MB-231; breast cancer

PP02: Profiling of microRNA expression in obese and diabetic-induced mice for biomarker discovery

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Abstract

Obesity is a potential risk factor contributing to the development of type 2 diabetes. Meanwhile, diabetes is one of the most prevalent chronic diseases, affecting 6.4% of the world's adult population. MicroRNAs (miRNAs) are short (-22 nucleotides) regulatory RNAs involved in many fundamental biological processes. They are involved in post-transcriptional regulation of gene expression. Dysregulated expression of microRNAs has been associated with a variety of diseases, including obesity and diabetes. The aim of this study is to identify microRNAs that are differentially expressed in obese, diabetic and control C57BL/6 mice by using small RNA sequencing. Total RNAs were extracted from the serum of the target groups of animal. Next, the small RNAs were sequenced using the TruSeq small RNA Library Prep Kit in a MiSeq Illumina sequencer. A total of 52 up-regulated and 54 down-regulated miRNAs were identified based on the comparison of the log2 fold change of obese and diabetic (with normal mice as control; FC ≥ 2). The obese groups showed 22 up-regulated and 25 down-regulated microRNAs. Meanwhile, in the diabetic group, 32 microRNAs were up-regulated and 29 were down-regulated. These findings will help better understand the mechanism of metabolic disorders and may influence future approaches for the diagnosis and treatment of obesity and diabetes.

Keywords: microRNA, obesity, diabetes, gene expression

PP03: A pilot acute toxicity study on the effect of *Orthosiphon stamineus* and gemcitabine combination treatment in athymic nude mice

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Abstract

Pancreatic cancer has the highest mortality rate of all major cancers due to its aggressive biology and lack of effective treatment. Gemcitabine is approved to be the first line anticancer drug for the treatment of pancreatic cancer. However, its efficacy may be reduced due to acquired resistance. *Orthosiphon stamineus* (*O.s*) is a medicinal herb which is used as a folk medicine in South-East Asia. Currently, there is no data available on the *in vivo* toxicity effect of gemcitabine and *O.s* when used in combination. This study aims to evaluate the toxicity effect of *O.s* either alone or in combination treatment with gemcitabine in athymic nude mice in order to select the safest dose for further anticancer studies. *O.s* (200 or 400mg/kg/day) alone and/or gemcitabine (10mg/kg/3days) were administered through oral gavage and interperitoneal injection respectively over a period of fourteen days. The mice in the control group were given distilled water. Different parameters including blood serum biochemistry, hematology, myeloid-erythroid ratio, incident of lethality, and histopathology analysis of liver, kidney, and spleen tissues were studied. Combination treatment of *O.s* and gemcitabine at the tested doses and treatment duration did not cause any sign of toxicity and damage to the organs in nude mice when compared to control group. The data obtained from this study will help to select the best dose for future pre-clinical studies. On-going work is being carried out to investigate the effect of *O.s* and gemcitabine in pancreatic xenograft tumor model.

Key words: Orthosiphon stamineus, herbal medicine, gemcitabine, pancreatic cancer

PP04: Circulating microRNA Expression Profiling in Nasopharyngeal Carcinoma: A Preliminary Result

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Abstract

Nasopharyngeal carcinoma (NPC) is one of the most common cancers in Malaysia. Majority of the cases were diagnosed at late stage, which complicate the treatment and disease outcome. The inaccessible location and inconvenient biopsy procedures of NPC make it difficult to detect early. MicroRNAs (miRNAs) was found to present in blood circulation in stable state and change with pathological state, including malignancy. Therefore, this study is aimed to assess the potential of circulating miRNAs as non-invasive biomarker for early detection of NPC. The total RNA was extracted from plasma of six NPC patients and five age- and gender-matched control subjects. The miRNA extracts were subjected to profiling using qPCR-array platform. The profiling data were processed and analysed statistically using ExpressionSuite software for normalisation and differential expression. The preliminary result found that twelve miRNAs were differentially expressed ($p<0.05$) in NPC patients as compared to control subjects, where nine miRNAs were up-regulated and three miRNAs were down-regulated. To the best of our knowledge, only hsa-miR-191 was previously reported to be detected in plasma and serum NPC, while the other elevens miRNAs were novel finding in this study. However, validation using qPCR must be performed to confirm the expression of dysregulated miRNAs in this study. As a conclusion, this study has found a list of miRNAs that were significantly dysregulated in NPC patients as compared to control subjects and the result need to be further validated to confirm the expression of those miRNAs.

PP05: Ultrasensitive, rapid and inexpensive detection of DNA using paper based lateral flow assay

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Abstract

Sensitive, specific, rapid, inexpensive and easy-to-use nucleic acid tests for use at the point-of-need are critical for the emerging field of personalised medicine for which companion diagnostics are essential, as well as for application in low resource settings. Here we report on the development of a point-of-care nucleic acid lateral flow test for the direct detection of isothermally amplified DNA. The recombinase polymerase amplification method is modified slightly to use tailed primers, resulting in an amplicon with a duplex flanked by two single stranded DNA tails. This tailed amplicon facilitates detection via hybridisation to a surface immobilised oligonucleotide capture probe and a gold nanoparticle labelled reporter probe. A detection limit of 1×10^{-11} M (190 amol), equivalent to 8.67×10^5 copies of DNA was achieved, with the entire assay, both amplification and detection, being completed in less than 15 minutes at a constant temperature of 37ºC. The use of the tailed primers obviates the need for hapten labelling and consequent use of capture and reporter antibodies, whilst also avoiding the need for any post-amplification processing for the generation of single stranded DNA, thus presenting an assay that can facilely find application at the point of need.

Keywords: DNA, aptamer, polymerase amplification, tailed primers

PP06: Rapid identification of clinical and environmental isolates of *Aeromonas* species by lab-on-chip based PCR-RFLP

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Abstract

Aeromonas taxonomy keeps expanding and the genus is currently composed of 27 species. *A. dhakensis* (*A. aquoriorum*) often indistinguishable from *A. hydrophila*, is emerging as a pathogen of clinical importance in severe soft tissue degloving infections as an occupational and recreational hazard, and bloodstream infections in immunocompromised individuals. However, correct identification remains problematic due to the phenotypic and genotypic heterogeneity of the species. The aim of this study was to develop a rapid, simple and reliable genotypic tool to differentiate *Aeromonas* at the species level based on a PCR-RFLP approach and microfluidic capillary electrophoresis targeting *rpoD* housekeeping gene. A pair of degenerated universal primers was designed to amplify the *rpoD* gene. Next *in silico* restriction analysis of targeted gene allowed the identification of a single restriction endonuclease (RE) *Alu*I which enabled distinct differentiation of the 25 species, except for *A. sanarelli* and *A. taiwanensis* in which required an additional RE *HpyCH*4IV. This method was first tested with 60 clinical and environmental *Aeromonas* isolates and the discriminatory power was validated using type (Figure 1). Using an Agilent Bioanalyzer, the developed PCR-RFLP assay unambiguously identified the tested isolates encompassing 12 *Aeromonas* species - *A. hydrophila, A. dhakensis, A. veronii, A. caviae, A. enteropelogens, A. salmonicida, A. jandei, A. media, A. allosaccharophila, A. taiwanensis* and *A. sanerellii*. The results of the tested samples were further substantiated by RFLP patterns of the 12 selected type strains.We believe this new method offers a rapid and accurate technique for molecular identification of *Aeromonas* species.

Keywords: Aeromonas complex; micro-fluid chip; molecular typing; PCR-RFLP; rapid

PP07: Evaluating the Potential of Autophagy as Biomarker for Colorectal Cancer (CRC)

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Abstract

Colorectal cancer (CRC) is the most and second most common cancer in male and female in Malaysia. Epidermal growth factor receptor (EGFR) is a promising target for antibody therapies against metastatic CRC (mCRC), but the therapies are only confined to RAS wild type tumour. Several studies have demonstrated the potent biomarkers for CRC, but little has been associated with KRAS mutation. Autophagy is a self-destructive mechanism that destroys the damaged cells by directing cellular components for lysosomal degradation. Here we aim to evaluate the potential of autophagy as biomarkers for advanced CRC in association with KRAS mutation. Normal (CCD114 and CCD841), wild-type KRAS (HT29 and SW48), and mutated KRAS (HCT116 and SW480) CRC cell lines were used in this study. Four autophagy markers (LC3A, LC3B, LC3C, and p62) were optimised, and LC3B and p62 were selected for further studies. Western blot analysis showed that LC3B and p62 were over-expressed in KRAS-mutated cell lines regardless of cellular stress. KRAS-targeting siRNA treatment of cell lines resulted in marked reduction of autophagy effector expression, similar to those treated with autophagy inhibitor LY294002. After 72-hour exposure of chemo-therapeutic drugs Cisplatin and 5-fluorouracil at respective inhibitory concentration $(IC)_{50}$, both LC3B and p62 expressions were significantly reduced. Similarly, gamma-irradiated CRC cell lines exhibited reduced levels of both autophagy effectors. These data suggest the therapeutic potential of autophagy for CRC treatment. We conclude that LC3B and p62 can be potentially developed into biomarkers for KRAS-associated CRC. These findings will be validated using patient formalin-fixed tissues, and correlated with treatment response and overall survival data.

Keywords: autophagy, KRAS, colorectal cancer, biomarker, therapeutic

PP08: Application of copper-chitosan nanoparticles in treatment of pathogenic local isolates bacteria

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Abstract

Development of nanotechnology, nanoparticles based product and its application is generating interest of many researchers due to its promising biological achievement. However, it is well known that inorganic nanomaterials are good antimicrobial agents, metal nanoparticles as copper assume special importance due to its low cost and easy availability .In this study the green synthesis method as eco-friendly approach is used to produce biologically copper oxide nanoparticlesfrom Ficus Carica leaf extract .The synthesized nanoparticles was characterized through the UV-Vis Spectrophotometer as it found to be 437 nm ,Transmission electron microscopy (TEM) that investigated particle sizes in the range 51-62 nm and typical XRD patterns of the formed CuO Nps with high phase purity were obtained , a chi¬tosan stabilizer as naturally occurring polymers was added to the prepared copper nanoparticles in different amounts .FTIR spectroscopy analysis was performed to copperoxide nanoparticle ,chitosan , copperoxide chitosan composite to confirm that CuO nanoparticle was mixed with polymer . The antibacterial efficacy of chitosan ,copper nanoparticles alone and polymer/metal composites(Co oxide-chitosan nanoparticle) was studied against 22 bacterial pathogen like methicillin-resistant S. aureus as gram positive bacteria , Escherichia coli o157 as gram negative bacteria that showed great antibacterial activity.The effect of the prepared Chitosan-CuO composite on ultrastructure of bacterial cells were evaluated by scanning electron microscopy (SEM), it was found that the antibacterial activity of Cu-chitosan nanoparticle composite is more greater than antibacterial activity of copper nanoparticles and chitosan alone that indicate the addition of chi¬tosan stabilizer enhance at great extent the antimicrobial activity of CuO Nps.

Keywords: Copperoxide nanoparticle; copperoxide –chitosan nanoparticle composite; Ficus carica leaf extract; antimicrobial activity

PP09: Human antibody phage display library generated T cell receptor (TCR)-like antibody for diagnostics and therapeutics.

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Abstract

Immunology has evolved dramatically with the rapid development in science and technology. Various strategies involving different immune components have been considered to be incorporated in both diagnostics and therapies. Recently, T cell receptor (TCR)-like antibody has drawn the attention of researchers worldwide, targeting various diseases such as cancer, viral infections and auto immune diseases. TCR-like antibody is a unique approach whereby the antibody is able to mimic the role of T cell in providing internal immunosurveillance and simultaneously executes its function as antibody to efficiently eliminate diseases, incorporating the advantages of both humoral and cellular immunity. Besides that, TCR-like antibody can also be utilized to diagnose diseases since certain pathogens are capable of immunoediting which affects antigen recognition and ultimately the MHC pathway. Tuberculosis is a disease caused by Mycobacterium Tuberculosis and is indicated as one of the top ten causes of death worldwide by World Health Organization (WHO). The available diagnostic tests such as tuberculin skin and immunological tests are found to be more efficient in diagnosing active TB infection rather than latent phase and most patients fail to comply with the lengthy treatment given resulting in poor recovery. In this study, TCR-like antibody is hypothesized to gain maximum benefits in terms of diagnostics and therapeutics. A high-throughput method for producing MHC-peptide complex via UV peptide exchange is generated. As the experiment models, MHC Class 1 molecule HLA-A2, HLA-A11 and HLA-A24 were used. The antibodies with the binding ability to the target peptide-MHC are generated by panning against the antibody phage display library.

Keywords: TCR-like antibodies; tuberculosis; diagnostics; therapeutics

PP10: Multiplex PCR for rapid and accurate diagnosis of acute leptospirosis

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Abstract

The gold standard for diagnosis of leptospirosis is by the detection of antibody towards *Leptospira* spp. by using micro-agglutination test (MAT). However early diagnosis might be missed due to fact that antibody mostly become detectable after tenth day of illness. Polymerase chain reaction (PCR) has been reported as a useful tool for early diagnosis of acute leptospirosis thereby can reduce mortality and morbidity. In this study, a multiplex PCR (mPCR) was successfully developed and evaluated for detection of two regions of gene encoding for 16s rRNA of *Leptospira* spp. The assay was tested with 37 *Leptospira* spp., 12 other bacterial species and 4 fungal species. Preliminary data showed positive results for almost all *Leptospira* spp. while all of other bacterial and fungal species were identified as negative results. . The analytical sensitivity of the assay was 1 cfu/ml. Therefore. our in-house mPCR has a potential to be used as rapid and early tool for diagnosing acute leptospirosis.

Keywords: mPCR; acute leptospirosis; 16S rRNA

PP11: A randomized study on isolation of *Salmonella enterica* serovar Typhi from gallbladder patients with hepatobiliary diseases in HUSM

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Abstract

Typhoid fever is caused by *Salmonella enterica* serovar Typi (*S*. Typhi) becomes a public health concern in developing and under developing countries with poor hygiene practice. It is estimated that number of typhoid fever episodes are 13.5 million new cases reported yearly. 1-5% of typhoid patients harbors *S*. Typhi for years as asymptomatic carriers and forms a crucial reservoir for the further spread of disease. Studies have shown that *S*. Typhi can be isolated from gallbladder, liver, spleen and bone narrow. By forming biofilm around gallstones in gallbladder, the bacteria can survive in human's high bile salt environment. To date, cholecystectomy (removal of gallbladder) remains the best alternative option for typhoid carriers with gallstones. However, the patient still remains becoming a reservoir due to dissemination of the bacteria in other organs. Randomized study has been performed to isolate *S*. Typhi from cholecystectomic gallbladder patient with hepatobiliary disease using culture technique, Typhoid-Carrier PCR kit and the Typhidot-C have been used for *S*. Typhi confirmatory test from the samples. Five culture techniques have been evaluated and optimized; direct incubation (technique 1), upper layer collection (technique 2), vortex (technique 3), upper layer and pellet isolation (technique 4) and bile dilution (technique 5) before proceed with PCR and Typhidot-C test. Out of 80 samples, 78 samples showed negative detection of S. Typhi but two samples showed presence of suspected salmonella species in XLD plate but negative for PCR. As a conclusion, this study unsuccessfully isolates *S*. Typhi from patient with hepatobiliary disease. Therefore, there is a need to refine inclusion criteria such as experienced typhoid fever before embarking in this study.

Keywords: S. typhi, typhoid; cholecystectomy; gallbladder; hepatobiliary disease

PP12: Gold Nanoparticles-based Colorimetric Aptasensor for Biomarker Detection

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Abstract

Biomarker detection is the measurement of a particular substance in an organism whose presence is highly associated to certain conditions, especially diseases. However, most traditional biomarker detections rely on ELISA, which is costly, time consuming and labour-intensive. In contrast, cysteamine-stabilised gold nanoparticles (cys-AuNPs) are newly introduced nanomaterials that act as signal probes to enable rapid colorimetric-based detection due to their interparticle-distance dependent optical properties, ease of preparation and fast response. We aim to exploit the electrostatic interaction between positively charged cys-AuNPs and negatively charged DNA aptamer (antibody-like DNA strand) in fabricating an aptasensor. Introduction of DNA aptamer electrostatically attracts nearby cys-AuNPs to close proximity, resulting in aggregation that changes the colloidal appearance from red to grey. We hypothesised that presence of targeted biomarker induces conformational changes on the aptamer and influences the subsequent cys-AuNPs aggregation, providing a mean of detection. Using thrombin as model, we discovered that our aptasensor exhibits bimodal behaviour when different aptamers were applied. Both 15- and 29-mer thrombin-specific aptamers were employed as capture probes individually. However, incubating thrombin with the former aptamer enhanced cys-AuNPs aggregation whereas with the latter aptamer reduced particles aggregation. The extent of enhancement or reduction was dependent on thrombin concentration with distinct sensitivity ranges for each aptamer. Despite early stage hitherto, we envision that once established, our aptasensor holds great potential to enable tuneable detection range and generalize for various biomarkers.

Keywords: cysteamine; gold nanoparticles; aptamer; aptasensor

PP13: Profiling of cytokines, chemokines and other soluble proteins as a potential biomarker in colorectal cancer and polyps

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Abstract

Soluble proteins, including cytokines, chemokines and growth factors, are small proteins that mediate and regulate immunity, inflammation, and hemopoiesis. These proteins are involved in the pathogenesis of many diseases. Their concentration in biological fluids and tissues suggests activation of pathways involved in an inflammatory response or disease development. They could serve as a tool for screening, diagnosis classification between stages of disease or surveillance for therapy. Enzyme-linked immunosorbent assays (ELISA) and bioassay have been used as a gold standard in cytokine level measurements in clinical practice. However, these methods allow only single cytokine detection at a time and ineffective for screening purposes. Multiplexing technology allows measurement of multiple soluble proteins simultaneously allowing rapid, cost effective and marked efficiency in analyzing small volumes of specimens. In this study, we explored the profiles of key inflammatory cytokines, chemokines and other soluble proteins derived from colorectal carcinoma (CRC, *n*=20), colorectal polyps (polyps, *n*=20) and healthy volunteers (control, *n*=20) using multiplexed bead-based immunoassays. We aimed to evaluate if the levels of these soluble proteins can classify these groups of populations and explore the possible application of the soluble proteins as biomarkers in early stage screening and/or surveillance. We observed significant high IL-4, FasL and TGF-β1 levels but lower levels for RANTES in polyps patients as compared to controls. Significant high IL-8, VEGF, MIP-1β, Eotaxin and G-CSF observed in CRC when compared to controls. Between CRC and polyps patients, significantly higher levels of Eotaxin and G-CSF but lower levels for TGF-β1 were detected in sera of CRC patients. Our findings may hold promise for the further development of serum screening assays which potentially useful in diagnosis as well as a target for therapy. Furthermore, this soluble protein profiles may be useful for the surveillance and evaluation of cancer vaccines in clinical trials.

Keywords: colorectal cancer; polyps; cytokine; chemokines; interleukin

PP14: Detection of invasive fungal pathogens utilizing Late-PCR

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Abstract

Polymerase chain reaction (PCR) based detection has been extensively used to detect and identify pathogenic fungi. Asymmetric PCR preferentially amplifies one DNA strand in a double-stranded DNA template and for use in DNA hybridization studies. Linear-After-The-Exponential-PCR (LATE-PCR) is an advanced asymmetric PCR method using primers at different concentrations, with innovative primer design to assure high efficiency and specificity. In the present study, we optimised LATE-PCR parameters to amplify and produce single stranded DNA of major fungal pathogens including *Candida* spp. and *Aspergillus* spp. The conserved fungal internal transcribed spacer (ITS) region was used to design limiting primer (ITS 4) and excess primer (ITS 1) for the LATE-PCR. The number of PCR cycles, primer annealing temperature, concentrations of genomic DNA, limiting and excess primers, $MgCl_2$ and *Taq* polymerase were optimized. Gel electrophoresis of LATE-PCR product showed a smaller band size compared to conventional PCR product indicating the presence of single stranded DNA. The single stranded product was hybridised with digoxigenin labeled complementary probe and detected using anti-digoxigenin antibody forming a conjugate by dot blotting. The conjugate then undergoes enzyme-catalysed colour reaction with phosphate substrate and tetrazolium salt producing the blue precipitate. LATE-PCR products of both *Candida* spp. and *Aspergillus* spp. successfully hybridized to respective oligonucleotide probes with no cross reactivity observed between each fungal genus probe and non-target LATE-PCR products. In conclusion, this advancement of PCR may be utilised for a rapid, membrane-based detection assay for detecting clinically important fungal pathogens.

Keywords: fungal pathogens; LATE-PCR; hybridisation assay

PP15: *Potential impact of BRCA1*-3'UTR- TG or TT variant (rs8176318G/T) in the Breast cancer populations of Saudi Arabia.

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Abstract

The Breast Cancer 1, early onset gene (BRCA1) encodes a tumor suppressor protein that functions as a negative regulator of tumor growth. Genetic mutation of breast cancer 1 (*BRCA1*) is one of the most notable factors responsible for a proportion of breast cancer cases. A germline, variant in the BRCA1 3'UTR (rs8176318C/T) was previously shown to predict breast and ovarian cancer risk in women from high-risk families, as well as increased risk of triple negative breast cancer. Thus, investigations of the underlying mechanisms that regulate *BRCA1* gene expression provide further insight into possible targets for breast cancer therapy. The aim of this study was to determine the frequency of T/T variant of BRCA1 3'UTR in breast cancer cases and its association with breast cancer progression. The study was conducted on 100 cases and 100 sex matched controls. DNA extraction was done for the FFPE specimens using NucleoSpin® DNA FFPE kit and for blood using DNAeasy kit from Qiagen. It was observed that patients with Breast cancer possessed significantly higher frequency of T/T variant of BRCA1 3'UTR gene (58%) than healthy controls (30%). Independent evaluation of the T/T variant of BRCA1-3'UTR revealed significant variation in baseline frequency by ethnicity, with a documented minor allele frequency in different populations of approximately 0.28. Similarly, a significant difference (p=0.0013) was observed in genotype distribution among cases and healthy controls. It was concluded that BRCA1 3'UTR variant (rs8176318C/T) is significantly associated with increased risk of Breast cancer among the population of Saudi Arabia.

Keywords: BRCA1 gene; BRCA1 3'UTR; rs8176318G/T

PP16: Identification of *Salmonella enterica* serovar Typhi virulence factors through bioinformatics analysis and yeast morphology assay

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Abstract

Typhoid fever is a symptomatic bacterial infection caused by *Salmonella enterica* serovar Typhi (*S*. Typhi) that usually occurs due to poor sanitation and poor hygiene. The identification of novel virulence factors (VF) of *S*. Typhi will allow for better understanding of the pathogenesis of typhoid infection and potentially help disease management. In this study, we used *Saccharomyces cerevisiae* as a model organism to identify *S*.Typhi VFs that cause morphological changes in yeast. The selection of VFs from the *S*. Typhi proteome in the available databases online (e.g. NCBI and UniProt) was carried out based on the VFs' ontology, function, subcellular location and biological process (e.g. adhesion, colonization, toxicity, motility, biofilm formation). The potential VFs were then cross-referenced to more specific databases for VFs such as VFDB (http://www.mgc.ac.cn/VFs) and PATRIC (http://patricbrc.org). These VF databases were established to provide current knowledge on various bacterial pathogens to accelerate and increase the accuracy of in silico prediction of VFs. A list of potential VFs are curated using extensive bioinformatics analysis and literature review. Beginning with the full proteome of S.Typhi CT18 of 4718 proteins and we selected 192 potential VFs for expression in yeast. 190 genes are successfully clone into plasmid bearing green fluorescent protein (GFP) using homologous cloning in high-throughput format. This is followed by expression of the VFs in yeast. The morphological changes cause by the VFs and the protein localization in yeast are observed.

Keywords: Salmonella typhi; virulence factor; high throughput; yeast morphology assay; GFP

PP17: Identification of *Salmonella enterica serovar* Typhi virulence factors using a yeast growth inhibition screen

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Abstract

The study of virulence factors (VFs) is crucial for the understanding of bacterial pathogenesis. When VFs are expressed in yeast *Saccharomyces cerevisiae*, they have been observed to be detrimental to yeast cells (e.g. causing growth inhibition). In this sense, yeast can act as a sensitive indicator to identify VFs. There are still many unknown VFs and for those already reported, their roles in pathogenesis are not completely understood. This study aims to identify *Salmonella enterica* serovar Typhi VFs by expressing them in *S. cerevisiae*. First, putative VFs were identified by bioinformatics analysis using online databases such as UniProt, VFDB and PATRIC. We selected 192 potential VFs from the full proteome of *S*. Typhi CT18 which contain 4718 proteins. The VFs were selected based on their gene ontology (GO) which covers function, biological process and subcellular location. Then, the selected VF genes were cloned and expressed in yeast in a 96-well plate format. Yeast growth was monitored quantitatively by measuring the optical density of the culture and qualitatively by checking the cell's viability on dilution assay. Of the 192 VFs selected, 176 VFs were successfully cloned and expressed in yeast, 24 VFs were found to inhibit the growth of yeast. These VFs will be subjected to further characterization studies.

Keywords: Salmonella; virulence factors; pathogenesis; yeast; growth inhibition

PP18: A preliminary report on proteomic-mediated response in mud crabs taken from Setiu Wetland lagoon, Terengganu.

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Abstract

Setiu Wetland lagoon Terengganu is a center for various water related-activities such as agriculture, fish farming and boating activities that contribute to toxic pollutants in its water that affect the organisms inhabit the surrounding areas. *Scylla* spp (known as wild mud crabs) are abundant at that area and important for commercial purposes. Poor water quality affects the health and biology of the crabs that cause changes in their proteins synthesis as part of defense mechanisms under stress conditions. To confirm this, tissues of gills, hepatopancrease and claws of mud crabs were subjected for proteomic analysis by 1D and 2D electrophoresis. Proteins of mud crabs were extracted from crab's tissues by using homogenize buffer, pH 7.8. For 1DE, 20 ug of protein samples were resolved on 10 % SDS gel. For 2DE, 200 ug of proteins samples were loaded on the strip for IEF. One high intensive band (~115 kDa) was detected from all tissues of mud crabs taken at all sampling locations. Interestingly, although 5 protein bands (~73, ~64, ~55, ~24, and ~19 kDa) were observed in all tissues at B and C sampling locations, these proteins were not expressed in hepatopancrease at A location. Protein separation in 2DE resulted 57 protein spots from gills, 32 protein spots from claws, and 55 protein spots from hepatopancrease of mud crabs. All these protein spots are observed at pH in the range of 3-9. Proteins expressed in various tissues of mud crabs observed in this preliminary study have potential as biomarkers for water quality at Setiu Wetland lagoon.

Keywords: wild mud crabs; Scylla spp; Setiu Wetland; proteomic

PP19: The identification of *Leptospira interrogans* virulent factors with a yeast growth inhibition screen

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Abstract

Virulence factors are pathogen-produced macromolecules that are capable to cause diseases. It can be effector proteins produced by pathogenic bacteria to help in invasion and evasion as well as enable the bacteria to replicate and spread in the host by affecting the host defense system. *Leptospira interogans* is an aerobic,Gram-negative spirochetes bacteria that is responsible for Leptospirosis, a fatal disease that can cause meningtis, kidney and liver failure. However, the knowledge about invasion mechanisms of *L. interrogans* remains inadequate. To identify the virulent factors of *L. interrogans*, we developed a high-throughput cloning system that can be applied to a 96-well plate format. A total of 278 potential virulence genes were selected and 230 were able to be cloned into a yeast expression plasmid. We are currently performing a yeast growth inhibition assay.

Keywords: Leptospira interrogans; virulent factors; high-throughput cloning; yeast inhibition assay

PP20: Establishment of a novel sirtuin inhibitor as an adjuvant therapeutic agent in colorectal cancer

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Abstract

Colorectal cancer (CRC) is the world's third most common cancer in men and the second most common in women. 5-Fluorouracil (5-FU) is the first line therapy for CRC. However, patients may acquire resistance to 5-FU, thus affecting treatment outcome and patient survival. Sirtuins (SIRTs) are highly conserved NAD+ dependent class III histone deacetylases (HDAC) that play a role in cancer. There are seven SIRT (1-7) in mammals. SIRT1 has been found to be upregulated in CRC. Although SIRT2 was studied to a lesser extent compared to SIRT1, the former was found to deacetylate p53 tumour suppressor gene that suppresses cell proliferation and tumour growth. We hypothesise that suppressing both SIRT1 and SIRT2 with our novel inhibitor may inhibit CRC cell viability through apoptosis. This project aims to study the role of our novel sirtuin inhibitor BZD9L1 in mediating chemosensitivity of CRC to 5-FU in vitro. The effects of treatments on HCT116 and HT29 colorectal cancer cell proliferation were determined using Cyquant. Clonogenic assay and scratch assay were performed to assess cell survival and cell migration respectively, post treatment. Combination treatment of BZD9L1 and 5-FU resulted in synergistic reduction in cell viability and the ability to form colonies compared to single treatment of either one in HCT116 cells, but not in HT29 cells. Combination or stand-alone treatment does not affect HCT116 cells ability to migrate and this could be due to concentration of SIRT1/2 inhibitor used in the treatment. The concentration used in this experiment is capable of increasing chemosensitivity of HCT116 cells towards 5-FU but it may not be enough to supress cell migration. Thus, understanding the molecular mechanisms affected by of these treatments in colorectal cancer is vital. Current work includes real-time PCR, senescence and immunoblotting to observe the downstream effect of these treatments.

Keywords: colorectal cancer; SIRT1/2; sirtuin inhibitor; adjuvant therapeutic agent; acquired resistance.

PP21: Development of rapid dot-blot flow through assay for HIV antibody detection with novel synthetic multiepitope peptide

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Abstract

The serological investigation remains the primary approach to achieving satisfactory results in STDs identification. However, the accuracy of the native antigen used in the current diagnostic kits has proven to be insufficient globally, so significant efforts have consistently been made to find alternative reagents as capture antigens/antibody. Consequently, multi-epitope peptides are promising diagnostic markers, with the potential for improving the accuracy of diagnostic kits. This research aims to perform a systematic review to assess the diagnostic accuracy of all reported recombinant antigens and multiple point-of-care rapid assay platforms for HIV detection according to standard methods and summarise test performance using meta-analysis to identify promising antigen for development of multiepitope peptide for detection of HIV/AIDS antigen and antibodies. Further to develop a diagnostic platform to detect HIV/AIDS antibodies using multiepitope peptides (MEP). The MEP is designed to include eight epitopic regions of 8 selected antigens fused to form a 330 amino acid peptide. Rapid dot-blot flow through assay was developed with MEP as antigen component at 320ng/ml antigen concentration and protein-A gold conjugate for detection of the antigen-antibody complex. On analysis of 53 known samples, 23 seropositive and 33 seronegative, HIV MEP flow through assay showed 87% sensitivity and 90.7% specificity over 47.8% sensitivity and 100% specificity of commercial MERIL Quadro HIV 1-2 Ab flow through assay. 100% reproducibility was achieved on analysis of 10 blinded reactive and five blinded non-reactive samples with three different batches. (With further optimisation, MEP based assays will be a promising antigen component in efficient HIV/AIDS diagnosis

Keywords: HIV/AIDS; multiepitope; rapid assay; dot-blot assay; antibody detection

PP22: Triple negative breast cancer: A review of molecular classification and potential target therapies

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Abstract

Breast cancer is the second leading cause of death among women worldwide. Triple negative breast cancer (TNBC) is defined by the immunohistochemical absence of estrogen (ER), progesterone (PR), human epidermal growth factor receptor 2 (HER2) expressions and erb-b2 receptor tyrosine kinase 2 (ERBB2) gene overexpression. Besides that, TNBC is also characterized by the poor prognosis and lack of therapeutic target as compared to hormone receptor positive and HER2 type breast cancers. TNBC comprises of about 15% of all breast cancer cases and has molecular features related to BRCA1 germline mutation carriers. The challenge for TNBC treatment is that they are unresponsive to either trastuzumab or hormone therapy. Therefore, to determine the presence or absence of a certain biomarker in TNBC could help to predict which therapy is the most suitable for targeted TNBC treatment. The aim of this review is to focus on the TNBC molecular features and new therapeutic options such as the use of EGFR antagonists, PI3K/Akt pathway, ARF1 regulation, PMCA2 downregulation, PARP inhibitors, VEGF and anti-angiogenics as potential therapy for TNBC. This approach will have great impact on development of new treatment tumor biology, to identify suitable biomarkers and customization of prognostics and therapies in TNBC patients.

Keywords: Breast cancer; molecular target; therapeutic strategies; biomarker; TNBC

PP23: Review: Recent Molecular Mechanism of Apoptotic Pathways in Cancer Cell Lines with Additional Apoptosis-Inducing Compounds in Natural Plants

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Abstract

Defective or inefficient apoptosis has become the hallmark of cancer cell. Extensive studies on molecular pathway reveal that targeting the apoptosis pathways in cancer can be used in many therapeutic treatments. In order to avoid apoptosis, cancer cells usually target several molecular mechanisms to become resistant to any apoptotic molecules. In this review, an understanding of the underlying mechanism of apoptosis pathways is provided to unravel novel cancer drug targets in treatment of various types of cancer. Recently, the use of natural herbs in treatment of cancer provides an alternative method to treat cancer patients without major side effects. A new unsung medicinal plant *Goniothalamus,* is known to have an apoptosis-inducing compound Goniothalamin. The biological property of curcumin has also been thoroughly studied and has been reported to induce apoptosis in many cancer cell lines. Thus, this review focuses on providing an overview of apoptotic molecular pathways in cancer and elucidates some of the apoptosis-inducing compounds in natural plants.

Keywords: Apoptosis; anticancer; Goniothalamin; curcumin

PP24: Functional annotation and classification of the hypothetical proteins of *Acinetobacter baumannii*

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Abstract

Acinetobacter baumanii is an opportunistic pathogen. There are many different species of Acinetobacter that can cause disease, but *A. baumanii* accounts for about 80 percent of reported *Acinetobacter* infections. It can cause diseases such as pneumonia and meningitis. It has become an increasingly important human pathogen because of the increase in the number of infections caused by this organism and the emergence of multidrug-resistant (MDR) strains. There is a need for identification of novel drug targets against this pathogen. In this study, we extensively analysed all available 964 hypothetical proteins (HPs) among *A. baumanii*. We performed extensive functional analysis of these HPs with the help of bioinformatics tools and assigned functions to 930 HPs. We classified 559 HPs were binding proteins, 330 HPs were lipid binding proteins, 11 HPs were enzymes, 17 HPs were receptor, 4 HPs were transporter, 9 HPs were nuclear receptor and 34 HPs were not functionally annotated by any of these tools. This functional classification will help to identify novel drug targets and also may help in the comprehensive understanding of pathogenesis, drug resistance, and adaptability to host for treatment of the diseases.

Keywords: pneumonia; meningitis; Acineobacter; bioinformatics

PP25: Functional annotation of conserved hypothetical proteins from *Salmonella typhi*

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Abstract

Salmonella typhi belong to Gram-negative enteric bacillus belong to the family Enterobacteriaceae. Infection of *S. typhi* leads to the development of typhoid, or enteric fever. This disease is characterized by the sudden onset of a sustained and systemic fever, severe headache, nausea, and loss of appetite. Typhoid fever affects roughly 17 million people annually around the globe. Due to emergence antibiotic resistance among various strains, the treatment of typhoid became a major public concern. There is immediate need of identification of novel drug targets against this pathogen. Our aim of the study is to combine a number of bioinformatics tools for function prediction of previously not assigned proteins in the genome of *Salmonella typhi*. The hypothetical proteins available in the genome were extensively analyzed. Amino acid sequences of all 770 hypothetical proteins were analysed and we successfully assigned a function to 559 hypothetical proteins. Out of 559 hypothetical proteins were functionally annotated, 118 proteins belong to enzyme, 36 proteins belong to transport protein, 30 proteins belong to structural protein, 6 proteins belong to Ion channel, 24 proteins belong to bacteriophage related proteins, 17 protein belong to cellular process regulator protein, 92 protein belong to miscellaneous function, 196 protein belong to Domain of Unknown Function (DUF) and 211 proteins were not able to functionally annotated by any bioinformatics tools. The outcome of this work will be helpful for a better understanding of the mechanism of pathogenesis and in finding novel drug targets for *Salmonella typhi*.

Keywords: Typhoid; drug target; hypothetical; bioinformatics

PP26: Computational functional annotation of putative conserved hypothetical proteins from *Klebsiella pneumonia*e HS11286

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Abstract

Klebsiella pneumoniae, a Gram-negative prominent nosocomial pathogen, is responsible for a variety of diseases in humans among immunocompromised patients. It is mainly responsible for septicemia, pneumonia, respiratory and urinary tract infections. As more *Klebsiella pneumoniae* strains are becoming highly resistant to various antibiotics, treatment of this bacterium has been rendered more difficult. This situation poses a threat to public health. Hence, identification of novel drug targets is necessary. Approximately 20% of the genome of *K. pneumoniae* HS11286 encodes hypothetical proteins. Hypothetical proteins are proteins with an unknown function where their sequences and structures are largely non-similar with other known proteins. Through computational tools, deciphering the functions of hypothetical proteins of this pathogen may give insight to possible novel potential drug targets. The present study was designed to functionally classify hypothetical proteins by using various bioinformatics tools available in *Klebsiella pneumoniae* HS11286. We have successfully characterized 731 out of 973 proteins. We classified 239 proteins as enzymes, 68 proteins as binding proteins, 41 proteins as transport proteins, 18 proteins as factor, regulators, 16 proteins as lipid binding proteins, 14 as bacteriophage related proteins, 13 proteins as cell cycle related, 10 proteins as signalling proteins, 4 proteins as ion channels, 2 proteins as nuclear receptor, 2 proteins as monoclonal, 1 protein as receptor, while 204 proteins predicted Domain of Unknown Function (DUF) and the rest of proteins were not functionally annotated by any of the tools. This computational functional classification of hypothetical proteins will help to identify potential novel drug targets among the classified drug targets.

Keywords: Klebsiella; pneumoniae; antibiotic; drug target; resistant

PP27: The Effect of Glucose Oxidase Concentration on the Performance of Indium Tin Oxide Glass Electrode for Glucose Detection

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Abstract

In this study we report the effect of glucose oxidase (GOx) concentration on the performance of the indium tin oxide (ITO) glass electrode modified with iron oxide nanoparticles (IONPs) and nafion for glucose detection. IONPs were synthesized using precipitation technique and surface functionalized using citric acid (CA) to provide hydrophilic surface and functional group for glucose oxidase (GOx) enzyme immobilization. The effect of GOx enzyme concentration (1mg/ml to 10 mg/ml) to the electrocatalytic performance of the modified electrode for glucose biosensor detection was studied. Increasing the concentration of GOx increases the electrocatalytic performance of the bioelectrode. This is because more enzymes would produce more hydrogen peroxide (H_2O_2) at the same concentration of glucose under the same condition. From the transmission electron microscopy (TEM) images analysis, the size of IONPs obtained was ~19 nm and the X-ray diffraction (XRD) spectra showed the presence of spinel cubic lattice of maghemite (γ-Fe_2O_3). The bioelectrode designated as Nafion/Gox/IONPs-CA/ITO shows good electrochemical performance for glucose detection with high sensitivity of 90.44 µAmM-1cm-2 for a linear range of 1.0-12.0 mM glucose concentration.

Keywords: Iron oxide nanoparticles; glucose biosensor; Nafion; enzymatic biosensor; citric acid functionalization

PP28: Comparison of carotenoid biosynthesis gene sequences and expression in wild type and a novel hyperproducing strain of *Xanthopyllomyces dendrorhous*

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Abstract

Xanthophyllomyces dendrorhous produces astaxanthin as its principle carotenoid, which was recently used in nutraceutical industries especially in cosmetic and pharmaceutical aspects because of its strong antioxidant properties. Mutagenesis by using chemical mutagen, 1-methyl-3-nitro-1-nitrosoguanidine, was carried out to obtain a hyperproducing strain, M34, as the astaxanthin production in wild type strain of *X. dendrorhous* is low. Wild type strain and mutant M34 were compared for carotenoid production and mRNA expression level of *idi*, *crtE*, *crtYB*, *crtI*, *crtR*, *crtS* carotenogenic genes to correlate carotenoid production with the transcript levels of these genes. The changes in the sequence of these genes were also studied to further elucidate the mutagenesis that lead to an increase in carotenogenesis in the mutant. At the end of stationary phase, total carotenoid yield of M34 was two folds higher than the wild type. For mRNA expression, both *crtE* and *crtS* genes showed higher expression, which are 1.3 and 3.8 folds respectively when compared to wild type. Besides, all six carotenogenic genes exhibited nucleotide changes, with *crtI* and *crtS* with just one nucleotide change after the mutation while *crtR* had the most changes of 18 nucleotides compared to wild type. This study will help in understanding the role of the carotenogenic genes in further improvement of carotenoid production.

Keywords: Xanthopyllomyces dendrorhous; carotenoid biosynthesis genes; astaxanthin- hyperproducing mutant

PP29: Optimization of LipL32-Loop-Mediated Isothermal Amplification (LipL32-LAMP) assay for faster detection of *Leptospirosis interrogans*

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Abstract

Molecular approaches, such as PCR and real-time PCR, have shown to be sensitive and specific methods in the early phase of leptospirosis; however, the needs of the sophisticated and expensive machine for both methods hinders its application in low-resource settings thus delays the proper treatment. As a rapid, simple and cost-effective detection method, loop-mediated isothermal amplification (LAMP) assay offers a better anticipation for early detection of leptospirosis. In this study, LipL32 gene, which is the specific marker to pathogenic *Leptospira interrogans*, was used as a target region for LAMP. The ability of the LipL32-LAMP assay to accelerate detection (100 copies/µl of synthetic plasmid) was optimized using four key components; reaction temperature, primers set design, Mg ion concentration and enzyme concentration. The reactions were incubated in tabletop thermo-block and evaluated manually by the presence of fluorescent green by naked eye every 5 minutes and time to results (TTR) were recorded accordingly. Results showed from three primers set of LipL32 (LipL32-1, LipL32-2 and LipL32-3) incubated in three different temperatures 60ºC, 63ºC and 65ºC, the primers set LipL32- 2 showed TTR of 20 minutes when incubated at 63ºC. Therefore, LipL32-2 primers set and 63ºC incubation temperature was chosen to be used throughout the experiment. The TTR for LipL32-2 assay was 15 minutes when 10 mM of Mg ions incorporated into the reaction. The TTR for LipL32-2 assay was then accelerated to 10 minutes when 1.6X of Bst3.0 DNA polymerase were incorporated. Thus, the best performance of the LipL32 assay within 10 minutes to positive results would offer a sensitive and specific rapid detection assay for leptospirosis.

Keywords: (Leptospirosis; Loop-mediated isothermal amplification; LAMP optimization)

PP30: Melioidosis: diagnostic value of IFAT IgM and IFAT IgG in comparison with qPCR

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Abstract

The annual incidence of the melioidosis in Malaysia is about 6.1 per 100,000 populations and the disease carries a high mortality of about 50%, most patients being diabetic with late presentation, Culture & sensitivity is a standard diagnostic method which takes at least 3 days to confirm the diagnosis while molecular testing by PCR is not routinely performed. In this comparative study 30 blood culture confirmed cases of melioidosis were followed up by IFAT and qPCR on peripheral blood samples collected on the day of confirmed diagnosis by conventional culture. The qPCR assay was previously developed in our laboratory in Basic Medical Sciences Department, Faculty of Medicine, International Islamic University Malaysia. The assay targeted the type III secretion system gene cluster of *Burkulderia pseudomallei* (Genbank accession number AF074878). Of 30 patients with positive blood culture for *B. pseudomallei* only 20 (66.7%) tested positive by qPCR on 1st day of obtaining the confirmed culture results i.e. ≥2 days after admission and empirical antibiotic treatment, while 72.5% tested positive by IFAT IgM and 60% tested positive for IFAT IgG using the cut off values of ≥20 and ≥80 respectively as determined previously by us based on ROC curve analysis. Two control groups were included in this study, patients with other infections and patients without apparent infections. In conclusion, it seems that the combined results from these 2 diagnostic tests might be of more diagnostic value than each alone.

Keywords: Melioidosis; IFAT; qPCR; comparison

PP31: Synthesis and characterization of gold nanoflowers as label in lateral flow dipstick

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Abstract

Lateral flow dipstick offers several advantages such as low-cost, rapid test, on site applications and simple to use for detection of various types of analytes. Spherical shaped gold nanoparticles (AuNPs) are commonly used as label in a dipstick because of its conjugation properties, easy to synthesis and visibility by naked eyes. However, AuNPs based dipstick show less sensitivity due to lower surface Plasmon resonance (SPR) peak compared to other dipsticks labels. In this work, flowers shaped or multi-branched gold nanoparticles (gold nanoflowers, AuNFs) were synthesized and characterized for labelling in dipstick to enhance its sensitivity. The AuNFs were synthesized using hydroquinone as mild reducing agent added to boiling gold salt solution. The solution then turned from yellow to blue after several minutes. This AuNFs were characterized using UV-Vis spectrometer, zeta-sizer and transmission electron microscope (TEM) microscopy. AuNFs show higher SPR peak at 701 nm due to its shape compared to sphere AuNPs. The size of AuNFs was 75 nm measured by zeta-sizer. Morphology of AuNFs was observed using TEM and flower-like shape with 10 to 15 projectiles was observed. AuNFs were successfully synthesized and characterized to be used as improved label in dipstick application.

Keywords: lateral flow dipstick; gold nanoflowers; rapid test; multibranched shape gold nanoparticle; surface Plasmon resonance

PP32: Optimization of Indirect Competitive ELISA for the Development of Immunosensor to detect Aflatoxin B_1 in peanut sample

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Abstract

Aflatoxin B_1 is a carcinogenic secondary toxic metabolite which leads to health effects through consumption of contaminated food. ELISA is an immunochemical method, which offers selective, sensitive, rapid and inexpensive technique to detect molecule in a matrix with simple sample preparation. In this study, multi-level factorial design was used to examine the effects of pH, incubation time and temperature towards the assay performance. Checkerboard titration was done to determine the specificity of the primary antibody, anti-AFB_1 towards the binding site of the coating conjugate, AFB_1-BSA. Skimmed milk was found to be the optimal blocking agent. Reducing the concentrations of both coating conjugate and antibody resulted in better sensitivity. AFB_1-BSA at 0.25 µg/mL with 1/5000 (v/v) of anti-AFB_1 antibody was chosen as the optimum concentrations for coating and antibody dilution which resulted in highest sensitivity with IC_{50} value of 0.0183 ng/mL. The assay performed well in buffer of pH 7 with 0.5 h incubation time at 25^0C. A non-linear calibration curve using AFB_1 standard with linear working range of 0.001 to 10 ng/mL and R^2 value of 0.9875 was obtained. The developed assay was successfully used to detect aflatoxin B_1 in peanut sample with minimal matrix effect.

Keywords: Aflatoxin B_1; Indirect Competitive ELISA; Immunosensor; Optimization

PP33: *In-vitro* cytotoxicity effect of Bismuth Oxide Nanoparticles (Bi_2O_3 Nps) synthesized at different temperature

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Abstract

Bismuth oxide nanoparticles (Bi_2O_3 NPs) recently had drawn tremendous attention in medical imaging, X-ray radiosensitizing and biomolecular detection due to its high atomic number (Z = 83) which directly possess high X-ray attenuation coefficient. However, exploration of this compound is hampered owing to challenges in synthesizing control for *in-vivo* stability. The aim of this preliminary study is to determine the cytotoxicity effect of Bi_2O_3 synthesized at different temperatures via hydrothermal method *in-vitro*. The Bi_2O_3 NPs synthesized at 60, 90 and 120 °C were each characterized using scanning electron microscope (SEM). Bi_2O_3 NPs cytotoxicity was evaluated using cell viability assay (MTT assay) upon 24 hours exposure to human hepatic cell line (WRL 68). MTT assay showed increase in cell viability as the synthetization temperature of each Bi_2O_3 NPs increase. The data suggest the response of WRL 68 to Bi_2O_3 NPs have a significant relationship with its synthesization temperatures, hence give a better understanding in Bi_2O_3 NPs synthesizing control to enhance its biocompatibility.

Keyword: bismuth oxide nanoparticles; synthetization temperature; cell viability; cytotoxicity

PP34: Development of immunochromatography based on Thyroid Peroxidase (TPO) as autoimmune marker for early detection of autoimmune thyroid diseases

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Abstract

Hypothyroidism is one of Autoimmune Thyroid Diseases (AITD) condition became a concerning for society. This disease is asymptomatic and should be aware especially for pregnant women because it will lead to decline in the infant's condition or born with mental or physical disabilities. The number of births is less healthy due to the worsening of the manifestation of symptoms in pregnant women who suffer from hypothyroidism, not in spite of the delay in determining the early detection and precise handling. Thyroid Peroxidase (TPO) antibody titer can be detected early before Triiodothyronine (T3) and Thyroxine (T4) hormone level alteration, and could be used for monitoring successful treatment. This work proposed to develop a reverse flow immunochromatography based detection using autoantibody of thyroid peroxidase as test line part. This test is conducted by using 20 µL sera and required 20-30 minutes test duration. This methods promise to have more specificity and sensitivity over commercial kits available and also not laborious. This works is started with preparation of recombinant human autoantibody of thyroid peroxidase from patients, then it was produce in *E. coli BL-21 cells* and purify before apply in cassette kits. Meanwhile, it was also prepared for the control lines which use goat anti mouse IgG to support test result interpretation. This platform also have promise to prevent hypothyroidism in pregnant women.

Keywords: hypothyroidsm; thyroid Peroxidase; detection kit; immunochromatography

PP35: Combination of A-1210477 and ABT-263 exhibit synergistic effect on cervical cancer cell lines – A preliminary study

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Abstract

Cervical cancer is an aggressive and a deadly cancer. Patients suffering from a recurrence and advance cancer built resistance to conventional treatment modalities namely chemo- and radiotherapy. Hence, novel treatment strategies are required to treat these patients. The anti-apoptotic proteins are expressed in many tumours and hence have become attractive targets for cancer therapy. The interest to target them increased with development of BH3-mimetics, which specifically target these proteins. BH3-mimetic ABT-263, which inhibits BCL-2, BCL-XL and BCL-w, demonstrated impressive single agent activity in most haematological tumours and small cell lung carcinoma (SCLC) but exhibited disappointing outcome as a single agent in most solid tumours. It has become clear that sensitivity to ABT-263 rely on expression of another anti-apoptotic protein, MCL-1. Thus, chemotherapeutic agents or targeted therapies that can repress or neutralize MCL-1 are predicted to synergize with ABT-263. Here we report that combination of MCL-1 selective inhibitor A-1210477 (AbbVie) and ABT-263 (Navitoclax, AbbVie) exhibited synergistic effects on cervical cancer cell lines SiHa, C33A, CaSki and HeLa. Furthermore, drug potentiation studies revealed that A-1210477 potentiated SiHa and CaSki to ABT-263 by 5- and 11-fold respectively. The potentiation in the opposite direction showed that ABT-263 was able to potentiate SiHa and CaSki to A-1210477 by 8-fold. Together these findings show that combination of ABT-263 and A-1210477 could be a potential treatment strategy for cervical cancer. Future studies, which involve testing this combination in 3D spheroids and xenograft models, are necessary to fully unleash the prospect of this combination to combat cervical cancer.

Keywords: ABT-263; A-1210477; cervical cancer cells; drug potentiation

PP36: Serotyping dengue virus with silver nanocluster DNA switch

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Abstract

Dengue is regarded as a prevalent mosquito-borne viral disease in tropical and subtropical countries[1]. There are four dengue serotypes (1-4). Infection of one serotype could confer to life-long immunity against that serotype but not to other three serotypes. Secondary infection is reported to associate to life-threatening diseases such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Hence, determination of dengue serotype is crucial for epidemiological and pathological studies to find out current and past infections[2]. DNA detection of dengue virus has the advantage of high limit of detection in sample. To serotype dengue virus in sample, DNA switch was constructed. DNA switch composed of two sets of DNA probes where main probe A (MP-A) anneals with dengue priming strand (DPS) serotype 1 and 2, while MP-B anneals with DPS serotype 3 and 4. Each of the DPS that annealed to the same main probe generate different colour of silver nanocluster to serotype dengue virus. In the presence of specific dengue target, specific DPS could be toehold out and isolated via streptavidin-biotin affinity interaction. Isolated DPS binds with common primer to initiate polymerization and nicking process to generate silver nanocluster strands. Incubation of silver nanocluster strands with silver nitrate and reduction with sodium borohydride generates fluorescent under UV. Dengue virus serotype is able to be determined via the colour of fluorescent emitted by silver nanoclusters.

Keywords: serotyping; dengue; nanocluster; DNA

PP37: Cassettes hybridization for vector assembly (CHyVAs): An alternative approach towards in vitro antibody affinity maturation

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Abstract

Vector assembly is a method in molecular synthetic biology that assemble DNA parts into a functional vector system. Most of the vector assembly approaches stipulate the starting materials have to be in single stranded form and endonucleases are usually employed to digest double stranded DNA into single stranded. Here, we proposed a new and efficient vector assembly method – cassettes hybridization for vector assembly (CHyVAs) – that uses stable double stranded DNA and hybridization between homologous overlapping regions on each DNA cassette to construct a new vector. This method was successfully applied to generate functional vectors with desired protein and antibiotics inserts. Therefore, we envisage the application of CHyVAs as an alternative method to achieve antibody affinity maturation. In conclusion, CHyVAs provides a simple yet feasible alternative to chain shuffling and construction of mini-libraries for selection of affinity matured antibodies.

Keywords: synthetic biology; DNA assembly; affinity maturation; chain shuffling

PP38: Identification of potential clones recognized anti-*Strongyloides* antibodies by cDNA library immunoscreening

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Abstract

Strongyloidiasis is a parasitic disease caused by the nematode *Strongyloides stercoralis*. In human, this parasite can cause long-term infection or can disseminate to other organs in an immunosuppressed individual, the latter commonly result in a fatal outcome. Most patients are asymptomatic or present with non-specific gastrointestinal complaints. There is no gold standard method to rule out the infection and serology is commonly used for laboratory diagnosis. The available commercial tests are based on native parasite antigen extract which have problems of cross-reactivity with other helminthic infections. A recombinant antigen-based test is a good alternative for improved diagnostic specificity and standardized test quality, thus the present study was conducted to achieve this goal. In this study, potential infection biomarkers against strongyloidiasis were identified by immunoscreening a *S. stercoralis* phage cDNA library using two secondary antibodies, i.e anti-human IgG-HRP and anti-human IgG4-HRP. Three consecutive phases of immunoscreenings were performed using individual pre-adsorbed patients and control serum samples, and this resulted in selection of 20 cDNA clones from each IgG- and IgG4-phage immunoblots. Finally, two cDNA clones, namely Ss3a and Ssla, were selected as having high potential diagnostic value. Both clones were reactive with all serum samples (n=14) from patients with confirmed infection based on parasitological and/or DNA detection of *Strongyloides* larvae in their stool samples. The diagnostic specificities of the clones were also high i.e. 90% and 87% (n=24) for Ss1a and Ss3a respectively. Subsequently, inserts of these clones were cloned and recombinant proteins produced for use in the development of improved serodiagnosis for strongyloidiasis.

Keywords: Strongyloides stercoralis; cDNA library; immunoscreening; antibodies, strongyloidiasis; diagnosis; recombinant proteins

PP39: Multiplex real-time polymerase chain reaction assay for detection of helminthes and protozoan parasites in stools of eight aborigine communities in Malaysian Peninsular

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Abstract

Parasitic infections remain endemic among the aborigines in Malaysia. The routine diagnostic method for stool examination using microscopy is not sensitive and time consuming, especially when concentration and staining techniques are performed. In this study, a multiplex real-time PCR was used to simultaneously detect *Entamoeba histolytica, Giardia lamblia, Ancylostoma duodenale, Ascaris lumbricoides, Strongyloides stercoralis* and *Trichuris trichuria*. A total of 130 stool samples from aborigine communities of Termiar, Jakun, Semai, Semalai, Mahmeri, Jahut, Temuan and Orang Asli ethnics from Perak, Selangor, Johor and Pahang were analysed. DNA extraction was performed using QIAMP DNA Stool Mini Kit. Two-tube multiplex real-time PCR assays were performed to detect DNA of the six parasites, and the results were compared with microscopic examination. The results showed that the real-time PCR detected parasite DNA from all samples (n=130), 125(96%) were positive for both helminthes and protozoa, all contained two to four species of helminthes and 125(96%) contained one to two species of protozoans. Meanwhile microscopic examinations were positive for only 89 (68.5%) samples. This study showed that the prevalence of parasitic infections among the aborigines was still very high. The rate of detection by the real-time PCR was 1.5 times higher than by microscopic examination. In addition, the real-time PCR allowed multiple species detection in a single run, thus shortening the time to obtain results. In conclusion the multiplex real-time PCR provides a more accurate prevalence data on the parasitic infections among the aborigines.

Keywords: helminthes; protozoa; aborigines; multiplex real-time PCR

PP40: Biopanning of antibody phage clones using 'Ping Pong' panning

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Abstract

Phage display is known as the most robust tool for isolating specific high affinity binding molecules against a variety of targets. The display technology is essential for diagnostic and therapeutic applications, typically the antibody discovery and generation. Biopanning is described as the affinity selection method for the screening of phage displayed combinatorial antibody libraries in search for the target-specific ligands. Despite the fact that phage displayed antibody libraries has proven promising in the identification of target-specific molecules, the problems associated with recombinant antigens are affecting the selection efficiency. Recombinant antigens are often designed, validated and expressed via various expression systems as targets for antibody selection. Although antibody phage selection is often conducted with purified antigen, some antigens are difficult to be expressed and requires laborious downstream purification. Hence, crude antigen can be used as targets without undergoing purification procedures. Crude proteins or antigens are presented as the native mixture of expressed biomolecules, however in a most complex state whereby the endogenous proteins are expressed alongside with the antigen. The affinity selection methodology can be customized and optimized to cater with antibody phage selection against crude antigen. A proposed idea for affinity selection against crude ubiquitin is conducted by 'fishing' the ubiquitin by anti-ubiquitin phage while negative selection of ligands against endogenous proteins in one go. It is demonstrated that the idea could be feasible to select antibody phage against crude antigen with enrichment of positive phages.

Keywords: phage display; recombinant antigens; crude antigen

PP41: Optimization of Protein Expression and Extraction of Zika (ZIKV) Non-Structural Protein for Antibody Selection

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Abstract

Zika Virus (ZIKV) is an arthropod-borne virus which contained single stranded positive sense strand of RNA. The outbreak of Zika Virus are a serious threat to public health by causing fever, rashes, headache, dizziness and neurological complication, such as Guillian-Barre syndrome and microencephaly. The polyprotein of Zika Virus constitute 3 structural proteins (Envelop, E; Membrane precursor, PrM; capsid protein) and 7 non-structural protein (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5). NS proteins are co-translated on the endoplasmic reticulum (ER) membranes to form replication competent complex. Thus, anti-NS can be useful in diagnostic or therapeutic purpose. To produce NS protein, sequence of NS protein were chosen, synthesized and cloned into pRSET-BH6, expressed in BL21 (DE3) with the helper plasmid, pRARE3 at 25 °C, 160 rpm for overnight. The main challenge in producing NS protein was the formation of inclusion bodies during protein expression. Thus, 8M urea buffer was used after lysing the cell with lysis buffer and lysozyme. Besides, optimization were done on expression hosts, additives and urea concentration. The protein band were confirmed with SDS PAGE and western blot. In conclusion, selected non-structural protein were successfully expressed and extracted out for purification.

Keywords: Zika; non-structural protein; protein expression; purification; antibody

PP42: Making sense of the mess; pre-panning process for improved antibody enrichment in phage display

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Abstract

Antigen B is a major protein component of *Echinococcus granulosis metacestode* that causes human cystic echinococcosis which now becomes common in many regions of the world. Development of antibodies against Antigen B is important for therapeutic and diagnostic applications. The antibody selection was done using phage scFv library. Biopanning with the library was carried out to enrich anti-Antigen B antibodies. A major complication with biopanning processes is the enrichment of non-specific binders. Therefore, optimization of the panning process was done to improve antibody enrichment. We adopted a pre-incubation step utilizing immunotubes coated with the interfering proteins to isolate non-specific from target specific clones. Phage library preparation was pre-incubated before binding with the immobilized Antigen B on microtiter plate. Blocking with 5% PTM was used for biopanning and polyclonal ELISA analysis. The introduction of pre-panning clean-up of the library was able to reduce the background during panning. Polyclonal antibody ELISA analysis shows improve in background reduction with an increase in enrichment output. In conclusion, the additional step of background subtraction using the pre-panning clean-up was able to yield good polyclonal antibody enrichment.

Keywords: phage display; antibody; biopanning

PP43: Preparation of stable conjugation gold nanoparticles to antibody for immunochromatographic strip assay for the rapid detection

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Abstract

Gold nanoparticles (AuNPs) conjugates have been used in a variety of biological applications, including in basic research and clinical diagnostic. Preparation of stable AuNPs conjugates is a simple process involves passive adsorption causes by electrostatic and hydrophobic interaction between AuNPs surface and antibodies. This process is optimally achieved at a pH near the isoelectric point (pI) of the antibody being conjugated. This study focuses on the stable conjugation efficiency of the antibody with different size AuNPs and concentration of antibody adsorbed to the AuNPs. Different size of AuNPs (10 nm, 20 nm, 30 nm and 40 nm) were prepared using the seeding- growth method to conjugate antibody for immunochromatographic strip assay for rapid detection. The concentration of antibody adsorbed to the AuNPs is a critical parameter in the preparation of AuNPs conjugates. If the concentration of antibody adsorbed to the gold surface is very small, aggregation takes place upon addition of electrolytes present in a standard buffer. Determination of the optimal gold-antibody concentration was achieved using the challenge method with 10% NaCl solution. The minimum concentration of antibody that did not exhibit a colour change from red to purple or grey revealed the most suitable amount for conjugation. The conjugation stability was investigated by UV-Vis NIR spectroscopy and particles size analysis. Based on optimized conjugation conditions, the use of 40nm AuNPs exhibited superior performance for the detection of immunochromatographic strip assay relative to other sizes of AuNPs.

Keywords: gold nanoparticles; conjugation; antibody, immunochromatographic strip assay

PP44: Contamination of *Leptospira* spp. in flood affected areas in Kelantan

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Abstract

Leptospirosis is a common yet neglected zoonotic disease mainly caused by pathogenic *Leptospira* species (spp.). Leptospirosis causes mild to life-threatening complications in animals and human. Outbreaks of leptospirosis around the world have been associated to heavy rainfall and flooding. These extreme weather events increased the risk of leptospirosis to those who live within *Leptospira*-contaminated environments and also the magnitude of outbreaks. We aimed to investigate the presence of *Leptospira* spp. in environmental samples collected from areas affected by flood in Kelantan occurred in January 2017. An amount of 52 water and soil samples were collected from three districts which were Tumpat, Pasir Mas and Kota Bharu. The samples were cultured and enriched in liquid EMJH, a selective media for *Leptospira* spp. followed by dark-field microscope (DFM) observation to determine positive morphology for *Leptospira*. Only positive samples under DFM were preceded for detection of pathogenic *Leptospira*, performed using PCR targeting *LipL32* gene, a known conserved virulence factor among pathogenic *Leptospira*. Our findings revealed 35 positive samples for *Leptospira* under DFM: 19 (54%) from Tumpat, 10 (29%) from Pasir Mas and 6 (17%) from Kota Bharu. Four samples (11%): 3 from Tumpat and 1 from Pasir Mas were detected as pathogenic *Leptospira.* Therefore, this study confirms that *Leptospira*-contaminated environments are associated with flood.

Keywords: leptospirosis; flood; LipL32

PP45: A Nanocluster Beacon to detect FOXP3 sequence

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Abstract

DNA-templated silver nanocluster is a new class of fluorescence probe that has been reported and favourable in many diagnostic application owing to their special properties like small size, photostability and water solubility. By using the advantages of AgNCs, we adapted the AgNCs to isolate regulatory T cells (Tregs). These Tregs are responsible for immune modulation and its impairment may lead to imbalance of the immune system, resulting in autoimmune diseases. Isolating Tregs enables a better characterisation of Tregs, but it has been a great challenge due to the fact that the FOXP3 distinct marker is located intracellularly. Therefore, internalisation of probe into the cells without killing the cells were needed. Here~~by~~, we introduced an optimised method for detection of FOXP3 target with hybridising silver nanocluster probe to its target. The successful hybridisation of three-way junction with AgNC, G-rich and FOXP3 target have generated a shift in fluorescence spectra with an increased fluorescence intensity. The AgNC design was also used to hybridise FOXP3 mRNA using total RNA isolates. Similarly, hybridisation to FOXP3 positive RNA generated a shift in fluorescence spectra and an increase in fluorescence intensity. This silver nanocluster system enables a successful detection of FOXP3 target sequence with a shift in excitation and emission wavelengths of AgNC, which allows a rapid and easy detection of DNA and RNA.

Keywords: Silver nanocluster; Fluorescence shift; DNA Hybridisation

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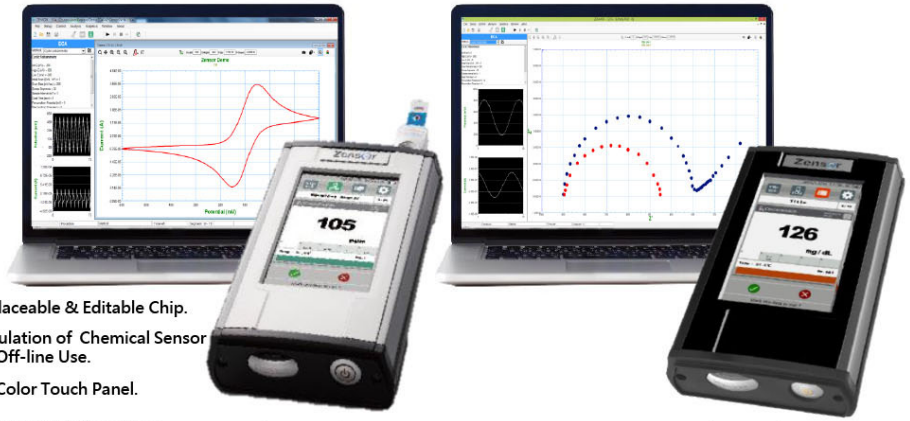

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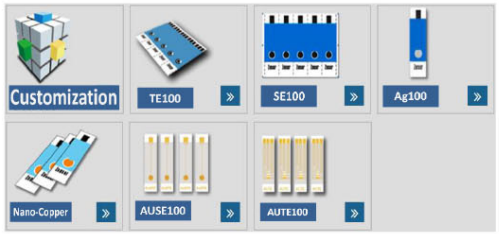

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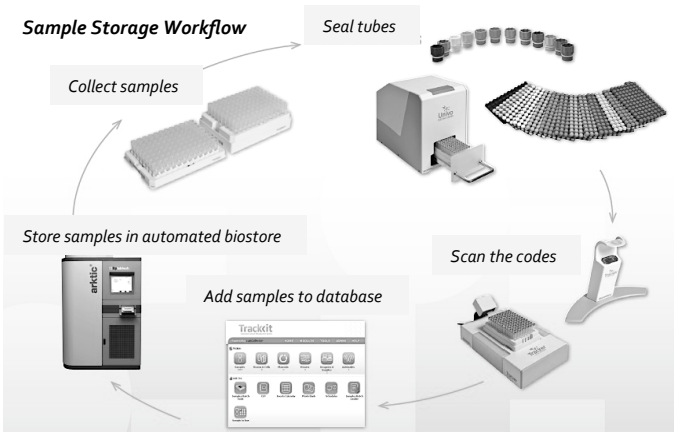

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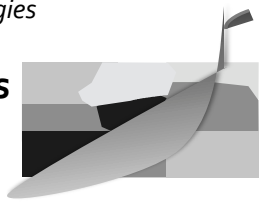

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