Daniel Turnberg Travel Fellowship Scheme

Alumni conference

19–21 November 2019
Landmark Hotel, Nicosia, Cyprus

The Academy of Medical Sciences

@AMS_Careers #AMSTurnberg

Daniel Turnberg Travel Fellowship Scheme

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The Academy of Medical Sciences

The Academy of Medical Sciences is the independent body in the UK representing the diversity of medical science. Our mission is to promote medical science and its translation into benefits for society. The Academy's elected Fellows are the United Kingdom's leading medical scientists from hospitals, academia, industry and the public service. We work with them to promote excellence, influence policy to improve health and wealth, nurture the next generation of medical researchers, link academia, industry and the NHS, seize international opportunities and encourage dialogue about the medical sciences.

Welcome

We are delighted to welcome you to the second Daniel Turnberg Travel Fellowship Scheme Alumni Conference.

Over the next few days, you will have the opportunity to:

- Present your own research and learn about the diverse and innovative projects being undertaken by your co-presenters
- Benefit from bespoke training focused on your career development
- Network with other alumni, Academy Fellows and invited guests
- Forge new collaborations.

During the 11 years, since it was launched, the scheme has supported over 270 Fellows from across the Middle East and the UK. We are delighted that it has again been possible to bring together a large number of the scheme's alumni, and we very much look forward to meeting you.

Thank you for joining us for this exciting event.

Leslie and Edna Turnberg
Lord and Lady Turnberg of Cheadle

Daniel Turnberg Travel Fellowship Scheme

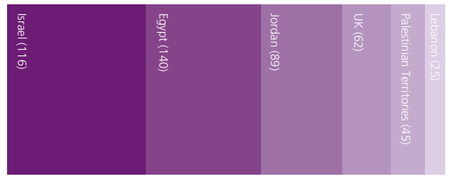
Applications

Number of applications

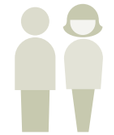
57%
Success rate

477 total applicants

Applicants' country of origin



Gender



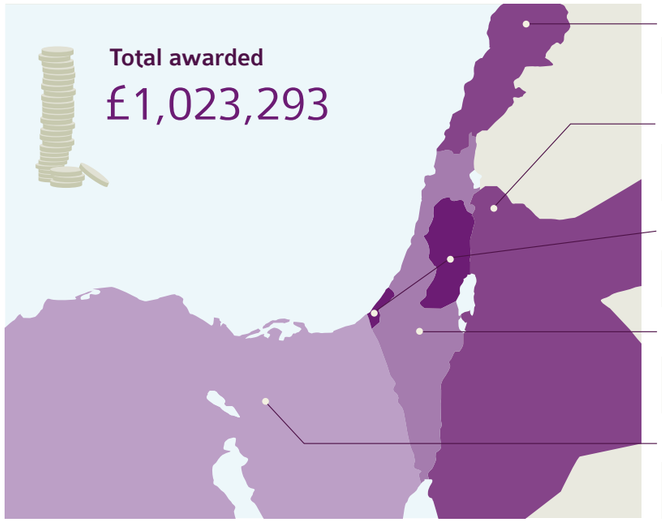
51% 49%

Fellowships

UK

47 Number of awardees
225 Number of visitors

Total awarded
£1,023,293



Lebanon

15 Number of awardees
4 Number of visitors

Jordan

38 Number of awardees
3 Number of visitors

Palestinian Territories

31 Number of awardees
1 Number of visitors

Israel

87 Number of awardees
37 Number of visitors

Egypt

54 Number of awardees
2 Number of visitors

Agenda

Day 1 – Tuesday 19 November 2019		
16:00	**Arrivals and Registration**	*Opposite Front Desk*
17:00	**Welcome Reception and Networking**	*Kantara Terrace*
18.00	**Conference Officially Opens/Pre-dinner Address** Lord Leslie Turnberg FMedSci	*Kantara A & B*
18.15	**Networking dinner**	*Kantara A & B*

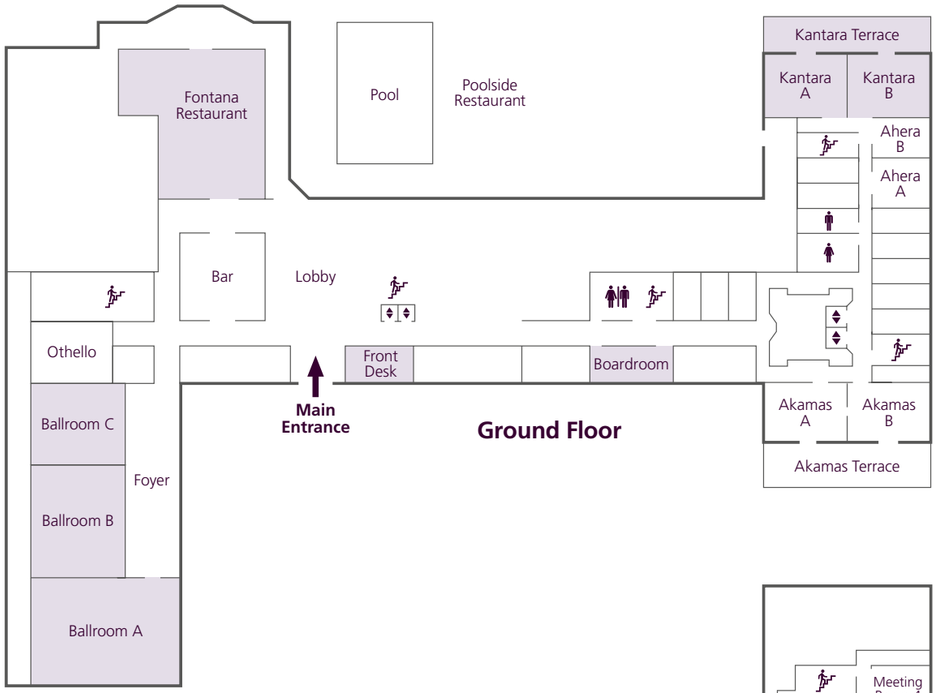
Day 2 – Wednesday 20 November 2019		
06.30 onwards	**Breakfast** **Poster Set-up**	*Fontana Restaurant* *Ballroom B & C*
09:00	**Welcome and Introduction to Day 2 of the Conference** Lord Leslie Turnberg FMedSci	*Ballroom A*
09:05	**Introduction to the Academy of Medical Sciences** Simon Denegri, Executive Director of the Academy of Medical Sciences	
	Oral Plenary Talks – 10 minutes each with 5 minutes for questions	
09:15	**Talk 1 – Dr Gal Dubnov-Raz,** Tel-Aviv University Prediction of Maximal Heart Rate in Children and Adolescents	
09:30	**Talk 2 – Dr Winnie Wefelmeyer,** King's College London The Emergence and Plasticity of Synapses at the Axon Initial Segment	
09:45	**Talk 3 – Dr Mohammed Alsbou,** Mutah University Alkaptonuria: From Basic Research to Clinical Trials – A Success Story from Jordan	
10:00	**Talk 4 – Dr Georges Daoud,** American University of Beirut Transcriptomic Profiling of Trophoblast Fusion Using BeWo and JEG-3 Cell Lines	
10:15	**Open Discussion of Talks 1-4**	
10:30	**Refreshments**	*Foyer*
10:45	**Talk 5 – Dr Heba Morsy,** Alexandria University Genetic Study of Egyptian Families with Suspected Primary Cilliary Dyskinesia	
11:00	**Talk 6 – Dr Yousef Najajreh,** Al-Quds University Genomic Studies for the Assessment of Platinum (IV) Susceptibility to Nucleotide Excision Repair (NER)	
11:15	**Talk 7 – Miss Lihi Ben-Reuven,** Weizmann Institute of Science NDE1 Role in Neurodevelopment: Characterization of Copy Number Variations of NDE1 gene using human brain organoids	
11:30	**Talk 8 – Dr David Greenberg,** University of Cambridge The Role of Empathy and Music in Social Conflict: An Investigation of an Israeli-Palestinian Youth Chorus	
11:45	**Open Discussion of Talks 5-8**	
12.00	**Lunch** **Poster Viewing**	*Fontana Restaurant* *Ballroom B & C*
13:00	**Poster Session Presentations** Attendees will be divided into groups	*Ballroom B & C*
14:50	**Refreshments**	*Foyer*
15:10	**Facilitated networking**	*Kantara A & B*
16:25	**Break**	*Foyer*
16:40	**Dr Maya Negev,** University of Haifa The impact of climate change on public health in the Middle East: from risk to opportunity	*Ballroom A*
17:00	**Keynote Lecture** **Professor Harry Hemingway FMedSci,** University College London 'The allure of the international classification of disease (ICD): big electronic health record data, phenomics and decision making for better health.'	
17:45	**Free time**	
18:30	**Pre-dinner Reception**	*Kantara Terrace*
19:00	**Conference Dinner**	*Kantara A & B*

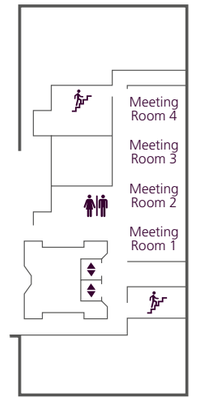
Day 3 – Thursday 21 November 2019		
06.30 onwards	**Breakfast and check-out** Please check-out before 1pm	*Fontana Restaurant*
08:25	**Welcome and Introduction to Day 3 of the Conference** Lord Leslie Turnberg FMedSci	*Ballroom A*
	Oral Plenary Talks – 10 minutes each with 5 minutes for questions	
08:30	**Talk 9 – Dr Sharon Anavi-Goffer,** Ariel University Effects of THC and CBD on Motor-like tics in Juvenile Mice	
08:45	**Talk 10 – Dr Mohamed Hamed,** Mansoura University The Role of MLK7 in Muscle Maintenance and Disease	
09:00	**Talk 11 – Dr Eman Alefishat,** University of Jordan Evaluation of factors affecting health-related quality of life in hypertensive patients using the EQ-5T tool in Jordan	
09:15	**Talk 12 – Professor Marei Sammar,** ORT Braude College-OBC Placental Derived Extracellular Vesicles Express Placental Protein-13 and Levels are Decreased in Preeclampsia	
09:30	**Open Discussion of Talks 1-4**	
09:45	**Refreshments**	*Foyer*

10:00	**Talk 13 – Dr Adnan Al-Hindi,** Islamic University of Gaza Epidemiology of Hydatidosis and Echinococcosis among Farmers and Dogs from Gaza strip, Palestine
10:15	**Talk 14 – Dr Polina Stepensky,** Hadassah Hebrew University Hospital Whole Exome Sequencing: a Decision-making Aid in Primary Immune Deficiency and Bone Marrow Transplantation
10:30	**Talk 15 – Dr Jad Abdallah,** Lebanese American University The Study of HSP90 inhibitor 17-AAG on neurobalstoma Stem Cells
10:45	**Talk 16 – Dr Mohamed Mandour,** University Catholique de Louvain Consequences of Infections on NK cell-mediated Cancer Immune Surveillance
11:00	**Open Discussion of Talks 13-16**
11:15	**Break** *Foyer*
11:25	**Career Development Session – Building effective partnerships – Part 1** *Ballroom B & C* Dr Steve Cross
12:20	**Lunch** *Fontana Restaurant*
13:00	**Career Development Session – Building effective partnerships – Part 2** *Ballroom B & C* Dr Steve Cross
14:00	**'Research in 3' – 7 talks of three minutes** *Ballroom A*
	Talk 1 – Dr Achraf Al Faraj, American University of Science and Technology Combination of anti-VCAM-1 and anti-IL4R alpha aptamers conjugated nanoparticles for efficient breast cancer diagnosis and therapy.
	Talk 2 – Dr Caroline Mullineaux-Sanders, Imperial College London The gut microbiota influences the in vivo lifestyle of the mouse pathogen Citrobacter rodentium.
	Talk 3 – Dr Vladimir Vinokur, Hebrew University of Jerusalem Neural stem cell-derived exosomes and cardioprotection.
	Talk 4 – Dr Randa Haddadin, University of Jordan Evaluation of antibiotic dispensing practice in community pharmacies in Jordan: A cross sectional study.
	Talk 5 – Mr Yiannis Philippou, University of Oxford Developing novel platforms for delivery and investigation of Vascular-targeted Photodynamic Therapy (VTP) of pre-clinical models of prostate cancer; towards multi-modality prostate cancer therapy.
	Talk 6 – Dr Shuli Svetitsky, Tel Aviv Sourasky Medical Center Pregnancy in women with nephrotic-range proteinuria
	Talk 7 – Dr Mohamed Abdel-Rahman, Suez Canal University Pyroptosis induced by scorpion venom antimicrobial peptides Smp24 and Smp43.
14:30	**Refreshments** *Foyer*
14:45	**Keynote Lecture** *Ballroom A* **Professor Maralyn Druce,** Queen Mary University of London From Daniel Turnberg Fellowship Awardee to Member of the Selection Panel
15:30	**Closing Address and Highly Commended Posters and Presentations Announced** Lord Leslie Turnberg FMedSci
15:45	**Close of Meeting**
Departures	

Conference map

The Landmark, Nicosia





Mezzanine Floor

Delegates are kindly reminded that they are expected to attend all sessions of the meeting.

The administration office is in the **Boardroom** should you need to speak to any of the organisers throughout the conference.

Speaker biographies

Lord Turnberg of Cheadle FMedSci

Leslie Turnberg was Professor of Medicine at the University of Manchester from 1973 to 1997, and consultant gastroenterologist at Hope Hospital, Salford and Dean of the Faculty of Medicine from 1986 to 1989. He was President of the Royal College of Physicians (1992 to 1997) and Chairman of the Academy of Medical Royal Colleges (1994 to 1996). He was President of the Medical Protection Society (1997 to 2007) and Chair of the Board of the National Centre for Replacement, Reduction and Refinement of Research in Animals (2004 to 2007). He was Vice President of the Academy of Medical Sciences (1998 to 2004) and served on the House of Lords Select Committee on Science and Technology (2001 to 2005).

Lord Turnberg is Chair of the Daniel Turnberg Memorial Fund and Travel Fellowship Scheme Selection Panel. He is a Trustee of The Wolfson Foundation and a number of other charities. He was knighted in 1994 and raised to a Peerage in 2000.

Professor Maralyn Druce

Professor Maralyn Druce undertook undergraduate training at Christ's College, Cambridge University and completed her clinical training at University College and Middlesex School of Medicine in 1994. She completed her higher medical training in Diabetes, Endocrinology and General Internal Medicine at the Hammersmith Hospital and Barts Hospital. She was awarded a Wellcome Trust clinical research training fellowship and obtained a PhD in physiology in Professor Steve Bloom's laboratory in Imperial College, focusing on gut hormones and their role in the peripheral and central control of energy homeostasis.

Maralyn went on to be awarded the Chadburn Lectureship at Barts and the London School of Medicine where she has remained since. She has a keen interest in teaching and completed her Masters in Medical Education (Dundee) in 2016. She is now Professor of Endocrine Medicine and Consultant Physician and Endocrinologist at Barts Health NHS Trust.

Current roles at Queen Mary University of London include Deputy Dean for Education (Postgraduate Taught Programmes) and Head of Governance for the Undergraduate MBBS and Dental programmes at Barts and the London. She is also Associate Dean for Undergraduates at the St Bartholomew's Hospital site.

Dr Steve Cross

Dr Steve Cross is a trainer and consultant to universities, museums and learned societies. He has worked with the Academy of Medical Sciences for a number of years, helping Fellows and awardees to develop communication, resilience and leadership skills, as well as teaching network-building and public engagement. Steve also works with various Universities including the University of Cambridge, Imperial College London and UCL, and funders including the Royal Society and the British Academy.

Steve was originally a lab scientist, with a PhD in the genetics of human heart development from the University of Nottingham. He then went on to be Head of Public Engagement at University College London, and has also worked for the Wellcome Trust, Science Museum and Centre for Life in Newcastle. Steve is a Fellow of Queen Mary University of London, a Wellcome Public Engagement Fellow and an Honorary Fellow of the British Science Association.

Professor Harry Hemingway FMedSci

As a clinician scientist and leader in using rapidly changing patient and population data resources for research, Professor Hemingway has helped establish, grow and evaluate the field of data science for health around the world. He aims to use insights gained from increasing scale and detail of data for health and healthcare within a framework of public trust.

A key focus of Professor Hemingway's current research is the human phenome project, for instance through the CALIBER resource. This open-access resource provides information, tools and phenotyping algorithms for UK electronic health records. By using large data this research can be applied to the 'patients like me' concept, stratifying patients into subgroups and moving towards more personalised medicine.

Professor Hemingway is Professor of Clinical Epidemiology and Institute Director at the University College London Institute of Health Informatics. Since 2018, he is also Research Director at Health Data Research UK, uniting five London universities in partnership for data science for health. In recognition of his contribution to advancing medical science and translating developments into benefits for patients and wider society, Harry was elected a Fellow of the Academy of Medical Sciences in 2019.

Simon Denegri OBE

Simon Denegri is the Executive Director of the Academy of Medical Sciences. Prior to taking up this role at the Academy, Simon was the National Director for Patients, Carers and the Public at the National Institute for Health Research (NIHR), and Chair of INVOLVE – the national advisory group for the promotion and support of public involvement in research funded by NIHR. He was Chief Executive of the Association of Medical Research Charities from 2006 until 2011 and, prior to this, Director of Corporate Communications at the Royal College of Physicians from 2003.

He also worked in corporate communications for Procter & Gamble in the United States from 1997 to 2000. He was awarded the OBE for services to the NHS, public health and social care research in the Queen's Birthday Honours 2018.

Networking activity

This conference is a great opportunity to make valuable connections with people spanning all career stages and specialities.

As well as including structured networking session on the main agenda, we've put together some networking checkpoints to help you make the most of your time here:

During the conference try to speak to:	
Someone delivering an oral presentation	☐
Someone from a different institution	☐
Someone who works in a different research field	☐
Someone who is at a different career stage	☐
A member of staff from the Academy of Medical Sciences	☐

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Daniel Turnberg Travel Fellowship Scheme

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Mrs Helen Abelesz Family Member
Professor Maralyn Druce Speaker & Panel Member
Professor Malcolm Rowland FMedSci Panel Member
Dr Steve Cross Guest Facilitator

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Miss Lauren Treacher Fundraising Officer, Academy of Medical Sciences
Miss Rachel Campbell Grants Officer, Academy of Medical Sciences
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Mrs Rachel Kelly Vivari Communications - Event Organiser
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Mr James Kendall AV Specialist

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Abstract: Abdallah et al.

The study of HSP90 inhibitor 17-AAG on neuroblastoma stem cells

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Institute where fellowship took place: The William Harvey Research Institute, Barts and The London Queen Mary University of London, London, UK

Background: Heat shock proteins (HSPs) function to ensure the proper conformation of substrate proteins when cells experience stress or damage. HSP90 is the most studied molecular chaperone that facilitates the maturation and stable conformation of several substrate proteins, many of which significantly contribute to tumor growth and survival. Therefore, the abrogation of their function using inhibitors is an attractive prospect, making HSP90 an interesting molecular target for drug discovery.

One of the original and most studied HSP90 inhibitors is a derivative of the geldanamycin antibiotic, 17-AAG. Through reversible binding to the ATP pocket of HSP90, 17-AAG potently disrupts its function, and ultimately induces tumor cell death.

Objectives: The aim of our study is to determine if the chemical inhibition of HSP90 using the drug 17-AAG would have a therapeutic effect on the malignant MYCN-amplified human IMR-32 and murine Neuro2A neuroblastoma cells, compared to the non-MYCN-amplified SK-N-SH human cells.

Method: We used siRNA for transcriptional knock-down (KD) of HSP90, and the drug 17-AAG for its chemical inhibition in the three cell lines. Cellular bio-function was assessed after siRNA KD or chemical inhibition of HSP90 including proliferation, migration and cell viability. Furthermore, differential protein expression of tumorigenic pathways was determined using western blot analysis.

Results: Our preliminary data show that targeting HSP90 by chemical inhibition with 17-AAG leads to anti-cancer activities, including inhibition of cell proliferation and viability. More interestingly, siRNA KD or the chemical inhibition of HSP90 leads to differential expression of other tumorigenic proteins including L1-CAM, prohibitin and HMGA1. Moreover, the transcriptional siRNA KD of HSP90 in IMR-32, Neuro2A and SK-N-SH does not alter cell proliferation nor cell migration.

Furthermore, HSP90 inhibition using 17-AAG reduced proliferation and viability in IMR-32 and Neuro2A cell lines. In addition, 17-AAG-mediated inhibition of HSP90 downregulates p-VEGFR and HMGA1 in IMR-32 but not in Neuro2A cells. Whereas 17-AAG-mediated inhibition of HSP90 induces apoptosis in IMR-32 cells.

Conclusion: HSP90 is a chaperon that assists in the correct folding and functionality of client proteins, some of which belong to tumorigenic pathways. Our preliminary data indicate that HSP90 inhibition may have therapeutic implications in the MYCN-amplified neuroblastomas. Cellular migration, cellular proliferation and viability are reduced after 17-AAG inhibition of HSP90. In addition, apoptotic rate increases in cells after drug treatment.

Abstract: Abdelghany et al.

Rapidly Dissolving Microneedle Arrays for Intradermal Delivery of Curcumin Nanosuspension

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Background: Rapidly dissolving microneedles (DMN) have attracted considerable interest, since they are composed of water-soluble polymers that completely dissolve or degrade in the skin. Lipophilic compounds do not dissolve in aqueous media; therefore, the incorporation of these compounds in DMN requires the formulation of these drugs in the nanosuspension form to allow homogeneous distribution of the drug in the DMN.

Objectives: The aim of this work is to enhance the intradermal delivery of curcumin via DMN. Intradermal administration of nano-formulated curcumin could allow sustained local administration, but also prolonged (weeks or months) systemic absorption, due to presence of the rich dermal microcirculation in the upper dermis. Microneedles create punctures in the stratum corneum and deposit their payload in the epidermal and upper dermal layers of the skin. Due to its low solubility in water, curcumin was formulated as a nanosuspension to reduce its size and then incorporated into DMN arrays. This offers a new avenue in enhancing intradermal delivery of curcumin for the treatment of local and systematic diseases, possibly including skin cancers and other skin disorders.

Method: Curcumin nanosuspension (CU-NS) was prepared using a nanoprecipitation method employing probe sonication. CU-NS was characterised for particle size, Scanning electron microscopy, and in vitro release. CU-NS was then formulated into CU-NS loaded microneedles (CU-MN), by two-layer centrifugation method. CU-MN was then characterised for mechanical strength, drug content, insertion capabilities in parafilm and in excised porcine skin, microneedle dissolution in porcine skin, optical coherence tomography, and finally, the deposition of curcumin in different layers of porcine skin following application of CU-MN.

Results: CU-NS particle size was 520 ± 40 nm, and the polydispersity was 0.27 ± 0.02. In vitro dissolution studies in 10% w/v Tween 80 showed that the CU-NS dissolved significantly faster than unmodified curcumin powder. CU-MN were able to withstand a compression force of 32 N for 30 s, which is comparable to hand insertion force. Moreover, these microneedles were able to penetrate excised neonatal porcine skin to a depth of 500 µm, dissolved completely in the skin within 60 min. After CU-MN dissolution, the drug diffused from the application site and migrated through the skin layers down to 2300 µm, significantly more than observed with topical application of CU-NS.

Conclusion: This suggest that the fabricated microneedles with the incorporated CU-NS could enhance the intradermal delivery of curcumin.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Abdelkader et al.

Challenges facing Egyptian forensic psychiatric services; a qualitative study of Egyptian forensic psychiatry health care provider's views

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Institute where fellowship took place: The University of Nottingham, Nottingham, UK

Background: There is a noticeable lack of gold standards for forensic psychiatric services in Egypt evidenced by long patient stays and a lack of standardized assessment tools which determine patient outcome.

Objectives: The current qualitative study aimed at exploring in depth the obstacles facing current forensic psychiatry services in Egypt in order to improve service provision and patients' quality of life.

Method: Purposive sampling was used to recruit participants. A structured interview guide was used in four focus groups consisting of 40 participants including doctors, nurses, psychologists and social workers working in the two forensic psychiatry governmental hospitals (Al-Abbassia and Al-Khanka).

Results: There were multiple limitations hindering the improvement of forensic psychiatry services in Egypt. They were presented as different themes, e.g.: prolonged periods of incarceration, lack of individualized rehabilitation and risk assessment, lack of systematized protocols for evaluation committees.

Conclusion: Egyptian forensic psychiatric services are in need of improvement. This could be solved by better collaboration between concerned parties (Ministry of Health and Ministry of Justice) to improve logistics and procedures of patients' handling together with applying international standards in assessment and management of forensic psychiatric patients as well as provision of counselling and training programs for health care staff.

Abstracts

Abstract: Abdel-Rahman et al.

Pyroptosis induced by scorpion venom antimicrobial peptides Smp24 and Smp43

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Background: Within the last decade, several peptides have been identified according to their ability to inhibit the growth of microbial pathogens. These antimicrobial peptides (AMPS) are a part of the innate immune system of all living organisms. Many studies on their effects on prokaryotic microorganisms have been reported; some of these peptides have cytotoxic properties although the molecular mechanisms underlying their activity on eukaryotic cells remain poorly understood. Smp24 and Smp43 are novel cationic AMPs which were identified from the venom of the Egyptian scorpion Scorpio *maurus palmatus.* Smp24 and Smp43 showed potent activity against both Gram-positive and Gram-negative bacteria as well as fungi.

Objectives: Here we describe cytotoxicity and mechanism of action of these peptides towards three non-tumour cell lines ($CD34^+$ (hematopoietic stem progenitor from cord blood), HRECs (human renal epithelial cells) and HACAT (human skin keratinocytes) and two acute leukaemia cell lines (myeloid (KG1a) and lymphoid (CCRF-CEM) leukaemia cell lines).

Method: Using a luciferase-based ATP luminescent assay and Hoechst 33342 and propidium iodide (PI) staining, qRT-PCR and electron microscopy, toxicity and molecular mode of action Smp peptides have been revealed.

Results: Treatment with Smp24 and Smp43 (4-256 µg/ mL) decreased the viability of all examined cell lines. There was a dose-dependent appearance of necrotic cells in all cell lines, although keratinocytes were markedly less sensitive. Cell membrane leakage as evidenced by the release of lactate dehydrogenase was evident in all cells and confirmed by scanning electron microscope studies which showed both pore formation and the formation of necrotic cell membrane blebs. Flow cytometry experiments using cells stained with PI provided evidence that Smp24 and Smp43 arrests cells in different phases of the cell cycle dependent on cell type. Investigating a range of necrotic genes by qRT-PCR indicated that the caspase-1 gene was uniquely up-regulated, and this was subsequently shown to be responsible for the downstream release of the inflammatory cytokine, IL-1B, using a dot-blot technique. Smp24 and Smp43 also induced formation of cell membrane blebs, appearance of autolysosomes, lipid droplets, residual bodies, multivesicular bodies and myelin lamellar structure as visualized by TEM.

Conclusion: Our results revealed a novel mechanism of action where Smp24 and Smp43 activated a cascade of events leading to acute cell pyroptosis through caspase-1-dependant pore formation and the release of the inflammatory cytokine, IL-1B.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Abdelsadik

Effect of hypercapnia on vascular remodeling and skeletal muscle atrophy in the fruit fly Drosophila melanogaster

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Institute where fellowship took place: The University of Nottingham, Nottingham, UK

Background: Lung diseases are common in children and adults. Variable and recurring symptoms, reversible airflow obstruction, and bronchospasm and episodes of wheezing, coughing, chest tightness and shortness of breath are common among lung diseases such as asthma and chronic obstructive pulmonary disease (COPD) which are a combination of genetic and environmental factors and sometimes are idiopathic.

Tissue remodeling can affect the entire bronchial tissue, including the vascular component of the mucosa. The bronchial mucosa is more vascularized in asthmatic patients than in healthy subjects, showing an increase in the number and dimension of vessels and vascular area. Moreover, peripheral muscle wasting is a common finding in advanced chronic obstructive pulmonary disease (COPD) and several other chronic diseases.

Objectives: To explore whether high CO2 can induce skeletal muscle atrophy in larval stages of Drosophila as in patients with lung diseases. To identify the tracheal vascular remodeling in response to hypercapnia and hypoxia.

Method: *We used the commonly used GAL4/UAS system in drosophila to track the changes in the muscles. Mef2Gal4>UASGFP fly line expression the green fluorescent protein (GFP) in the muscles of flies. We had exposed the animals for* 48hrs normocapnia (ambient air), hypercapnia (10% CO_2, 18.2% O_2) and hypoxia (5% oxygen). In addition, we used the normal and *Mef2Gal4>UASGFP* flies to count the thick terminal branches (TTBs) in the control and treated flies.

Results: Flies experienced different gaseous status showed several conformational changes in the tracheal branches. We tracked the larval newly formed tracheal branches in *Drosophila* in response to *hypoxia* or *hypercapnia.* We found a massive decrease when flies being in hypercapnia which is worsened over time. This effect is contradictory to larvae exposed to *hypoxia* where the number of tracheal branches is increased.

Moreover, we found a decrease in muscular mass of hypercapnia experienced larvae; this muscular atrophy is reversible when animals returned to ambient air. This effect is particular to specific muscles and not all-over the body and is not accompanied by any overall phenotypic changes.

Conclusion: In conclusion, tracheal system dynamically responds to imbalances in the ratio of oxygen to carbon dioxide (O_2/CO_2 Ration). A greater knowledge of the molecular mechanisms that underpin this challenge may provide an entry to understand the changes occur in asthma.

Abstracts

Abstract: Abou-Kheir

Life in 3D: Establishing Patient-Derived Organoids And Implications For Personalized Medicine

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Institute where fellowship took place: The Institute of Cancer Research, Surrey, UK

Background: Prostate Cancer (PCa) is the second most frequently diagnosed cancer and the second most frequent cause of cancer-related death in men worldwide. It is a heterogeneous disease, and the currently available cancer models fail to recapitulate the progression of PCa. The three dimensional (3D) organoid culture systems are rapidly emerging as potential models to investigate both basic developmental processes and disease mechanisms.

Objectives: The aim of this work is to employ fresh tissue specimens from a treatment-naïve cohort to optimize and establish 3D patient-derived organoids as an in vitro disease model for PCa progression and drug response. In addition, our aim was to generate novel PCa patient-derived cell lines.

Method: Fresh radical prostatectomy specimens were collected from different treatment-naïve patients (one unaffected and one tumor). Briefly, fresh tissue samples were digested enzymatically, and the resulting cell suspensions were plated in a 3D environment that employs Matrigel as an extracellular matrix. A cocktail of essential factors was used to enhance the establishment of organoids. Organoids and the corresponding tissue specimens were characterized using immunofluorescent analysis and immunohistochemistry. Furthermore, patient-derived organoids were employed for the assessment of drug response. Furthermore, PCa patient-derived cell lines were generated and their culture conditions were optimized. These cells were further characterized using immunofluorescent analysis. Statistical analyses were performed using Graphpad prism 6 software to test for the significance of results.

Results: More than 90% of fresh tissues were successfully established as organoids and also as 2D cells using the same culture media. The presence of prostate luminal (Cytokeratin 8, Androgen Receptor, Prostate Specific Antigen) and basal (Cytokeratin 5, Cytokeratin 14, and P63) epithelial lineages was confirmed by immunofluorescent analysis. In addition, the results showed differential drug response between patient samples. Moreover, our results demonstrated the ability to grow and maintain patient-derived organoids using only 5 factors components instead of the 12 initial components. In addition, we optimized the culture and maintenance of patient-derived 2D cells by plating on collagen type I and we have reduced the medium requirement to include EGF only as an essential component.

Conclusion: This study provides a repertoire of novel patient-derived organoids and cells from a unique cohort of treatment-naïve patients, as our results demonstrate that we succeeded in delineating the essential components needed to grow prostate organoids and primary cells with a high success rate and long-term maintenance in culture.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Abu-Youssef et al.

Targeting axon transport for optic nerve repair and retinoprotection

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Institute where fellowship took place: University of St Andrews, St Andrews, Scotland, UK

Background: As a part of the central nervous system (CNS), the optic nerve cannot regenerate after birth, whether injured by trauma or nerve degeneration. Growth of the axon, the longest branch of a neuron, relies on transport of membrane lipids and proteins to the axon tip by endosomes, the neuron's transportation organelles. Endosome activity is regulated by GTPases, enzymes that provide energy to cells by hydrolysing the energy molecule GTP. One GTPase that transports protein cargo is Rab11, and is regulated by a parent GTPase, Arf6. When activated, Arf6 moves endosomes retrogradely, while Arf6 inactivation moves endosomes anterogradely towards the axon tip. Yet the odds are stacked against neurons: expression of the Arf6 activator Efa6 increases with age, while the Arf6 inactivator Acap1 does not exist in the CNS. This prevents axon entry of membrane proteins like integrins and the neuronal growth factor receptor TrkB. Alongside proteins, axon growth requires lipid membrane precursors. The transport of membrane-carrying vesicles is regulated by the GTPase Rab10, whose activator Lgl1 is enriched in embryonic neurons.

Objectives: The project studies whether overcoming the axon restriction of protein and lipid membrane cargo leads to optic nerve regeneration and/or survival after injury.

Method: Adeno-associated viral constructs (AAVs) of Acap1, Efa6 siRNA, and the endosome cargo Rab11, integrins, and TrkB, will be tested, as will AAVs for Rab10 and Lgl1. *In vitro,* brain cortex neurons were transfected with the AAVs, with GFP as control. Axons were cut using live-imaging laser axotomy, and imaged for regeneration up to 14 hours post-injury. The amount and localization of Rab11, integrins, and TrkB entering the axon will be assessed by immunocytochemistry. Live-cell imaging of axon transport of endosome cargo in transfected neurons will be done using spinning disc confocal microscopy. The fraction of endosomes that move anterogradely or retrogradely will be quantified, as well as their velocity. *In vivo,* AAVs will be injected into the mouse/rat eye, and the optic nerve will be injured either via optic nerve crush as a trauma model, or laser-induced glaucoma as a neurodegenerative model. Axon regeneration and/or survival will be imaged using confocal microscopy of retina and optic nerve tissue.

Results: Retina imaging shows that our injected AAVs do target optic nerve neurons. Laser-axotomized Acap1-transfected neurons show almost twice as many regenerating axons than GFP-transfected neurons (58% vs. 30% respectively).

Conclusion: Results so far show that overcoming the blockade of growth cargo into the axon may boost CNS regenerative ability.

Abstracts

Abstract: Adams et al.

Developing a chick embryo slice model of spinal injury for screening new therapies

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Institute where fellowship took place: Bar-Ilan University, Tel-Aviv, Israel

Background: Implantation of therapeutic hydrogels could be effective for spinal cord repair. However, during technological development, testing is often performed in live animal models which are technically complex, expensive and associated with ethical implications. To address this issue we previously developed an organotypic spinal cord slice injury model using rodent tissue. Importantly, these systems are 3D tissue mimetic models with similar cellular composition, cytoarchitecture and 3D synapse and cell-cell contacts as found in vivo. Using these slices, we proved that major neuropathological features can be replicated in response to a transecting injury. Whilst useful, rodent tissue can be expensive, not readily accessible and is associated with ethical issues.

As an alternative, chick embryos replicate many features of mammalian spinal cord; possessing all major nervous system cells arranged in characteristic neuroarchitecture, suggesting they may also be used to establish slice cultures. Embryos are cost-effective, easily manipulated and are non-protected animals before embryonic day 14 (E14) offering significant 3Rs impact. However, they have never been tested as a model for testing new therapies in sites of spinal cord injury (SCI).

Objectives:
1. Investigate histopathology of the chick embryo organotypic slice model of SCI.
2. Examine injured tissue responses to new therapies.

Method: Chick embryos were sacrificed at E14 and the spinal cord extracted. Longitudinal slices were taken and cultured at an air:medium interface. Injuries were introduced using a scalpel and slices were cultured for 4-12 days to examine injury responses overtime. To investigate how injured tissue responds to new therapies, a clinical grade hydrogel was implanted into the injury site and injury responses monitored at 12 days post-intervention.

Results: Organotypic slices of chick embryo spinal cord showed characteristic pathological responses to a transecting injury, including glial scarring (which appears to develop over time), disrupted myelination, limited nerve fibre outgrowth and immune cell invasion. After implantation of the clinical grade hydrogel, scarring appeared to be disrupted and extensive nerve fibre outgrowth was observed in the scaffold.

Conclusion: Our data suggest that the chick embryo slice model could be used to investigate injury pathology and responses to new therapies in sites of SCI. Whilst live adult animal testing cannot yet be abandoned for therapeutic testing prior to clinical use, the chick embryo slice model may be used as a cheap, rapid, reproducible and replacement model within which to test new therapies.

Abstract: Ahmed

A short video Educational Channel for building a community of practice

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Institute where fellowship took place: The University of Nottingham, Nottingham, UK

Background: Creating a collaborative environment that fosters interprofessional development is a task required mainly in affirmation of the importance of interprofessional team functioning in healthcare. To create functional health teams that deliver quality service, there has to be a number of available factors and situations that set health care providers to accept and capitalize on diversity within teams. Among these factors is the capacity to accept and contribute to a shared educational pool.

Objectives:
The objective of this intervention is to create a portal for educational material that can be used in an interprofessional way by all actors in health care in an equal and mutually beneficial way that allows them all an opportunity to contribute and utilize eachothers' contributions.

Method: The FAIMER fellowship is designed to develop interprofessional professionals to build respect in the training setting in hope that this will be transferred to the hospital wards. The Egyptian Chapter of the fellowship that has adapted itself to the nature of the Middle East and North Africa Region that it serves. Identifying the need to create an open source venue for the products of the program we created a YouTube channel with playlists hosting videos that are produced by the fellows of the program all over the region under themes that reflect the fellowship themes; Educational methods, Assessment, Teaching Methods, Technology in teaching, Professionalism, Project management, Quality assurance and the products of the distant learning themes (ML Web) under creative commons license. The channel analytics were studied and learner feedback was taken. (https://www.youtube.com/channel/UCF53wrxV2XWv8g8qkr06ntg)

Results: Videos were found to be accessed at peaks that were coincidental with the dates of their ML Web online courses indicating that the use of the channel to fellows was for academic purposes. 29% of hits on videos were actually performed from outside Egypt. This reflected the utility of the channel to fellows outside the circle if the MENA FRI Institute. 90% of videos were closed after 2 minutes and so the average estimated time for new video production was 2-3 minutes. Upon requesting feedback from fellows, 89% were found to access the channel more than once a week. 67% thought that the channel was a good way to get their work visible.

Conclusion: Using a short video open channel to post educational material is acceptable as a tool to engage in a community of practice.

Abstract: Akhtar

Micromechanical and Ultrastructural Degradation of the Cornea

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Institute where fellowship took place: Nour Al Haya Eye Center, Heliopolis, Cairo, Egypt

Background: Keratoconus is the most common ectatic disorder of the cornea. Keratoconus is progressive and leads to irreversible visual loss due to increasing irregular corneal astigmatism, ultimately resulting in a decline of the quality of life of patients. The keratoconic cornea is characterized by a conical shape, due to the progressive thinning and protrusion. Furthermore, the loss of biomechanical properties is an important factor associated with keratoconus, with a localised reduction in stiffness in specific regions of the cornea. Given the increased prevalence of keratoconus worldwide, there is a need to better understand corneal degradation.

Objectives: This study aimed to develop an in vitro experimental model which can be used to understand how the biomechanical properties and ultrastructure of the cornea are altered with corneal degradation. Specifically, the project aimed to understand how the micromechanical properties and collagen ultrastructure are altered with in vitro degradation with α-Amylase (Amy) or collagenase (Col) enzymes, both of which are known to degrade the collagenous structure of the cornea.

Method: One hundred and twelve porcine corneas were obtained from a local abattoir. They were grouped into a control group (8 corneas) and 13 groups (8 corneas each) incubated for different periods (1, 2, 3, 4, 24, 48 hours) in varying amylase (10, 20 mg/ml) and collagenase (1, 2 mg/ml) concentrations. The epithelium layer was peeled off before incubation.

The biomechanical properties were determined with a Nanoindenter G200 system with a DCM-II head (KLA-Tencor, USA) to measure the micromechanical properties, with the corneas fixed in a holder and pressurised at normal intraocular pressure (15 mmHg) during the testing. Atomic force microscopy (AFM) with a Bruker Multimode 8 instrument was used to assess the collagen fibril organisation following the in vitro degradation.

Results: The elastic modulus decreased in the corneas as the concentration of either amylase or collagenase and incubation time increased. The maximum reduction in the elastic modulus (61%) was observed when the corneas were incubated in a solution contains both amylase and collagenase for 4 hours. Amylase and collagenase treatment dramatically affected collagen fibril morphology and digested the proteoglycans, leading to a deterioration of mechanical properties.

Conclusion: Amylase and collagenase treatment decrease the localised mechanical properties and disrupt the collagenous structure of the cornea. This enzymatic degradation method may serve as a model for understanding ectatic corneal conditions such as keratoconus.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Akiva Kabiri et al.

Pitch-Color Synesthesia and Absolute-Pitch

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Institute where fellowship took place: The University of Nottingham, Nottingham, UK

Background: Synesthesia is a neurological condition in which otherwise normal individuals experience two commonly independent perceptions as joined together. In pitch-color synesthesia a musical pitch evokes an additional, concurrent perception of a color. Pitch-color synesthesia is often associated with Absolute Pitch (AP), which is the ability to identify pitch tones without an external tonal context.

Objectives:
The present study aimed at testing the importance of absolute pitch (AP) in pitch-color synesthesia.

Method: AP and non-AP pitch-color synesthetes were presented with a Stroop-like task where they were asked to name the color on the screen and ignore the accompanying musical pitch. The synesthetical color elicited by the pitch could be congruent or incongruent with the color presented.

Results: When the musical pitch was auditory, only AP possessors presented a congruency effect whereas when the pitch was presented visually (as a written note) both groups presented a significant congruency effect. These results suggest that in pitch-color synesthesia additional color perception, in response to musical pitches, is automatic and impossible to suppress. However it is also possible that color synesthetical association could be elicited by auditory pitches or musical notes, depending on AP ability.

Conclusion: While AP is characterized by that ability to automatically label pitch, the results suggest that synesthetical associations in pitch-color synesthesia are semantically mediated and related to the name of the pitch. In this case, pitch-color synesthesia is not necessarily related to the auditory experience of hearing musical pitches but rather to pitch identification.

Abstracts

Abstract: Akour et al.

Urinary megalin in association with progression markers of Diabetic Nephropathy

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Institute where fellowship took place: Newcastle University, Newcastle upon Tyne, UK

Background: Megalin is a 600-kDa protein expressed in renal proximal tubular cells and it is involved in the reabsorption of vitamin D binding protein. Recently, urinary megalin excretion has been evaluated as a potential urinary marker of nephropathy.

Objectives: The aim of this study is to evaluate the correlation between the urinary megalin, as a potential marker of diabetic nephropathy, and serum vitamin D levels.

Method: This was a pre-post interventional study in 63 patients with type 2 diabetes mellitus. Vitamin D was administered to participants for six months, then their clinical parameters (Blood pressure, glycemic control, lipids) as well as urinary megalin levels were compared to those of baseline. ELISA was used to measure megalin levels, and SPSS® version 20 was used to perform statistical analysis.

Results: A stepwise forward logistic regression which was adjusted for Blood pressure, plasma glucose, and calcium levels showed that there is a significant inverse association between vitamin D levels and megalin levels in urine (OR= 0.281, p-value=0.047). There was a significant improvement in kidney function, as showed by an increase in glomerular filtration rate (GFR) and a decrease in Albumin excretion (ACR), with concomitant decrease in urinary megalin and increase in vitamin D3 serum levels. The decrease in megalin was more pronounced than ACR, which indicates that megalin is more sensitive than ACR to changes in renal function over a shorter period of time.

Conclusion: Urinary megalin is a new potential marker for diabetic nephropathy and its progression factors, and it is more sensitive than albumin.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Al Faraj

Combination of anti-VCAM-1 and anti-IL4Rα aptamers conjugated nanoparticles for efficient breast cancer diagnosis and therapy

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Institute where fellowship took place: King's College London, London, UK

Background: Targeting of specific biomarkers overexpressed on tumor cells is considered as promising approach for enhanced cancer management. Aptamers are considered as potential candidates for both diagnostic and therapeutic applications.

Objectives:
Anti-VCAM-1 and anti-IL4Rα aptamers were assessed as therapeutic and diagnostic tool for breast cancer. Following intravenous injection of SPIO nanoparticles-conjugated aptamers, their selective targeting to tumor site and enhanced therapeutic efficiency was monitored using noninvasive MRI and Bioluminescence imaging (BLI).

Method: Biocompatible SPION were conjugated to anti-VCAM-1 or anti-IL4Rα aptamers and their conjugation efficiency was assessed by measuring the Fluorescence and UV-Vis absorption. The viability of Luciferase-expressing 4T1 cancer cells in the presence of anti-VCAM-1 and/or anti-IL4Rα aptamers were assessed by monitoring their bioluminescence signal and the changes in the absorbance and the fluorescence of Alamar blue dye. Tumor-bearing mice underwent biweekly BLI to monitor the growth of the tumor site. The therapeutic efficacy was then longitudinally assessed following each treatment condition (i.e. individual or combined injection of aptamers-conjugated SPION) for up to 4 weeks by quantifying the tumor volume in the mammary fat pad of mice using noninvasive MRI on a 4.7T magnet.

Results: Cells treated with anti-VCAM-1 and anti-IL4Rα aptamers showed no significant increase in the absorption and fluorescence intensity of Alamar dye compared to non-treated cells or cells incubated with truncated anti-VCAM-1 aptamers. Aptamers specifically target the VCAM-1 and IL4Rα receptors with high affinity. When the aptamers bind to the receptor, they block and inhibit their biological functions and thereby suppress the growth of the tumor cells. In vitro bioluminescence assay confirmed the suppressing of the cells incubated with both aptamers. Quantification of tumor signal and size using noninvasive BLI and MRI revealed that, while the radiance efficiency and tumor volume in non-treated mice increased gradually in a time-dependent manner, they were found to significantly decrease following injection of either anti-VCAM-1 or anti-IL4Rα aptamers conjugated SPION. Remarkably, this attenuation effect was significantly more prominent when combining both aptamers-conjugated nanocarriers.

Conclusion: Anti-VCAM1 and anti-IL4Rα aptamers were used as theranostic tool for breast cancer. Cell viability and bioluminescence assay confirmed that these specific aptamers suppress the function of VCAM-1 and IL4Rα receptors and promote tumor cells apoptosis. The enhanced treatment was confirmed in vivo as assessed by monitoring tumor inhibition using noninvasive BLI and MRI. A synergetic and more prominent effect was observed when combining both aptamers.

Abstracts

Abstract: Albakain

New era for analyzing drugs exist in environmental and biological samples

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Institute where fellowship took place: Queen's University, Belfast, UK

Background: Analytical, Bioanalytical and Environmental Chemistry.

Objectives: Before moving to the step of wastewater treatment, scientists try to find new method for green analysis of environmental and biological compounds may exist in water, soil, etc... Supercritical fluid chromatography is considered as a green technique due to the low consumption of organic solvents. While the mechanisms involved in is complex because they are influenced by: temperature, pressure, chemistry of the mobile phase and nature of the stationary phase. Herein, for the first time, a new and technique was used to analyze drug may exist in the environmental or/and biological samples.

Method: A set of 14 drugs of different pharmaceutical families was selected to test and classify the 8 selected stationary phases: XBridge HILIC (HILIC), Silica (Silica), Diol, 2-Ethylpyridine (2-Et), C4, Amino (NH2), Cyano (CN), and Propylpyridylurea (PPU) under 12 conditions. Gradient elution of methanol proportion was implemented. The tested drug residues have been injected separately at 3.0 µL. UV detection was carried out at 220 nm. All runs were operated at a flow rate of 2.0 mL/min. The statistical analysis was performed using MATLAB.

Results:
PARAFAC Output in Condition-Dimension PARAFAC plots indicated that the tests fall roughly into two distinct categories. The results reveal that the experimental conditions were grouped according to the gradient elution similarity. The influence of temperature and pressure on clustering of conditions also needs to be commented upon but less than the temperature effect.

PARAFAC Outputs in Drug-Dimension Drugs were grouped according to their acid-neutral versus basic characteristics as follows: group A which is a mix of neutral and acidic compounds (ibuprofen, diclofenac, etodolac, warfarin, theophylline, hydrocortisone, ipriflavone, caffeine, and antipyrine) and group B (basic compounds) (nadolol, terfenadine, haloperidol, toremifene, and carvidolol). Herein, antipyrine is a weak base, which behaved like neutral in our conditions, so it is clustered with neutral hydrocortisone. Theophylline also is a weak acid and behaved as neutral in the current running conditions; thus it was clustered with neutral caffeine and ipriflavone.

Conclusion: The wide ranges of the studied chromatographic conditions and drugs were clustered to uncover the complex retention mechanisms often involved in SFC. SFC columns were grouped when they exhibited comparable mechanisms for retaining different drugs including primary and secondary interactions. Regarding the effect of the parameters on column classifications, the gradient elution of % MeOH was the dominating parameter over the temperature and the pressure. Moreover, (1) different conditions in SFC could be minimized into only two clusters since some conditions were clustered together and (2) for similar kinds of operational conditions, columns, and experiments, a reduced set of drugs of different chemistries could be involved in the future.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Alefishat et al.

Evaluation of Factors Affecting Health-related Quality of Life in Hypertensive Patients Using the EQ-5D Tool in Jordan

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Institute where fellowship took place: The University of Nottingham, Nottingham, UK

Background: Hypertension(HTN) is a major risk factor for CVD, it is an epidemic health problem with 1 billion people affected, causing four million deaths annually worldwide which pushes HTN to be the third leading cause of death with mortality rate of 13% [2]. The lack of symptoms in patients with elevated blood pressure create a challenge for clinicians to educate patients about the long-term consequences of hypertension and to improve patient medication adherence[4].

Objectives:
The aim of the present study is to assess Health-related quality of life (HRQoL) in patients with hypertension and the variables associated with poor HRQoL among them.

Method: Three hundred hypertensive patients visiting outpatient clinics (cardiology and internal medicine) were recruited from four hospitals in Jordan. Patients' Socio-demographic and medical data were collected from patient interviews and medical files, and the Arabic version of EQ-5D tool was used to evaluate their HRQoL. Simple linear regression was performed to assess patients factors associated with poor HRQoL.

Results: During the study period, 300 patients were found to have hypertension. The mean score of the EQ-5D index of the 300 participants was 0.732 (SD= 0.29, range from -0.594 to 1.0).

Many participants reported some problems, with the highest percentage for some problems shown to be for the mobility dimension (43.3%) and the lowest percentage for self-care (13.9%). Extreme problem represented less than 10% for all dimensions. Using simple linear regression analysis, seven variables were significantly found to predict the EQ-5D index value (P-value <0.05). These were: gender, monthly family income (medium, low and poor income), number of medical conditions, number of medications, number of hypertensive medications, duration of hypertension, and the presence of any ASCVD.

Conclusion: The current study highlights indicators associated with HRQoL that can guide healthcare providers through to improve the outcome in hypertensive patients. The ability to identify indicators of poor HRQoL has been proposed to be crucial for determining targets of intervention for the prevention and treatment of disease and improving clinical care.

Abstract: Al-Hindi et al.

Epidemiology of Hydatidosis and Echinococcosis among farmers and dogs from Gaza strip, Palestine

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Institute where fellowship took place: College of Science & Technology, School of Environmental and Life Sciences, University of Salford, UK

Background: Zoonotic diseases are important issue in Gaza strip. Echinococcosis is a disease caused a causative organism, the dog tapeworm *Echinococcus granulosus,* is transmitted cyclically between cannines and numerous herbivorous livestock animals, which can serve as intermediate hosts (including sheep's and rodents). When tissues of human or intermediate host are infected with hydatid cyst this is called hydatidosis.

Objectives: The aim of the present study was to study the epidemiology of the of Hydatidosis and Echinococcosis among farmers and dogs in Gaza Strip.

Method: We collected 300 sera samples from farmers in Gaza and 37 stool samples from dogs. Serum samples (*n*=296) were collected from farmers in Biet-lahia (North Gaza) and stored at -20°C until used. Sera samples were examined using AgB5 and DNA was extracted from dogs faecal samples using DNA extraction mini kit according to the Manufacture instructions. PCR and sequencing were performed at Salford University (Cestode group).

Results: The molecular examination of *Ecchinococcus granulosus* isolated from dogs, proved that the prevalence was 6/38=15.7%.

In this investigation, serum samples (*n*=296), were collected from an area of Gaza and subjected to analysis by ELISA to evaluate the incidence of cystic echinococcosis. Optical density values above the cut-off point (0.31) were considered to be positive. Hydatid cyst fluid antigen and AgB showed seropositivity with a frequency of 13.8% 13.5% respectively.

Conclusion: The present findings of DNA confirm the existence of Hydatid cyst disease in faecal samples from dogs in Gaza, and the he genotype was G1. In addition, the seropositivity of sera samples for hydatid cyst disease. **It is recommended to:** Control of stray dogs especially in boarders' regions. Education of Palestinian public towards transmission methods of the disease. Demonstration the seriousness of the slaughtering inside the houses on the health of the people is their lack of knowledge and the nature of hydatid.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Al-Kadi

Automated liver cancer detection and segmentation

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Institute where fellowship took place: Institute of Biomedical Engineering, University of Oxford, Oxford, UK

Background: The ability to rapidly and accurately identify tumor location in ultrasound images is limited due to inherent low contrast. Early diagnosis of liver cancer can assist clinicians for faster and more reliable treatment outcomes. Employing artificial intelligence for automated liver cancer detection and segmentation would positively impact on the efforts in dealing with this disease.

Objectives: The research aims at extracting large number of quantitative features from raw 3D ultrasound imaging data via employing a hand-crafted technique (based on fractal dimension characteristics) and deep-learning (U-Net architecture) technique for liver tumour segmentation.

Method: The work involves statistical modelling of the backscattered echo by applying stochastic-based models for quantifying self-similar patterns. Different patches representing the tumour area and surrounding tissue regions were extracted and transformed to localized fractal dimensions. These hand-crafted features are combined with the learnt features using the U-Net convolutional neural network for automated liver tumour segmentation.

Results: Initial experiments suggest that statistical modelling of the backscattering echo can better characterise the change in tumour shape, and by investigating the acquired spatial scatterer fractal patterns, important cues on tumour morphology can be revealed.

Conclusion: Statistical modeling of the backscattering echo based on the fractal dimension and deep learning effectively characterize the changes in tumor shape, and hence provide better delineation of tumor boundaries.

Abstracts

Abstract: Al-Rahamneh et al.

The Prevalence of Risk Factors among Hypertensive Individuals during the 5 Years that Precede Hypertension Diagnosis

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Background: Hypertension is an important risk factor for heart attacks, heart failure, stroke, renal failure and kidney disease. Controlling BP with antihypertensive agents can reduce strokes by 35-40%, heart attack by 20-25% and heart failure by more than 50% (Chobanian et al., 2003).

Systolic blood pressure (SBP) is defined as the maximum pressure produced during the cardiac cycle. It is recorded during systole. Therefore, it is called SBP. Systolic blood pressure depends mainly on the cardiac output (Q). While diastolic blood pressure (DBP) is defined as the minimum pressure recorded during the cycle, it depends mainly on the peripheral resistance (Pal and Pal, 2005).

Objectives: The aim of the current study was to assess the prevalence of risk factors of hypertension among individuals with hypertension during the five years that precede the disease diagnosis from medical specialists.

Method: The study sample consisted of (514) males and females with hypertension, (257 males and 257 females). Inclusion criteria were; his or her age is ≥ 35 years, diagnosed with hypertension. The study population consisted of all Jordanian male and female adults, aged ≥ 35 years and diagnosed with hypertension. The descriptive approach was employed. The researchers designed a questionnaire for data collection. Content validity and reliability was established for the questionnaire. Data were analyzed using SPSS version 16. Means, standard deviation and chi-square techniques were used to analyze the data.

Results: The results showed that hypertension was more common among low educated individuals, perceived stress scale was moderate among persons with hypertension, and 47% of the sample were obese (M: 30.2 ± 5.4 Kg\m^2, F: 31.6 ± 5.8 Kg\m^2) during the 5 years that precede hypertension diagnosis. The results also showed that 81.9% of the study sample consumed moderate to very high amount of salt, and 64% of the study sample did not use to exercise at moderate or high intensity during the 5 years that precede hypertension diagnosis.

Conclusion: The researchers recommend healthy individuals to adopt healthy lifestyle to avoid hypertension incidence. These includes: exercising at low to moderate intensity 3-5 times a week, monitoring their weight, quitting smoking, avoiding high amount of salt intake and sugar, controlling and avoiding stress.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Al-Saraireh et al.

Inhibition of cell surface polysialic acid biosynthesis modulates tumor cell migration

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Institute where fellowship took place: University of Bradford, Bradford, UK

Background: Polysialic acid (polySia) is a carbohydrate polymer expressed on the surface of NCAM (neuronal cell adhesion molecule) in many cancer cells where it modulates cell-cell and cell-matrix adhesion, migration, invasion and metastasis. PolySia-NCAM expression is strongly associated with poor clinical prognosis and correlates with aggressive/invasive disease in small cell lung cancer, pancreatic cancer, neuroblastoma and many other tumors principally of neuroendocrine origin. SiRNA knockdown of polysialyltransferase ST8SiaII (STX), the enzyme primarily responsible for polySia synthesis in tumors, has been shown to abolish tumor cell migration . Besides brain regions with persistent neuronal plasticity, polySia is essentially absent from the adult body. STX inhibition thus presents a novel, selective, highly attractive and largely unexplored therapeutic opportunity to reduce dissemination of polySia-expressing tumors.

Objectives:
1. To design and synthesize compounds that inhibits the polysialylation of NCAM.
2. To develop particular assays to quantify the reduction of level of polysialylation of NCAM and determine the effect of reduction of polysialylation on tumor cell migration and invasion.

Method: Using endoneuraminidase, an enzyme that specifically cleaves polySia chains from NCAM, we can assess the rate and extent to which polySia growth is inhibited in the presence of agent in cellular systems. In addition, an in vitro scratch assay was established to evaluate modulation of cell migration using a transfected isogenic cell line system (C6-STX: polySia +, ST8SiaII + / C6-WT: polySia -, ST8SiaII) and neuroblastoma cell lines known to express polySia-NCAM, ST8SiaIV and ST8SiaII (SHSY-5Y and IMR-32).

We have designed and synthesised inhibitors of STX and the polysialylation process. The potency of these compounds has been increased by chemical modification, resulting in greater lipophilicity. Using an isogenic cell line system and human neuroblastoma cells these compounds were evaluated for their ability to reduce polySia expression and to modulate cell migration in vitro.

Results: We have identified CMP-sialic acid precursors, including compounds ICT-3172 and ICT-3176, which reduced polySia expression and tumor cell migration by up to 70%. These effects were only found in cell lines expressing STX and polySia.

Conclusion: We have identified a number of key modifications to polySia biosynthetic precursors which dramatically decrease cell migration in cells over-expressing STX through modulation of polySia assembly. The potential of the polySia biosynthesis pathway, and in particular STX, as attractive therapeutic targets in metastatic tumors is discussed.

Abstracts

Abstract: Alsbou

Alkaptonuria: from basic research to clinical trials - A success story from Jordan

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Institute where fellowship took place: Royal Liverpool University Hospital, Liverpool, UK

Background: Alkaptonuria (AKU) is a rare autosomal recessive disorder with an incidence of 1:250,000 worldwide. It is characterized by a lack of homogentisate 1,2 dioxygenase enzyme, causing excretion of homogentisic acid (HGA) in urine and accumulation of HGA in connective tissues. Clinical manifestations include dark urine, dark-black pigmentation of connective tissues (ochronosis), and arthritis of large joints and spine. No previous studies have been conducted so far in Jordan. This is the first study to highlight the AKU in Jordan.

Objectives:
The objectives of the study were to identify AKU patients in Jordan, create AKU patients registry and to identify the disease causing mutations, to find treatment for AKU patients, and to establish collaboration and networking with AKU sisters societies worldwide. Finally to raise the awareness about AKU among healthcare providers and the community in Jordan.

Method: Urine samples were collected from all suspected patients and all family members with history of the disease and laboratory investigations were perform to confirm the diagnosis of AKU. Quantitative measurement of HGA levels in urine samples was done by using Gas chromatography mass spectrophotometer (GCMS). Blood samples were collected from AKU patients, carriers of the disease and genetic analysis was performed.

Results: We identified 80 cases with AKU in Jordan (age range, 2 months-77 years), two third of patients were under the age of 30 years. AKU research office and Jordanian AKU society were established to support patients and their families. Novel mutations were identified in AKU patients. 19 patients from Jordan were involved in DevelopAKUre Project, which is an international clinical trial funded by the European Commission to find a cure for AKU.

Conclusion: The prevalence of AKU among Jordanian is likely to be greater than prevalence rates worldwide due to the high rate of consanguineous marriages. Further studies and effective screening program are needed to detect undiagnosed cases of AKU, to provide genetic counselling, and ultimately to prevent the occurrence of new case of AKU.

Abstract: Altaani

Taste Masking of Clarithromycin by Eudragit EPO using Hot Melt Extrusion for the Preparation of Orally Disintegrating Tablets

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Institute where fellowship took place: Queen's University Belfast, Belfast, UK

Background: Clarithromycin is a bitter tasting drug used in the treatment of infections. The bitter taste of clarithromycin decreases its acceptance and reduces patient compliance. Many patients cannot swallow tablets such as children and elderly patients. It is desirable to prepare the drug in dosage form that is easy to swallow with acceptable taste.

Objectives: The objective of this research is to mask the bitter taste of clarithromycin using a carrier processed by hot melt extrusion technology. The product will be used in the preparation of orally disintegrating tablets (ODT).

Method: Clarithromycin was embedded in Eudragit EPO using hot melt extrusion technology. Polymer to drug ratio and temperature during extrusion were varied. The extruded product was milled using ball mill. The product were characterized for drug loading, particle size, powder flow and yield. XRD, DSC and FTIR were used to evaluate the solid state of the drug.

The products were used in the preparation of ODT. XL-PVP or Primojel were used as superdisintegrants. Tablets were evaluated for tablet dimensions, hardness, friability, tensile strength, porosity and disintegration time. Drug release from ODT was tested at different pHs. ODT were evaluated using 10 human volunteers for disintegration time, roughness and bitterness.

Results: Drug loading of the milled extruded products varies depending on polymer to drug ratio. The results shows minimal drug loss during extrusion with yield between 88.9-96.7%. The particle size ranges between 138- 330 micron with narrow particle size distribution. Powder flow were passable to poor indicating the need for lubrication. XRD, DSC and FTIR results indicates that clarithromycin is present in form II. Testing of the tablets showed that as the ratio of the polymer increases, the tablet were denser, harder and the disintegration time were longer. Tablets prepared with XL-PVP tend to be denser, harder, less porous and of longer disintegration time than tablets prepared with Primojel. In vivo testing showed that tablets prepared with XL-PVP have better taste with longer disintegration times than those prepared with Primojel and as the ratio of polymer increases, the taste of the tablet were less bitter and disintegration time is longer.

Conclusion: Hot melt extrusion of bitter tasting drugs in Eudragit EPO is an excellent technique to mask the drug taste. The extruded product can be used to prepare ODT.

Abstract: Anavi-Goffer et al.

Effects of THC and CBD on motor-like tics in juvenile mice

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Institute where fellowship took place: Ariel University Center of Samaria, Ariel, Israel

Background: Delta-9-tetrahydrocannabinol (Δ^9-THC), the principle psychoactive cannabinoid of *Cannabis sativa*, reduces DOI-induced head twitch response. These results are further supported by clinical reports describing a significant amelioration of symptoms when cannabis was used by patients with Tourette syndrome. However, the effect of cannabidiol (CBD), the main non-psychoactive cannabinoid of *Cannabis sativa*, has not yet been investigated. In this study we selected to focus on the effects of CBD on 2,5 dimethoxy-4-iodoamphetamine (DOI), a potent agonist of the serotonin 5-HT_{2A}/5-HT_{2C} receptors, which increases head twitch response. DOI-induced head twitch response has been proposed to model motor tics of Tourette syndrome.

Objectives:
To study the effects of Δ^9-THC and CBD on DOI-induced head twitch response in juvenile mice.

Method: The behaviour of juvenile C57BL/6J male mice was tested in the presence or absence of DOI. The number of head twitches and the frequency of grooming behaviour were recorded in the open field cage.

Results: Our results show that DOI induces dose-dependent head twitch response and increased grooming behaviour in juvenile C57BL/6J male mice, resembling the onset of motor tics in children with Tourette syndrome.

CBD had a small, but significant, reversal effect on head twitch response. However, CBD had no effect on DOI-induced grooming behaviour.

Surprisingly, CBD alone significantly increased the head twitch response in healthy juvenile mice.

Conclusion: In the DOI model, our results show that CBD cannot effectively reverse motor-like tics and compulsive-like behaviour in juvenile mice. These results suggest that CBD may not effectively treat motor tics in children and may even exacerbate tics in a population of patients.

Abstract: Arafa et al.

Expression of immunohistochemical markers panel in relation to prognostic parameters of endometrial carcinoma

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Background: Endometrial carcinoma is the most common gynecological malignancy. Histopathological examination plays a central role in the management plan of the patients.

Objectives: This study aims to assess the relation between the expression patterns of estrogen receptors (ER), progesterone receptors (PR), HER2 and the Ki-67 index with the different histopathological prognostic parameters in endometrial carcinoma (EC).

Method: We examined 109 cases of endometrial carcinoma (EC) regarding the expression of ER, PR, HER2 and Ki-67 by immunohistochemistry in relation to the age, tumour size, FIGO stage and grade, depth of infiltration, cervical and ovarian involvement, lymhovascularspace invasion (LVSI) and lymph nodes (LN) metastasis.

Results: The mean age of patients was in this study was (59.8 years ± 8.2). Low ER and PR expression scores and high Ki-67 showed high significant association with non-endometrioid histology *(P=0.007 &P<0.001&P<0.001)* and poor differentiation *(P=0.007 &P<0.001&P<0.001).* Low PR score shows highly significant association with advanced stage *(P=0.009).*Low ER score is highly asscociated with lymphovascular invasion *(P=0.006),* and low PR scores is associated significantly with LN metastasis *(P=0.026).* HER2 expression significantly associated with advanced stages *(P=0.04)*, increased depth of infiltration *(P=0.02)*, lymphovascular invasion *(P=0.017)*, ovarian involvement *(P=0.038)* and LN metastasis *(P=0.038).* There was a high statistically significant association between HER2 expression and cervical involvement *(P=0.009).* Higher Ki67 values is associated with LN involvement *(P=0.012).*

Conclusion: The overexpression of HER2 and Ki-67 and low expression of ER and PR seems to indicate a more malignant behavior and should be contributed to an immunohistochemical panel for the identification of high-risk tumors.

Abstract: Azab et al.

Survey of End-of-life care in Intensive Care Units in Ain Shams University Hospitals, Cairo, Egypt

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Institute where fellowship took place: Ethox Centre, Nuffield Department of Population Health, University of Oxford, Oxford, UK

Background: Studies of end-of-life care revealed different practices of limiting life support therapy between countries and regions. Available data about physicians' practice regarding end-of-life care in ICUs in Egypt is very limited.

Objectives: This study aimed to investigate physicians' attitudes toward end-of-life care and the reported practice in adult ICUs in Ain Shams University Hospitals, Cairo, Egypt.

Method: The study included 100 physicians working in several ICU settings in Ain Shams University Hospitals.

Results: Most of the participants agreed with implementation of ''do not resuscitate'' (DNR) orders and applying pre-written DNR orders (61% and 65% consecutively); whilst only 13% almost always/often order DNR for a terminally-ill patient.

The majority of the respondents (52%) agreed with usefulness of limiting life-sustaining therapy in some cases, but they expressed fear of legal consequences. 47% of them found withholding life-supportive treatment is more ethical than withdrawing it. This was evident in their practices as 16% of them almost always/often withheld further active treatment but continued current ones but only 6% almost always/often withdrew active therapy for terminally-ill patients.

Conclusion: Absence of a definite policy and guidelines for end-of-life care in ICUs, at Ain Shams University Hospitals was the main influential factor of participants' practice and attitudes towards it.

Therefore, development of a consensus for end-of-life care in ICUs in Egypt is mandatory. Also, training of physicians in ICUs on effective communication with patients' families and surrogates is important for planning of limitation of life-sustaining treatments.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Bar-Sade et al.

Female reproductive function is modified by early life immune challenges

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Institute where fellowship took place: The University of Nottingham, Nottingham, UK

Background: Challenging environmental conditions encountered by pre-pubertal women affect their subsequent reproductive function, as shown in studies by our collaborators on Bangladeshi women immigrants in the UK. High incidence of inflammatory diseases, due to bad sanitation conditions and poor medical treatment in Bangladesh, was found to correlate with delayed menarche and early menopause as compared to Bangladeshi women who spent their childhood in the UK. Environmental conditions might affect reproductive function through epigenetic modifications, which result in altered gene expression.

Objectives: Elucidating the mechanisms leading to alteration in reproductive function as a result of pre-pubertal immunological stress.

Method: We have established a mouse model for early life immunological stress in which young female mice are given DSS in their drinking water to induce temporal colitis. Ovarian follicles were counted in stained sections, under a light microscope. mRNA levels were determined using RNA-seq or qPCR, and DNA methylation analysis was performed using Illumina EpicMethylation array or DNA bisulfite conversion and deep-sequencing.

Results: Puberty onset was significantly delayed by 6 d in DSS-treated mice compared to untreated littermates, and ovarian follicle counts revealed lower numbers of developing follicles and larger numbers of atretic follicles in DSS-treated mice compared to controls. Ovarian RNA-seq analysis indicated 105 differentially expressed genes, several of which are involved in signaling pathways that increase follicle development. Moreover, analysis of the Bangladeshi women buccal tissue revealed altered methylation in some of these genes, which correlates with their expression levels in the mice. One of the down-regulated genes was *Srd5a1*, which encodes the enzyme 5α reductase-1. This gene was more methylated in women who spent their childhood in Bangladesh, and in the DSS treated mice. We found that also in the hypothalamus, but not in other tissues of DSS-treated mice, mRNA levels of *Srd5a1* were reduced compared to controls.

Conclusion: Enhanced follicle development and increased atresia of follicles might lead to early depletion of the ovarian follicle pool, and thus early menopause in the Bangladeshi women. Furthermore, the neuroactive steroids produced by the action of 5α reductase-1 are reported to alter GnRH secretion at puberty onset. Thus, the reduction of *Srd5a1* expression in the hypothalamus might explain the delayed puberty in both DSS-treated mice and women who grew up in Bangladesh. Our findings suggest that pre-pubertal exposure to immunological stress affects reproductive strategy in the adult through epigenetic regulation.

Abstract: Ben-Reuven et al.

NDE1 role in neurodevelopment: Characterization of Copy number variations (CNVs) of NDE1 gene using human brain organoids

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Institute where fellowship took place: The University of Edinburgh, Scotland, UK

Background: Neurodevelopmental brain disorders include a spectrum of diseases, ranging from malformations such as microcephaly (small brains) and lissencephaly (smooth brains), forms of epilepsy, to Intellectual Disability (ID), Autism Spectrum Disorders (ASD), and Schizophrenia. The notion that these diseases present a spectrum of the same pathophysiology continuum is underscored by the findings that different mutations in a single gene result in a wide range of brain disease.

Copy number variations (CNVs) of NDE1 (nudE Nuclear Distribution E homolog1), the model gene in our study, were shown to cause severe brain malformations in human patients. A homozygous point mutation in the NDE1 was characterized in patients as the cause of microlissencephaly (small and smooth brain). A different frame shift mutation which caused a premature stop codon was described in patients with similar phenotypes. In Scottish genetic studies, individuals with CNVs in NDE1, resulting in an overexpression of the prtein, were also diagnosed with Autism and Schizophrenia.

Objectives: We study the role of NDE1 in human brain development. We characterize different CNVs in human Stem Cells (hESCs) and in brain Organoids.

Method: Our lab developed a novel on-chip device for growing brain organoids. We were able to show several hallmark features of the in vivo human neuroepithelium, including the folding of the outer surface as the organoids grew. We conducted cell lines that recapitulate NDE1 CNVs that were observed in human patients, such as NDE1 truncated protein and NDE1 overexpression. Then, we applied our “mini-brains” system to observe the developing brain organoids in live imaging for weeks.

Results: The organoids exhibit changes in size and a smoother surface, similarly to that observed in the respective patients. The known role of NDE1 in cell-cycle was also emphasized in our results, as different NDE1 CNVs resulted in changes in the cell-cycle in the ESCs stage and in the forming neuroepithelium. We also observed changes in the elasticity of the cells and in the gene expression.

Conclusion: We were able to recapitulate the changes in brain size and the reduced gyri folding, that were observed in human patients, using a novel system to grow human brain organoids. We reveal an important role of NDE1 in regulation of proliferation of neuronal progenitor cells and explore the suggested molecular pathways, which may represent a potential pharmacological target and/or for future downstream studies.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Ben-Shachar

Upstream missense variants approximately located in Hikeshi gene cause Hypomyelinating leukodystrophy

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Institute where fellowship took place: Manchester Center for Genomic medicine, Manchester, UK

Background: A founder Ashkenazi missense variant, Chr11:86017416 G>C (p.Val54Leu), in *Hikeshi* gene *(C11ORF73)*, encoding HSP70 nuclear transporter protein was found to cause hypomyelinating leukodystrophy, associated with spasticity and intellectual disability. At present, no further pathogenic variants in the gene have been described. We detected two additional missense variants in the gene causing similar phenotype.

Objectives: To better characterize the genetic and clinical characteristics of Hikeshi related Hypomyelinating leukodystrophy.

Method: We have performed trio exome sequencing of patients with leukodystrophy and their parents as part of a clinical evaluation. We further validated the results and tested the familial carrier status using Sanger sequencing. Clinical data was obtained from the medical records.

Results: We have detected a missense variant, CHR11: 86017488 T>C (p.Pro78Ser) in homozygous state in an 18 year-old male of Christian Arab origin, with leukodystrophy, severe intellectual impairment and spasticity. His healthy consanguineous parents were found to be heterozygous to the variant, while his healthy two sibs were detected to be heterozygous for the variant as well.

A compound heterozygous for the founder Ashkenazi variant and the CHR11:86017330 T>C (p.Phe25Ser) variant has been detected in a Russian boy of partial Ashkenazi Jewish origin), presented with similar albeit milder phenotype. The two novel variants detected, were detected only very rarely among normal population (Allele frequency of 4.064e-6 for both , gnomAD browser). Brain MRI showed a similar characterization of the leukodystrophy in all cases.

Conclusion: We have detected two novel missense variants in *Hikeshi* gene among patients with a characterized leukodystrophy, adding to the one pathogenic variant, previously described. These approximately located variants, suggest that this region may have a functional importance. We suggest to add *Hikeshi* gene sequencing in each gene panel related to leukodystrophy.

Abstract: Beshtwai et al.

The Effects of Corneal Collagen Cross-Linking Repeated Treatment- Histological Analysis of Eye-Banked Human Corneas, in-vitro

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Institute where fellowship took place: The University of Manchester, Manchester, UK

Background: Riboflavin/UV-A treatment has successfully been used to induce new cross-links between the collagen fibers and treat keratoconus. An increase in the biomechanical properties of the cornea after applying collagen cross-linking treatment in-vitro and in clinics has been documented. However the corneal collagens renew every 2-7 years, indicating the possible need of repeating the treatment. Scanning acoustic microscopy is a novel tool to measure the stiffness of tissue pixel by pixel with a high spatial resolution.

Objectives: To evaluate the effect of repeated collagen cross-linking (CXL) treatment on corneal structure, in-vitro.

Method: Thirty human corneas were included in this study. In group (A), five corneas were treated once with cross-linking. In group B&C the corneas had 2 and 3 treatments, respectively, 24-hours apart with cross-linking. The contralateral control corneas in each group were treated with riboflavin only. Corneal thickness was measured by Oculus Pentacam. Endothelial cell density was assessed using trypan blue. The corneas were then assessed histologically using haematoxylin and eosin staining (H&E), immunofluorescence staining, TUNEL and immunohistochemistry analysis.

Results: The percentage change in central corneal thickness in the cross-linked corneas in groups A, B and C was found to be 6.34% ± 1.38%, 3.58% ± 2.76% and 6.14% ± 1.71% respectively, while it was 3.91% ± 1.00%, -2.54% ± 2.41% and -0.29% ± 1.64% in the contralateral control corneas respectively. The keratocyte loss in the CXL corneas varied between the three groups. Cell loss was found to be down to 250µm depth in group A and down to 380µm and 450µm in group B and C respectively. No signs of cell apoptosis in the posterior cornea were found in the CXL corneas in group A and B, but apoptosis in the posterior stroma was found in the corneas in group C.

Conclusion: Repeated treatments over short periods of time appear to cause deeper changes in the cornea. A decrease in endothelial cell density and an increase in cell death markers in the endothelium and posterior stroma were evident after three treatments which would be considered unsafe.

Abstract: Cooper et al.

Transient blood–brain barrier disruption is induced by low pulsed electrical fields in vitro: an analysis of permeability and trans endothelial electric resistivity

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Institute where fellowship took place: King's College London, London, UK

Background: The blood–brain barrier (BBB) is limiting transcellular and paracellular movement of molecules and cells, controls molecular traffic, and keeps out toxins. However, this protective function is the major hurdle for treating brain diseases such as brain tumors, Parkinson's disease, Alzheimer's disease, etc. It was previously demonstrated that high pulsed electrical fields (PEFs) can disrupt the BBB by inducing electroporation (EP) which increases the permeability of the transcellular route.

Objectives: To study the effects of low PEFs, well below the threshold of EP on the integrity and function of the BBB.

Method: Ten low voltage pulses (5–100 V) were applied to a human in vitro BBB model. Changes in permeability to small molecules (NaF) were studied as well as changes in impedance spectrum and trans-endothelial electric resistivity. Viability and EP were evaluated by Presto-Blue and endogenous Lactate dehydrogenase release assays. The effect on tight junction and adherent junction protein was also studied.

Results: The results of low voltage experiments were compared to high voltage experiments (200–1400 V). A significant increase in permeability was found at voltages as low as 10 V despite EP only occurring from 100 V. The changes in permeability as a function of applied voltage were fitted to an inverse exponential function, suggesting a plateau effect. Staining of VE-cadherin showed specific changes in protein expression.

Conclusion: The results indicate that low PEFs can transiently disrupt the BBB by affecting the paracellular route, although the mechanism remains unclear.

Abstract: Daoud et al.

Transcriptomic Profiling of Trophoblast Fusion Using BeWo and JEG-3 Cell Lines

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Background: Abnormal placental development and more specifically abnormal trophoblast fusion is implicated in many pregnancy related disease such as Down syndrome, HELLP and preeclampsia. However, little is known about the genes that regulate trophoblast fusion.

Objectives: Identify a set of genes that control trophoblast differentiation and fusion.

Method: Two placental cell lines (BeWo and JEG-3 cells) are used to identify a set of genes responsible of trophoblast fusion. Cells were treated with forskolin for 48 hours to induce fusion. RNA was extracted, hybridized to Affymetrix HuGene ST1.0 arrays and hosphor using system biology. Cell culture and differentiation was evaluated by real time PCR and immunocytochemistry analysis. Microarray data were analysed using system biology and bio-informatic analysis. Moreover, some of the identified genes were validated by real time PCR and their functional activity by western blot using hosphor-specific antibodies.

Results: Our results identified a list of 32 altered genes in fused BeWo cells compared to JEG-3 cells after forskolin treatment. Among these genes, 4 were validated by RT-PCR including salt inducible Kinase 1 (SIK1) gene which is specifically upregulated in BeWo cells upon fusion and activated after 2 min with forskolin. Finally, SIK1 showed to be at the center of many biological and functional processes which suggest that it might play a major role in trophoblast differentiation.

Conclusion: This study identified new target genes implicated in trophoblast fusion; a process implicated in the etiology of many pregnancy-related diseases such as preeclampsia, IUGR, and gestational diabetes.

Abstract: Dubrov-Rav et al.

Prediction of maximal heart rate in children and adolescents

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Institute where fellowship took place: Children's Health and Exercise Research Centre, University of Exeter, Exeter, UK

Background: The predicted maximal heart rate (MHR) is commonly used in exercise testing and prescription, for both adults and children. Numerous prediction equations exist, but most were developed for adults and have a very low accuracy in children.

Objectives:
1. To test the performance of all adult prediction equations in predicting MHR of children and adolescents.
2. To develop a prediction formula for MHR in children and adolescents using clinical and anthropometric variables.

Method: Data from 627 treadmill maximal exercise tests performed by 433 paediatric athletes (age 13.7±2.1 years, 70% males) were analysed. Data extracted from each test included age, sex, sport type, stature, weight, BMI (absolute and percentiles), body fat, fitness level, resting and maximal heart rate. Stepwise multivariate linear regression was used to identify predictors for MHR. A linear mixed model was used to control for repeated measures in the same individual. The relationships between existing prediction equations and MHR were also evaluated using Pearson's correlation.

Results: Observed MHR was 197±8.6 b·min^{-1}. Existing adult equations showed a very low correlation with observed MHR (r=-0.03-0.34) in children and adolescents. Stepwise linear regression revealed that resting heart rate, fitness, weight and fat percent were predictors of MHR (R^2=0.25,p<0.001), while age was not. Resting heart rate explained 15.6% of MHR variance, weight added 5.7%, fat percent added 2.4%, and fitness level added 1.2%.

Conclusion: A new equation to predict MHR in children and adolescents was developed, but it had a low prediction of MHR, similar to adult equations applied on children. Considering the narrow range of MHR in youth, we propose using 197 b·min^{-1} as the mean MHR in children and adolescents (or 200 b·min^{-1}, for simplicity), with 180 b·min^{-1} the minimal threshold value (-2 standard deviations).

Abstract: Elbehairy et al.

Patterns of breathlessness and associated consulting behaviour: results of an online survey

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Institute where fellowship took place: Imperial College London, London, UK

Background: Breathlessness is a common symptom among the general population that can be related to ageing, lung or heart disease, a lack of fitness or anxiety.

Objectives:
The British Lung Foundation (BLF) developed an online survey tool, the 'BLF Breath Test', that members of the public could use to assess their breathing and possible contributing factors. Survey responses provide an opportunity to analyse the relationship between breathlessness, common sociobehavioural risk factors and interaction with healthcare.

Method: Members of the public were invited via social media to complete a simple online survey about their breathing and possible risk factors. Based on individual responses, subjects were given tailored advice. For those who agreed, a follow-up survey was distributed to evaluate the behavioural response to the breath test approximately one year later (Elbehairy et al. Thorax 2019, doi: 10.1136/thoraxjnl-2018-212950).

Results: We analysed data from 356 799 responders: 71% were ≥50 years old and 18% were smokers. 20% reported limiting breathlessness (Medical Research Council breathlessness score ≥3), and the majority of these (85%) worried about their breathing; of these, 29% had not sought medical advice. Of those who had, 58% reported that the advice received had not helped their breathlessness. Limiting breathlessness was associated with being older, physically inactive, smoking and a higher body mass index.

The follow-up survey was distributed to the 13,444 subjects. 1072 responses were received; 562 remembered taking the BLF Breath Test and were included in the current analysis. 40% of this sample reported limiting breathlessness and the majority of these (73%) already had a diagnosis of a respiratory condition before taking the test. 47% of the subjects reported that taking the online BLF Breath Test increased their awareness that breathlessness can be a sign of a serious disease. Following their test, 33% reported that they had changed their lifestyle and 20% consulted their general practitioner (GP) about their breathlessness. Specifically, 18% increased their exercise level, 17% modified their diet, 6% successfully quit smoking while 3% had tried to quit but failed.

Conclusion: These data suggest a considerable unmet need associated with breathlessness as well as possibilities for intervention. Our data also show that limiting breathlessness is a common problem affecting mainly older people, a demand that is currently suboptimally met and requires further attention with the aim to timely diagnose and treat patients and improve healthcare services.

Abstract: Elgezawy et al.

The Prognostic Value Of High Expression Of ALK Gene In Upper Egypt Childhood Neuroblastomas: Correlation With Other Biological Markers

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Institute where fellowship took place: Haematological Sciences, Institute of Cellular Medicine, Newcastle University, Newcastle-upon-Tyne, UK

Background: Neuroblastoma is one of the most frequent and challenging childhood tumours. The mutated Anaplastic lymphoma kinase (ALK) gene has been identified as a potential and major predisposition oncogene in human neuroblastomas (NBLs). The uniqueness of this tumour depends on its biological markers, which classify neuroblastomas into favourable and unfavourable, with 5-years survival rates ranging from almost 30- 100%.

Objectives: To determine the level of ALK mRNA gene expression in childhood neuroblastoma and to assess its prognostic value in relation to clinicopathologic characteristics and other genetic prognostic factors of neuroblastoma.

Method: Quantitative real-time (RT-PCR) was applied to examine the expression level of ALK mRNA and detect the prognostic value in seventy nine childhood neuroblastoma patients. Those patients were diagnosed clinically as well as pathologically and tested for DNA ploidy, MYCN amplification and TrkA expression. Immunohistochemical staining was used to check the expression level of ALK proteins.

Results: Analysis of seventy-nine patients with sporadic primary NBL who met study criteria, 46 of them were favourable and 33were unfavourable according to Shimada's pathological classification. High ALK gene expression was reported in 46 patients (58%), most of them were unfavourable ($p<0.001$). Regarding other biological biomarkers, we recorded that significantly high expression of ALK mRNA in patients with amplified copies of MYCN ($p<0.001$) and low TrkA expression level ($p<0.001$), all these factors are known to be associated with poor prognosis in neuroblastoma. Of interest, immune-histochemical study revealed positive ALK expression in ALK-amplified tissues. Further more, high expression of ALK gene was significantly associated with poorer survival ($p<0.05$).

Conclusion: We concluded that high expression of ALK gene is associated with poor prognosis of NBL. Moreover, it might play vital role in cell growth as well as proliferation representing a good target for ALK inhibitors in the treatment of NB.

Abstract: Elhadidy

Unraveling the black box of Campylobacter epidemiology: Source Attribution of Clinical Campylobacter Infection from Environmental Sources

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Institute where fellowship took place: University of Bath, Bath, UK

Background: The foodborne bacterial pathogen *Campylobacter* is among the most common causes of human gastroenteritis with consumption and mishandling of retail chicken is considered one of the most important infection sources. The alarming increasing rates in antibiotic resistance of *Campylobacter* isolates raised the concern about studying the molecular mechanisms of resistance.

Objectives: 1-Assign risk-based binary typing of *Campylobacter* isolates from human and environmental using comparative genomic fingerprinting (CGF) and multilocus sequence typing (MLST) to evaluate a basis for subtyping that could also be related to the risk to human health from individual strains 2-Determine the dynamic of antibiotic resistance and investigate the clonal structure and genetic determinants of resistance 3- Determine the extent that the dynamics in genomic content of endemic *Campylobacter* contributes to clinical disease severity, transmission routes, and source attribution.

Method: *Campylobacter* isolates from human, broiler carcasses, milk and dairy products were used in this study. The isolation and enumeration of *Campylobacter* strains from different food matrices was performed according to the ISO 10272-1. CGF40 fingerprints were generated from 8 Multiplex PCRs as previously published. Paired-end sequencing was performed on the Illumina MiSeq platform. MLST, genetic variation at pan-genome loci, antimicrobial resistance genes were determined from whole genome sequence (WGS) data and by comparison of the sequences to the PubMLST database (http://pubmlst.org/campylobacter) on BIGSdb. Probabilistic assignment of Egyptian clinical isolates to their most likely origin was performed separately using STRUCTURE software.

Results: The comparative genome analysis identified core and pan genome of *Campylobacter* species and how this is related to population structure, evolution of host/niche adaptation, and maintenance of *Campylobacter* species. The sequence information is uploaded into a central worldwide database, thus providing a community resource enabling researchers to enrich knowledge about the global diversity, transmission, population structure, ecology, and evolution of this important human pathogen.

Conclusion: Data from environmental isolates provided novel insights on the importance of different potential sources of transmission of *Campylobacter* species, thus identifying potential intervention strategies and targets. Such findings are critically needed to reduce human disease burden from zoonotic pathogens in Egypt and other developing nations.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: El-Khoury

Profiling cellular bioenergetics using the Seahorse technology

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Institute where fellowship took place: Department of Cell & Developmental Biology at University College London, London, UK

Background: The research department of the Faculty of Medicine at the American University of Beirut is currently planning to acquire the Seahorse Analyzer, a relatively novel instrument that uniquely enables measurements of oxygen consumption from small populations of cells. This initiative, which I have started, is supported by many local scientists from different research areas who expressed their interest in such a technology.

Objectives: The main purpose of the visit was to seek the assistance of Professor Duchen and his team for their extensive expertise in mitochondrial biology in order to get acquainted with the Seahorse technology.

Method: In order to fulfill the objectives of my visit, we used with the assistance of several members of Professor Duchen Laboratory the Seahorse XF24 analyzer of the Core Facility for Metabolic and Mitochondrial Studies.

Results: The visit was highly enriching at both the personal and the scientific level. I was able to familiarize myself with the theoretical as well as the practical aspects of the Seahorse technology and most importantly recognize its strengths and limitations.

Conclusion: Currently, Seahorse technology developed by Agilent is the most suitable approach used to assess cellular bioenergetics as it allows live, time-resolved and non-invasive investigations. The Turnberg fellowship that I have obtained in May 2018 enabled me to spend one month in Professor Michael Duchen's research laboratory where I was able to have deeper insights into the Seahorse technology. The short-term visit was therefore an essential step that will be of considerable importance for completing the initial procedures that will eventually lead to the acquisition of the Seahorse analyzer. Moreover, it will be essential for the implementation of the new technology once the instrument is purchased. Having such a technology will definitely strengthen our mitochondrial related research capacities and allow scientists from different fields to potentially unravel novel bioenergetics features that might be essential in different cellular processes.

Abstracts

Abstract: Elmahallawy et al.

Pharmacological and functional characterisation of Schistosoma mansoni cyclic adenosine monophosphate (cAMP) phosphodiesterases in a unique protozoan expression system

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Background: Schistosomiasis is neglected tropical disease caused by parasitic worms of genus *Schistosoma*. The disease is considered the second devastating parasitic disease in poor societies with unclean water and inadequate sanitation. Despite several schistosomal research, the drug of choice, as main line to control the disease, is still out of reach. On the other hand, Phosphodiesterases (PDEs) are among the most exciting new drug targets in several parasites. Given the above information, targeting the Phosphodiesterases in *Schistosoma* seems promising drug targets.

Objectives: *Schistosoma mansoni* PDEs, enzymes of cAMP signalling pathway were cloned and systematically, one-by-one expressed in a novel protozoan expression system for functional and pharmacological characterisation.

Method:

1. Having theTbrPDEB1 fragment PvuII - C-terminal (designated B1-C) synthesized then transforming it into *E. coli* followed by miniprep overnight.
2. Obtaining pRPa$^{i+TbrPDEB1\text{-}6myc}$ plasmid then allow it to grow in bacteria – with ampicillin, miniprep and digestion with PvuII-HF and XbaI. This removes the original catalytic domain-plus-C-terminal sequence of TbrPDEB1 but leaves the 6xMyc tag.
3. Selection the coorect colonies and verfication by sequencing and digest the contrsuct by doucble digestion using *MfeI*-HF and *Bgl*II.
4. Amplification of SmPDE4A, SmPDE7var, SmPDE11 and TbrB2 catalytic domains, miniprep, digestion of these amplified products using *MfeI*-HF and *Bgl*II and selection the correct colonies and verfication by sequencing.
5. Ligation the product of step 4 with the product of step 3 then transforming the ligations into *E. Coli* then screening of the posotitive colonies.
6. Growing up the positive colonies, Miniprep, verfication by sequencing, linearise, transfect into *T. brucei* TbrPDEB1/B2 sKO (single knowcked out).
7. Once have verified clones with correct PDE inserted, knocking out second allele of TbrPDEB1/2 – with TbrB1-B2 KO Pur-TK plasmid.

Results:

1. Cloning and expressing the catalytic domain of SmPDEs 4a, 7var and 11 in the complementation strain of T. brucei, through domain swap with TbrPDEB1 in the pRPa,i-6myc plasmid and switching TbrB2 catalytic domain in as a control to confirm inhibitor specificity.
2. Verification of this expression using qPCR to quantify the amount of *Schistosoma* mRNA and protein, respectively, being expressed.

Conclusion: Taken together, The project pursued a promising and innovative strategy to gain novel insight into a critical part of *Schistosoma* biochemistry and exploit this for the development of new drugs against the parasite.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Elrafie et al.

Forensic-psychiatric services in Egypt - Challenges and Efforts

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Institute where fellowship took place: Institute of Mental Health - Jubilee Campus, The University of Nottingham, Nottingham, UK

Background: Forensic psychiatry deals with the assessment and treatment of mentally disordered offenders in prisons, secure hospitals and the community. Forensic psychiatric services in the Arab world (including Egypt) are Underdeveloped with faulty Cultural beliefs and Social stigma. The current Egyptian system differs from systems in other countries in some respects. Admission to hospital is governed under the 'Law for the Care of the Mentally Ill Patient' which came into force in 2009. A lot of national and international projects are currently being implemented to conduct evidence-based studies and to provide staff training to overcome the challenges facing the services in Egypt.

Objectives: The aim of study 1 was to describe basic sociodemographic, clinical and offending characteristics of the entire forensic-psychiatric population in Egypt (N=638) as well as length of stay and discharge decisions related to this group of patients. A second study is being conducted, aiming at testing the effects of novel staff training programs on the ward environment of the patients.

Method: The first is a cross-sectional study that included all patients at Khanka (N=601) and Abbasia (N=37) high secure forensic-psychiatric hospitals. These are the only two forensic services in Egypt; admitting male and female patients respectively. The other study is a 6-month randomized controlled trial (the first of its kind in Egypt) that includes conducting customized training programs for the staff members of half of the forensic psychiatric population's wards and comparing the seclusion hours and offensive incidents with the other half that wil not receive such trainings.

Results: Study 1: Patients were predominantly male, single, had low socioeconomic status, were first time offenders, had an index offence of murder, had a diagnosis of Schizophrenia, had a length of stay of < 5 years and no discharge recommendation. Factors which predicted higher length of stay were increased age, increased age at index offence and improvement to treatment.
Study 2: Study is still being conducted.

Conclusion: We hope that understanding the characteristics of this population and conducting tailored Egyptian trainings can shape the quality of care to be more patient orientated. The current projects' outcomes include Translated HCR-20 V3, Hands on Trainings, Research papers and Joint thesis supervisions. This work will also aid future work of the discharge committee to establish an evidence-based system for these decisions.

Abstracts

Abstract: El-Tholoth et al.

Recombinase Polymerase Amplification -Nucleic Acid Lateral Flow Immunoassays for Newcastle Disease and Infectious Bronchitis Viruses

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Institute where fellowship took place: Brunel University London, Uxbridge, UK

Background: Newcastle disease (ND) and Infectious bronchitis (IB) viruses are frequently affecting the respiratory tract of chickens and cause great economic losses in poultry industry. Rapid detection of these viruses is important to start implementation of appropriate control measures.

Objectives: The aim of our study was to develop field, simple and rapid molecular diagnostic method for Newcastle disease and infectious bronchitis viruses.

Method: Recombinase polymerase amplification assay combined with nucleic acid lateral flow (RPA-NALF) immunoassay was used for NDV and IBV using modified Primers.

Results: The results revealed that RPA-NALF immunoassay detected both viruses after 40 minutes at 38 °C and only NDV after 20 minutes. The least limit of detection was 10 genomic copies / RPA reaction.

Conclusion: In conclusion, RPA-NALF assays were developed for specific and rapid identification of NDV and IBV that could be used for rapid, on site molecular detection of NDV and IBV as the result detected by naked eye without the need for measuring fluorescence signal. Furthermore, the NALF device could be adapted to detect other infectious agents.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Foda et al.

Relation of E-cadherin and Fascin expression to clinicopathological features and prognosis of spinal and intracranial meningiomas

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Institute where fellowship took place: Mansoura University, Mansoura, Egypt

Background: E-cadherin and Fascin are adhesive proteins that are expressed in many tumors. It was supposed that loss of expression of these proteins is associated with increased aggressiveness of the tumor. Whether spinal and intracranial meningiomas express adhesion proteins in different rates is not yet known.

Objectives: We aimed to investigate the expression of E-cadherin and Fascin in a large number of meningioma specimens and determine if clinical and prognostic significance exists.

Method: 134 spinal and intracranial meningioma samples were collected. Manual TMA blocks were constructed and immunohistochemistry for E-cadherin and Fascin was done. Focal or diffuse staining was considered positive.

Results: Intracranial meningioma occurred in significantly younger age than spinal ones. Most of spinal meningiomas were of transitional histology. E-cadherin was expressed in 38.8% of cases. Spinal meningiomas showed statistically significant negative expression of E-cadherin than intracranial tumors. All atypical meningiomas showed negative E-cadherin expression. Fascin was expressed in 9% of cases with significant expression in atypical cases.

Conclusion: Aggressive behavior of meningioma could be explained in part by loss of E-cadherin and overexpression of Fascin especially in spinal meningiomas. Further studies are suggested to explore the biological aspects of spinal and intracranial meningiomas for constructing tailored targeted therapies.

Abstracts

Abstract: Ghosh

Peptide-biopolymer based coassembledsystems formineralization and osteogenesis

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Institute where fellowship took place: Queen Mary University, London, UK

Background: Skeletal deficiencies resulting from trauma, tumors, abnormal development frequently require surgical intervention. Bone guided regeneration is an alternative approach to restore and regenerate bone tissue. Elastin-like polypeptides (ELPs) are recombinant proteins which shows bioactivity, ease of design and production, possibility to form robust and elastic materials. Alternatively, short aromatic peptides can form fibrous hydrogels under physiological conditions that is stable across a broad range of temperatures and at a wide pH range. We are trying to develop a co-assembled system combining both to serve as a superior mineralization matrix.

Objectives: The aim of the proposed research is to develop a biocompatible co-assembling system based on the conformational modification of elastin-like recombinamers (ELRs) by short aromatic peptides in order to tune the physical and mechanical properties of the new hybrid systems. Thus allowing to develop a therapeutic bone regenerative matrix for cell proliferation, mineralization and osteogenesis.

Method: We developed here protein/short aromatic peptide based systems that can be maintained for substantial periods of time with a control over its assembly. Cell adhesive RGDS motifs were included in the negatively charged ELP molecules whereas the peptide molecules were designed with amino acids having overall positive charge and supporting mineralization and imparting mechanical stiffness to the developed system.

Results: Following the formation of the self-assembled systems we did morphological characterization of the systems with optical, scanning electron and confocal microscopy. Optical images showed the formation of membrane and gel with two different peptides. Fluorescent images under confocal microscopy demonstrated the co-existence of both peptides and ELP at the interfacial region suggesting the role of both in the formation of the systems developed. Scanning electron microscopy (SEM) revealed nanofibrous leyered system for both membrane and gel.

The self-assembled systems formed were non-deformed in cell culture media for 48 hours indicating sufficient stability of these systems under physiological conditions. Finally, the systems were used for the mineralization studies both in vitro in a solution containing 5 wt% HAP and fluoride in water at 37°C for 7 days and also in vivo bio mineralization with preosteoblast cells.

Conclusion: The results suggested a new polymer/peptide based co-assembled system with superior morphological and mechanical features. The systems were stable at physiological conditions over a substantial period of time. They showed tunable properties to support in vitro mineralization and biocompatibility and cell adhesion, mineralization and osteogenesis.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Gilbar

Disclosing genetic test results to the patient's relatives: How does the law influence clinical practice?

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Institute where fellowship took place: Department of Nursing, Faculty of Medicine, Tel- Aviv University, Israel

Background: Disclosure of genetic test results to relatives is the subject of extensive scholarly debate and empirical research. This is because genetic test results may have serious implications not only for the patient but also for the relatives. However, the patient's legal right to confidentiality makes disclosure to relatives problematic if the patient refuses disclosure. One aspect which has not yet received sufficient scholarly attention is how clinicians deal with the legal framework within which they operate.

Objectives: This paper aims to fill this gap by presenting findings from a qualitative study conducted with Israeli clinicians who provide counseling and treatment to healthy women undergoing BRCA1/2 testing.

Method: The study was based on semi-structured, face-to-face, one on one interviews with 28 clinicians who diagnose and treat healthy women who undergo BRCA1/2 testing.

Results: The findings indicate that clinicians follow the law. They respect their duty of confidentiality and generally refrain from informing the relatives without the patient's consent. However, the findings also indicate that they find the law restrictive when patients explicitly refuse to inform their relatives. Furthermore, the law does not help clinicians to resolve the difficulties regarding patients' passive non-disclosure, namely when the patient agrees to inform the relatives in the encounter with the clinician but refrains from doing so after leaving the clinician's office. In addition, the law does not help clinicians to overcome the practical difficulties of tracing relatives when patients are not cooperative and refuse to provide contact details.

Conclusion: The law should leave it to the discretion of the clinicians to decide whether or not to initiate a process of disclosure without the patient's consent. In tort law terminology, a legal duty to the relatives should be recognized, but the question of whether and how to initiate a process of disclosure without consent should remain at the discretion of clinicians. Such a legal rule, which shifts the discussion from the duty stage to the breach-of-duty stage, would require clinicians to dedicate more thought to the criteria justifying disclosure without consent. In addition, it would require clinicians to change their underlying attitude to confidentiality and disclosure and consider them with equal moral and legal weight.

Abstracts

Abstract: Goldberg

Pediatric Systemic Lupus Erythematosus as a manifestation of Constitutional mismatch repair deficiency

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Institute where fellowship took place: University of Oxford, Oxford, UK

Background: Biallelic mutations in any of the four mismatch repair genes *MSH2, MSH6, MLH1,* and *PMS2* result in one of the most aggressive childhood cancer predisposition syndromes, termed constitutional mismatch repair deficiency syndrome (CMMRD). In addition to a very high tumor risk, the CMMRD phenotype is often characterized by the presence of signs reminiscent of neurofibromatosis type 1. Pediatric Systemic Lupus Erythematosus (pSLE) is very rare. It has been reported so far in three CMMRD patients and has not been considered a diagnostic feature of the syndrome.

Objectives: To describe the link between these two rare conditions.

Method: Two female patients from two different families diagnosed clinically with pSLE presented with features suggestive of CMMRD and were found to have bi-allelic pathogenic mutations in *MSH6*.

Results: We report two CMMRD female patients diagnosed with pSLE and compare them to the three reported cases. Hence, there are a total of five out of approximately 200 (2.5%) currently reported CMMRD patients that also have pSLE.

Conclusion: Given the rarity of both CMMRD and pSLE this phenotype is significant and should be further explored. pSLE should raise the possible diagnosis of CMMRD if supported by additional indicative features.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Goldman Wohl et al.

Immune cells at the maternal fetal interface remember pregnancy

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Institute where fellowship took place: Wellcome Trust/MRC Building, Addenbrooke's Hospital, Cambridge, UK

Background: Subsequent pregnancies are more robust than first pregnancies. Preeclampsia and several of the "Great Obstetrical Syndromes" that have as a basis poor placental development, are associated with first pregnancies. We have shown that Natural killer cells, which are abundant at the fetal maternal interface, have builder properties in addition to their known role as killer cells. These decidual natural killer cells (dNKs) produce cytokines, growth and angiogenic factors beneficial for the development of the placental bed.

Objectives: We sought to investigate the cellular and molecular basis for better outcomes in subsequent pregnancies. We investigated differences in decidual NKs in pregnancies of primigravid (first pregnancy) vs parous (subsequent pregnancy) women.

Method: dNKs isolated from elective pregnancy terminations from primigravid and parous women, and endometrial NKs, were characterized by assays including FACs, RNA-seq transcriptome and epigenetic analysis and angiogenic and growth factor experiments as well as single cell RNA sequencing (scRNAseq).

Results: We discovered an NK cell population unique to pregnancies of parous women, possessing a novel transcriptome and epigenetic signature, characterized by high expression levels of the receptors NKG2C and LILRB1, which interact with ligands expressed on invasive trophoblasts. Activation of these receptors leads to increased production and secretion of IFNγ (interferon gamma) and VEGFα (vascular endothelial growth factor), the latter found to support vascular sprouting and trophoblast-tumor growth. Overall, the dNKs of parous women were found to have a unique epigenetic profile. More specifically, focusing on IFNγ and VEGFα, the NKG2C^{high} cells were shown to have a more "open" chromatin configuration. Furthermore, the unbiased technology of scRNAseq enabled detection of immune cell populations, including previously undescribed subpopulations of dNK.

Conclusion: NK cells of the maternal fetal interface "remember" past pregnancies. These "memory" immune cells impart enhanced properties of development to the placental bed. These immune cells with memory, residing in the epigenome between pregnancies and with their heightened growth factor expression, afford in part a possible explanation for the robustness of subsequent pregnancies and the observed increased risk in first pregnancies for several of the "Great Obstetrical Syndromes" that are based in poor placentation. Understanding the molecular and cellular bases of improved outcomes of subsequent pregnancy may lead to the development of treatment modalities designed for women at high risk for pregnancy disorders originating at the maternal–fetal interface.

Goldman-Wohl D 2019 PMID: 30802436.

Abstract: Greenberg et al.

The role of empathy and music in social conflict: An investigation of an Israeli-Palestinian Youth Chorus

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Institute where fellowship took place: Bar-Ilan University, Ramat Gan, Israel

Background: Deficits in empathy impede social communication and understanding at the group level. Music is one tool that promotes empathy, and in a recent paper we hypothesized how music can increase empathy in cultures in conflict.

Objectives: The study will investigate the effects of biopsychosocial markers including empathy, "brain types", and social perception, via group musical interaction in Israelis and Palestinians. The measures will be administered to high school students of the Jerusalem Youth Chorus at several time points throughout the year. Video and audio recordings will be analyzed with machine learning methods. Data collection will commence in the Fall 2019. Therefore the present abstract provides four preliminary studies testing how music listeners perceive social cues from music using "big data" methods.

Method: In Study 1, participants from the US listened to 25 musical excerpts, and rated the prototypical fans of each. In Study 2, 6,279 participants completed self-reports of their personality traits and provided observer personality ratings for an artist of their choosing (from a selection provided to them). In Study 3, we analysed 75,296 US users of the MyPersonality project who completed a self-report of their personality traits while voluntarily opting in to share their Facebook likes, including Likes for at least one of the artists presented to the participants in Study 2. In Study 4, we investigated 4,902 participants to see whether the match between a person's personality profile and that of an artist–could predict a participant's preference for the music of an artist.

Results: Results from Study 1 showed that individuals perceive consistent and transparent patterns of social cues from music features. Study 2 and 3 showed that the perceived personality traits of artists correlates with the personality traits of their listeners, and Study 3 showed that the fit between the personality of the listener and the artist is a more important predictor of musical preferences than the fit for gender, age, and even the music's audio features.

Conclusion: The findings across the four preliminary studies showed that music is a way for people to define and reinforce in- and out-group boundaries, supporting group-level process theories and adaptationist accounts of music. This evidence sets the stage for the study of the Jerusalem Youth Chorus which will investigate the role empathy and social perception in Israelis and Palestinians in conflict.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Hadas et al.

Hyaluronan-NK cell Interaction Controls the Primary Vascular Barrier during Early Pregnancy

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Institute where fellowship took place: The Weizmann Institute of Science, Rehovot, Israel

Background: Successful embryo implantation is associated with a unique spatial pattern of vascular remodelling, characterized by profound peripheral neo-vascularization surrounding a peri-embryo avascular niche. Hyaluronan, a major component of uterine extra-cellular matrix (ECM), has been demonstrated as a vascular morphogen numerous physiological processes.

Objectives: We hypothesized that hyaluronan controls the formation of the unique vascular pattern encompassing the embryo.

Method: This hypothesis was evaluated by inhibition of maternal hyaluronan synthesis and by genetic modification of hyaluronan metabolism specifically targeted to the trophectoderm.

Results: The outcome of altered hyaluronan deposition on uterine vascular remodeling and post-implantation development were analyzed by MRI, detailed histological examinations and RNA-sequencing of uterine NK cells. Our experiments revealed that eliminating the anti-angiogenic hyaluronan, led to elevated expression of MMP-9, VEGF-A and its receptor VEGFR-2, accompanied by reduced recruitment of uterine NK cells. Further local decrease in VEGFR-3 resulted in impaired formation of vascular sinuous folds, ectopic angiogenesis and dysfunctional uterine NK cells. Conversely, enhanced deposition of hyaluronan caused the expansion of the maternal-embryo barrier, leading to an increased diffusion distance and aborted implantation.

Conclusion: These results demonstrate a pivotal role for hyaluronan in successful pregnancy by fine-tuning the peri-embryo avascular niche and maternal vascular morphogenesis.

Abstracts

Abstract: Haddadin et al.

Evaluation of antibiotic dispensing practice in community pharmacies in Jordan: A cross sectional study

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Institute where fellowship took place: Queen's University Belfast. This research was conducted in Jordan

Background: It is well known that the emergence of antibiotic resistance is linked to the misuse and overuse of antibiotics. Misuse includes self-medication and the inappropriate use of antibiotics because of improper dosage or improper duration than recommended.

Objectives: This study aimed at investigating three patterns of dispensing antibiotics in a sample of community pharmacies in Jordan. This included dispensing antibiotics by prescription or over-the-counter either by direct request or upon a pharmacist's recommendation.

Method: The study was a cross sectional observational study. Ethical approval was obtained for the study. Research assistants (n=7) were distributed in seven community pharmacies in four cities in Jordan. Research assistants were requested to observe all patient-pharmacist interactions that involved antibiotics whether by prescription or not. When antibiotic dispensing to the customer was conducted, the researcher intervened to collect the necessary information from the customer and the prescription (if present). The information collected from the customers was recorded in a data collection form. The form included information about the customer and the patient such as age, gender, education, diagnosis or symptoms and complaint, others such as (comorbidities, chronic diseases, allergies and pregnancy), antibiotics dispensed (trade name, active ingredient, strength), dosage, duration of treatment, cost, and the dispensing practice whether by prescription, direct self-medication (i.e., requesting a specific drug), or indirect self-medication (i.e., presenting symptoms to the pharmacist). The antibiotics dispensed were evaluated in terms of indication, appropriateness of dose, and duration of treatment based on the empirical treatment suggested by selected references: Lexicomp (2017) and UptoDate (2017) and the manufacturer's recommendations.

Results: Of the 457 antibiotics dispensed, almost one third were without prescription. Of the antibiotics dispensed with prescription or without prescription, 31.5% and 24.6% respectively were appropriate dosage and duration (p=0.002). In the three patterns of dispensing, beta lactam antibiotics were the most commonly dispensed. In addition, it was noticed that there was a tendency to prescribe or dispense higher generations of antibiotics to cases that could have been treated with lower generation or safer antibiotics. Furthermore, 12.2% of the antibiotics were dispensed to treat infections that are not indicated for them.

Conclusion: The study indicates the importance of enforcing the Jordanian regulations prohibiting the dispensing of nonprescription antibiotics and the implementation of continuous education to physicians and pharmacists to increase awareness about the emergence of antibiotic resistance.

Abstract: Hamed et al.

The role of MLK7 in muscle maintenance and disease

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Institute where fellowship took place: University of York, York, UK

Background: Muscle weakness and disease can be caused by rare genetic defects. Here, I will be characterizing in detail a mouse model that recapitulates a rare chronic disease in humans caused by mutations in a protein called MLK7. MLK7 belongs to the so called "stress proteins" family because these proteins activate pathways in response to stressors such as heat, osmotic pressure, mechanical load, etc. This disease exposes for the first time that a stress signaling protein is essential for skeletal muscle maintenance, as attested by the symptoms of the patients lacking MLK7. In particular, the symptoms and histology from patients and the preliminary data obtained in mice points to a critical role for this signalling pathway in the maintenance of postural muscles. The mouse model will allow us to characterize the disease in much greater detail that could ever be possibly in humans.

Objectives:
1. Histopathological characterization of Mlk7 -/- mice.
2. Analysis of the MLK7beta→ MKK6→ p38g pathway in control and mutant muscles.
3. Identification of MLK7 substrates in differentiating myoblasts.

Method:
1. **Histopathological characterization of** *Mlk7* -/- mice. Using Histopathological and immunofluorescent staining.
2. **Analysis of the *MLK7beta→ MKK6→ p38g* pathway.** Antibodies against total and phosphorylated specific forms of *MLK7*, MKK6 and p38g **were used.**
3. **Identification of MLK7 substrates in differentiating myoblasts.** We will undertake a phosphoproteomics approach using the recently developed protocol for the C2C12 myoblast cell line.

Results:
Histopathological examination of hindlimb Tibialis/EDL regions show clear signs of pathology in these mice with a significant number of fibres showing central nucleation. Moreover, we have confirmed that soleus shows a shift towards slow type muscle fibres, in agreement with the report in human patients.
Analysis and Identification of MLK7, MKK6 and p38g pathways in *Mlk7* -/- mice in comparison to control groups displays significant variations. the MLK7, MLK6 and P38g are down expressed in the *Mlk7* -/- mice in contrary to the control groups. Thus the MLK7 substrates (stress proteins) explain to what the extent this kinase is involved in other phosphorylation events that contribute to the strength of the muscle fibre.

Conclusion: This research into MLK7 myopathy will provide hope to patients and their families. From a basic research perspective, it will contribute to clarifying the role of MAP kinases in muscle maintenance, paving the way to assess the impact that these signalling pathways may have in the pathogenesis of more common muscle diseases such as Duchenne muscular dystrophy.

Abstract: Kabiri et al.

Fertility preservation for male patients: comparing the effectiveness of three human testicular tissue cryopreservation methods

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Institute where fellowship took place: MRC Centre for Reproductive Health, The University of Edinburgh, Scotland, UK

Background: Due to remarkable advances in cancer treatments, we are witnessing a growing population of long-term survivors of childhood malignancies. However, fertility in adult life may be severely impaired by gonadotoxic therapies. Since prepubertal boys cannot produce spermatozoa, banking of testicular tissue prior to gonadotoxic treatment is a crucial step towards fertility preservation for this population. Several centers around the world are now cryopreserving testicular tissue for prepubertal boys in anticipation that future technologies will allow the utilization of the banked samples for fertility restoration.

Objectives:
The objective of the study was to compare three methods of testicular cryopreservation (Controlled Slow Freezing, Uncontrolled Slow Freezing, and Vitrification), in order to develop efficient protocols for cryopreservation of viable prepubertal human testicular tissue.

Method:
Human testicular tissue was provided from prepubertal and adult males undergoing orchiectomy due to various indications. A testicular biopsy was performed, manually dissected and cryopreserved using three freezing protocols: Uncontrolled Slow Freezing (USF), Controlled Slow Freezing (CSF) and Vitrification.

After thawing, intact tubules were evaluated for the presence of different markers. The tubules number per 1500X1000uM, and the number of MAGE-A4, Oct4 and Vimentin positively stained cells per tubule were calculated from 3-5 random slides.

Results:
Histological evaluation of fresh and thawed tissues demonstrated no significant differences in tissue architecture, structural integrity and cellular morphology between fresh and cryopreserved fragments.

Conclusion: The research demonstrates the feasibility of those three methods for human testicular tissue cryopreservation and significantly contributes to the potential future utilization of the frozen samples for sperm production and fertility preservation.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Kahale et al.

Identifying participants with missing data in reports of randomized controlled trials: guidance for authors of systematic reviews

Lara Kahale[1,2], Gordon Guyatt[3], Thomas Agoritsas[3], Matthias Briel[3], Jason Busse[3], Alonso Carrasco-Labra[3], Assem Khamis[1], Yuqing Zhang[3], Shaun Treweek[4], Lotty Hooft[2], Rob Scholten[2], Elie Akl[1]

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Institute where fellowship took place: University of Aberdeen, Scotland, UK

Background: Authors of systematic reviews (SRs) frequently deal with missing data for the outcomes of trial participants. 42% of SRs and 63% of randomized controlled trials (RCTs) reported on participants with missing data. Missing data may seriously bias results of RCTs. Thus, inferences from SRs of RCTs may be misleading if authors do not handle missing data appropriately. For authors of SRs to handle missing data in (RCTs), they need to first identify the number of trial participants with missing data. This task can become quite complex, when RCTs do not clearly report this information.

Objectives: To provide guidance for authors of SRs on how to identify participants with missing outcome data in RCTs.

Method: Guidance statements were informed by a review of studies addressing the topic of missing data and an iterative process of feedback and refinement, through meetings involving experts in health research methodology and authors of systematic reviews.

Results: The judgment of missingness relies on how trial authors report on the categories and handle them in their analyses.

Practically, for their primary analysis, systematic reviewer authors should choose how to identify participants with missing outcome data (i.e., use either ‘definitely missing data’ or ‘total possible missing data’), then select a method for handling missing data in meta-analysis. Sensitivity analyses should be undertaken to explore consistency with competing options for classifying patients as having missing data.

Conclusion: Our approach uses categories of participants described in RCT reports, and who might have missing data, and relies on how trial authors report on those categories and handle them in their analyses. Adopting the proposed guidance will help promote transparency and consistency regarding how missing data is managed in systematic reviews.

Abstract: Karaky et al.

Novel Effective Antimicrobials Against The Planktonic and Biofilm Forms of Multidrug Resistant Isolates of Klebsiella pneumoniae

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Institute where fellowship took place: King's College London, London, UK

Background: The burden of antimicrobial resistance in bacteria is a daily challenge in clinical settings, especially in intensive care units. The escalating trends of multidrug-resistant (MDR) bacteria which are reported worldwide today, and the loss of effective antimicrobials undermines the ability to fight infectious diseases. The development of novel antibacterial agents is urgently needed in healthcare settings to reduce potential nosocomial infections.

Objectives: This study aimed to assess the antibacterial efficacy of eighteen metal ion solutions individually, and in combination with graphene or graphene oxide (GO) against MDR isolates of Klebsiella pneumoniae.

Method: Minimal inhibitory concentration, minimal bactericidal concentration and crystal violet biofilm assay assessed the antimicrobial effect of the metal ion solutions against the bacterial planktonic and biofilm states, respectively. Synergy between metal ion solutions with graphene or GO was tested using fractional inhibitory concentration. Scanning electron microscopy (SEM) was used to detect the bacterial morphological changes after treatment.

Results: When tested individually against the four isolates in both planktonic and biofilm states, molybdenum, silver, gold, tin, platinum, palladium and gallium exhibited the greatest antimicrobial activity at concentrations of 13 mg/L to 52.08 mg/L. GO demonstrated no antimicrobial effect (>500 mg/L), whilst graphene showed an antimicrobial activity at 125 mg/L. When tested in combination, graphene produced a synergistic effect with platinum, gallium, tin, gold, molybdenum, silver and palladium ($p<0.05$) and inhibited the biofilms of the four resistant isolates. Following treatment with metal ion solutions or graphene compounds, SEM revealed clear morphological damage characterized by the formation of grooves or cuts in their cell walls. The bactericidal effect of the metal ion solutions, and their synergistic effect when combined with graphene derivatives against biofilms of K. pneumoniae may result in the production of potential novel antimicrobials. Currently, the effects of the compounds is being investigated on different aspects. Genome sequencing was performed to determine the effect of the tested compounds on the molecular level, while cell cytotoxicity assays are being established to predict the effect of the tested combinations on cell viability. Furthermore, confocal laser scanning microscopy is used to determine any conformational changes in the treated biofilms. Corresponding results will be presented during the conference.

Conclusion: The tested combinations can be incorporated into novel formulations for antimicrobial cleansers/ surgical scrubs that can be used in clinical settings against MDR/ chlorhexidine resistant K. pneumoniae.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Kliper et al.

Cognitive state following stroke: the predominant role of preexisting white matter lesions

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Institute where fellowship took place: The Centre for Clinical Neuroscience, St Georges, University of London, London, UK

Background: Stroke is a major cause of cognitive impairment and dementia in adults, however the role of the ischemic lesions themselves, on top of other risk factors known in the elderly, remains controversial.

Objectives: To determine the respective impact of the new ischemic lesions' volume, preexisting white matter lesions and white matter integrity on post stroke cognitive state.

Method: Consecutive first ever mild to moderate stroke or transient ischemic attack patients recruited into the ongoing prospective TABASCO study underwent magnetic resonance imaging scans within seven days of stroke onset and were cognitively assessed one year after the event using a computerized neuropsychological battery. The volumes of both ischemic lesions and preexisting white matter lesions and the integrity of the normal appearing white matter tissue were measured and their contribution to cognitive state was assessed using structural equation modeling path analysis taking into account demographic parameters. Two models were hypothesized, differing by the role of ischemic lesions' volume.

Results: Structural equation modeling analysis of 142 patients confirmed the predominant role of white matter lesion volume (standardized path coefficient $\beta = -0.231$) and normal appearing white matter integrity ($\beta = -0.176$) on the global cognitive score, while ischemic lesions' volume showed no such effect ($\beta = 0.038$). The model excluding the ischemic lesion presented better fit to the data (comparative fit index 0.9 versus 0.092).

Conclusion: Mild to moderate stroke patients with preexisting white matter lesions are more vulnerable to cognitive impairment regardless of their new ischemic lesions. Thus, these patients can serve as a target group for studies on cognitive rehabilitation and neuro-protective therapies which may, in turn, slow their cognitive deterioration.

Abstracts

Abstract: Kozlakidis et al.

Representativeness of the flu surveillance in the Belgian Sentinel Network of Laboratories using one clinical microbiology laboratory's data

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Institute where fellowship took place: LHUB - ULB, Pôle Hospitalier Universitaire de Bruxelles (PHUB), Brussels, Belgium

Background: With 15 participating clinical microbiology laboratories (CMLs) across different geographical areas, the Belgian Sentinel Network of Laboratories is able to describe trends and monitor changes in 12 groups of pathogens both at national and regional levels. As elsewhere in Europe, Belgian CMLs undergo a process of consolidation involving a shift towards laboratory amalgamation and closer real-time informational linkage.

Objectives: The impact(s) of such centralization on infectious disease surveillance (IDS) remain undefined. Anticipating some consequence of such merging on IDS, we evaluated whether influenza infection trends could be estimated from only one CML serving the Brussels area in comparison to available laboratory surveillance data in Belgium and the UK.

Method: The incidence of influenza reported cases in the LHUB-ULB (01/2016 to 12/2016), a merged CML in Brussels, was compared to the regional and national level incidences. The genomes of 100 randomly selected Influenza A isolates obtained from patients attending the emergency room of two Brussels University Hospitals (02/2016 to 03/2016), were sequenced and compared to equivalent sequences deposited at the Epiflu database for the same location and period and against UK-derived sequences from the same time period.

Results: In 2016, 1310 Influenza infections were reported by the LHUB-ULB. This represents 79.3% and 11.6% of all Influenza cases reported by the BSNL at the local and national level respectively. There was no significant difference in the observed trends between the regional and national levels and those reported by LHUB-ULB. Among the 100 sequenced isolates, no significant genomic differences were observed within the LHUB-ULB samples or against deposited genomes from the same location and time period. However there is distinct genomic grouping between the UK and LHUB-ULB sequences.

Conclusion: Our results illustrate that the real-time integration of high-throughput whole genome sequencing platforms available in consolidated CMLs into the public health surveillance system is credible and perhaps advantageous to use for future surveillance and prediction purposes. This can be most effective when coupled with multiple layers of information and timely implementation of control strategies. The genomic analyses of randomly selected samples underlined a consistent genomic similarity within the Brussels-derived samples, which were in turn genomically distinct to the UK-derived samples of the same time period.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Krivoy et al.

The scandal of lost years: Is medical services utilization a moderating factor of early excess mortality in patients with schizophrenia

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Institute where fellowship took place: Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

Background: Unlike the general population, patients with schizophrenia have excess of chronic physical morbidities such as diabetes, cardiovascular and respiratory disorders. In addition, they do no gain from primary and secondary medical services due to gaps in the accessibility and quality of those services. The result is shorter life expectancy of about 20 years mostly due to preventable physical illnesses, of otherwise people with an exclusive brain disorder.

Objectives: To explore how does utilisation of medical services moderate the association between physical morbidity and early mortality in schizophrenia patients.

Method: A retrospective cohort study derived from Clalit Medical Services electronic database (the largest health provider in Israel, covers 53% of the nation population). A three years follow-up (2012-2014) of 24,679 individuals with a diagnosis of schizophrenia (ICD 10 Code: F.20) and control general population (N=2,295,579), up to 75 years old age.

Results: Schizophrenia was associated with HR 3.52 (95% CI 3.35-3.72) for mortality, adjusted for age, sex and socioeconomic status. Patients' mortality rate was 5.6% with about half dying from physical illnesses (cardiovascular, neoplasms, respiratory, and digestive disorders). Metabolic syndrome parameters were more prevalent in the schizophrenia population, with the exception of hypertension. While the adjusted Odd Ratio (OR) for primary physician (GP) contact was 0.42 for schizophrenia patients, the OR for hospitalisation was 1.25 with more than double mean length of hospitalisation. Higher number of contacts with GP or specialists was associated with lower mortality in patients with metabolic disturbances.

Conclusion: Patients with schizophrenia tend to die earlier, mostly from preventable physical illnesses also in Israel. Utilising primary and secondary medical service was associated with better survival rates when having metabolic dysregulation. The main Health Policy implication is to stablish a national system to detect and manage physical morbidity by increasing the accessibility of primary and secondary medical services for this high-risk population.

Abstracts

Abstract: Lavi et al.

The Role of Parental Emotion Reactivity and Regulation in Child Maltreatment: A Meta-Analytic Review

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Institute where fellowship took place: King's College London, London, UK

Background: The prevalence and impact of child maltreatment make the scientific investigation of this phenomenon a matter of vital importance. Prior research has examined the associations between problematic patterns of emotion reactivity and regulation and different forms of child maltreatment (e.g., Lesnik-Oberstein, Koers, & Cohen, 1995; Moretti & Craig, 2013).

Objectives: However, the strength and specificity of these relationships is not yet clear.

Method: To address this issue, we conducted a meta-analysis of substantiated maltreatment cases involving children aged up to 18. Eighteen studies were located and included (encompassing 1,508 families). We incorporated studies addressing families with welfare cases regarding child abuse, neglect and emotional maltreatment. Our focus was the magnitude of the link between parents' emotion reactivity / emotion regulation and maltreatment of their children.

Results: As expected, results indicated problems with reactivity and regulation in maltreating parents. In comparison to non-maltreating parents, maltreating parents experience more negative emotions, display more negative emotion behavior, and are more dysregulated and impulsive.

Conclusion: Theoretical implications of these findings are discussed, presenting a model of emotion dysregulation as a core psychological factor, relating to both child maltreatment and to risk factors of child maltreatment (e.g., psychopathology, social relations). In addition, implications for prevention and treatment are presented.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Mandour et al.

Consequences of infections on NK cell- mediated cancer immune surveillance

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Institute where fellowship took place: Deduve Institute, University Catholique de Louvain (UCL), Belgium

Background: At early stages of cancer development, appropriate immunosurveillance eliminates most of the transformed cells. In addition to cytotoxic T cells, innate immune cells such as natural killer cells and NK/T cells play a major role in this protection against cancer development, especially through production of interferon-gamma (IFN- γ). Toll-like receptors (TLRs), the eminent innate pattern recognition receptors, have a crucial role in stimulating a competent anti-microbial immune response via recognition of attacking microbes or precise agonists. Recently, the connection between cancer and infections has attracted major attention. Since infections deeply modulate the immune microenvironment and particularly its innate components, we investigated their role in cancer immunosurveillance.

Objectives: To investigate the role of infections in cancer immunosurveillance both in a mouse model of acute viral infection and via ligation of various TLRs (simulating a broad range of microbial infections).

Method: The effect of infections on plasmacytoma (TEPC.1033.C2) and mesothelioma (AB1) cell growth was analysed in BALB/c mice after infection with lactate dehydrogenase-elevating virus (LDV), a usually non-pathogenic mouse nidovirus. Infections were also mimicked by ligation of various Toll-like receptors (TLRs). The mechanisms of immunosurveillance were analysed by using anti-NK cell depleting polyclonal antibody and cytokine neutralizing monoclonal antibodies.

Results: Acutely infected animals were significantly protected against both plasmocytoma and mesothelioma development. The protection was mediated by NK cell activation, through IFN- γ production. In addition, TLRs 3, 7 and 9 ligation significantly protected the mice against mesothelioma development but not plasmacytoma. This protection was attributed to the induced IFN- γ.

Conclusion: Our results indicate that modulation of the mouse immune microenvironment, and especially of innate immune responses, following either a non-pathogenic viral infection or TLR ligation protects against mesothelioma and plasmacytoma early development. This would provide a promising approach for understanding the prophylactic role induced by infections against cancer which might have important therapeutic and prophylactic applications.

Abstracts

Abstract: Manikam

The Protection Needs Inside Syria in 2018: A Rapid Review of Humanitarian Literature and Systematic Review

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Institute where fellowship took place: American University of Beirut, Beirut, Lebanon

Background: Due to the prolonged nature and growing complexity of the Syrian Crisis, the protection needs of individuals within Syria continue to increase in severity and be unmet by the international community. This study evaluates the most recent protection needs of this population for the year 2018 using a Socio-Economic Model (SEM) of health and well-being.

Objectives:
1. Identify protection needs among this population.
2. Compare how needs vary by governorate.
3. Identify institutions, actors and policies relevant to the protection needs of Syrian civilians.

Method: We are undertaking a systematic review using database searches, complemented by a rapid review of humanitarian and grey literature databases. The aim is to take a 12-month snapshot of protection among civilians currently in Syria and gaps in protection needs. Documents are to be quality assessed using the AACODS checklist, and synthesised using weight of evidence methodology.

Results: Systematic review is ongoing. Preliminary findings from the rapid review indicate that there continues to be a lack of basic needs for healthcare services, WASH services, food, and education; yet these appear to be the downstream effects of more complex needs related to movement restriction, documentation to receive humanitarian assistance, and access to livelihoods. Additionally, protection needs are not homogenous, and there is extreme variation depending on governorate.

Conclusion: Overall this research provides a practical and current document for health workers and decision makers working within the context of the Syrian Crisis.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Meerson et al.

Obesity impacts the regulation of miR-10b and its targets in primary breast tumors

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Institute where fellowship took place: Research was carried at MIGAL; samples were provided by collaborator Lorna Harries at University of Exeter Medical School, Exeter, UK

Background: Obesity increases breast cancer (BC) risk in post-menopausal women by mostly unknown molecular mechanisms, which may partly be regulated by microRNAs (miRNAs).

Objectives: Our study aimed to characterize obesity-associated effects on miRNA expression changes in BC and identify cancer-relevant miRNAs with levels significantly affected by obesity.

Method: We isolated RNA from paired benign and malignant biopsies from 83 BC patients and determined miRNA profiles in samples from 12 women at the extremes of the BMI distribution by RNA-seq. Candidates were validated in all samples. Associations between miR-10b expression and validated target transcript levels were explored. Additionally, we assessed the effects of targeted manipulation of miR-10b levels in a primary BC cell line (BT549) on proliferation, invasion potential and target gene expression.

Results: Of the 148 miRNAs robustly expressed in breast tissues, the levels of miR-21, miR-10b, miR-451a, miR-30c, and miR-378d were significantly associated with presence of cancer. Of these, miR-10b showed a stronger down- regulation in the tumors of the obese subjects, as opposed to the lean. In ductal but not lobular tumors, significant inverse correlations were observed between the tumor levels of miR-10b and miR-30c and the mRNA levels of cancer-relevant target genes SRSF1, PIEZO1, MAPRE1, CDKN2A, TP-53 and TRA2B, as well as tumor grade. Suppression of miR-10b levels in BT-549 cells increased cell proliferation and invasive capacity, while exogenous miR-10b mimic decreased invasion. Manipulation of miR-10b levels also inversely affected the mRNA levels of miR-10b targets BCL2L11, PIEZO1 and NCOR2.

Conclusion: Our findings suggest that miR-10b may be a mediator between obesity and cancer in post-menopausal women, regulating several known cancer-relevant genes. MiR-10b expression may have diagnostic and therapeutic implications for the incidence and prognosis of BC in obese women.

Abstracts

Abstract: Mhanna et al.

The sulfation of biomimetic glycosaminoglycans controls growth factor binding and subsequent cell proliferation and differentiation

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Institute where fellowship took place: Institute for Science & Technology in Medicine, Keele University, Guy Hilton Research Centre, UK

Background: Glycosaminoglycans (GAGs) are major components of the extracellular matrix that possess structural and functional roles in many tissues. The sulfation arrangements of GAGs have been tightly correlated with biological events including morphogenesis, tissue repair and aging. However, it is not clear how such events are affected by sulfation. Elucidating the mode of action of sulfated GAGs will enable the synthesis of biomimetic 2D and 3D substrates that can be used in the treatment of diseases and injuries.

Objectives: The objective of the current research was to mechanistically determine how the degree of sulfation (DS) of sulfated GAG mimetic materials affect their binding to growth factors such as fibroblast growth factor (FGF-2) and how such binding can influence the growth and differentiation of cells.

Method: Alginate was sulfated at different sulfation degrees and then biotinylated in an end-on fashion. The biotinylated sulfated alginates were then used to modify gold or polystyrene substrates. Binding of growth factors including fibroblast growth factor (FGF), epidermal growth factor (EGF) and nerve growth factor (NGF) to the substrates was assessed quantitatively using quartz crystal microbalance with dissipation monitoring (QCM-D) and enzyme-linked immunosorbent assay (ELISA) and validated qualitatively with immunostaining. Finally, the morphology and growth of cells including normal and tumour breast epithelial, neuroblastoma and lung cancer cells was evaluated via ImageJ, 3-(4,5-dimethythiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and 5-bromo-2'-deoxyuridine (BrdU) assays.

Results: Sulfated GAG modified substrates with different degrees of sulfation were constructed and assessed using QCM-D. Growth factor binding was found to increase with increased sulfation of GAGs. These findings were confirmed with ELISA and immunostaining. Cell proliferation was typically hindered when sulfated materials were added in solution. However, when neuroblastoma cells were cultured on sulfated substrates, they exhibited more stem cell spheres on the more sulfated substrates.

Conclusion: The ability to prepare sulfated substrates with controlled sulfation levels has strong implications in the biomedical field. Sulfated substrates can be used to induce different levels of growth factor binding, and to increase or inhibit cell proliferation which has major implications in tissue engineering and cancer therapy.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Morsy et al.

Genetic study of Egyptian families with suspected primary ciliary dyskinesia

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Institute where fellowship took place: Institute of Child Health, University College London, London, UK

Background: Primary ciliary dyskinesia (PCD), a genetically heterogeneous condition enriched in some consanguineous populations, is caused by recessive genetic mutations affecting cilia structure/motility. Early diagnosis is the key for attenuating diseaseprogression, which improve the quality of life of patients. In Egypt, a country with limited resources and high rate of consanguineous marriage, the prevalence could be even higher. Currently, diagnosis requires multiple expert tests. Recently, Genetic testing is increasingly used, however, PCD shows high allelic and locus heterogeneity with mutations in about 40 genes, known so far, lead to PCD.

Objectives: To evaluate the genetic diagnostic yield of targeted next generation sequencing (NGS) and mutation spectrum in a cohort of Egyptian families where PCD is highly clinically suspected.

Method: The study included 44 patients from 33 unrelated families, who were recruited from Alexandria University Children's Hospital, in the period between April 2016 and April 2018. Informed consent was obtained from all participants or their guardians.

All patients were screened by targeted next generation sequencing. Sequencing data were processed at North East Thames Regional Genetics Service using an in-house bioinformatics pipeline. Confirmation of the prioritized variants in the affected individuals and segregation within the available family members was performed using Sanger sequencing.

Results: Out of the 44 affected patients enrolled in the study, only one affected individual was 33 years old at the time of recruitment. All other 43 participants were below 18 years old (1 month – 18 years). Parental consanguinity was reported in 73% of the families. The majority of the participants showed typical PCD clinical symptoms.

Variants in known PCD genes were identified in 25 families of the 33 families (76%). Bi-allelic variants in 13 autosomal recessive genes were identified, Sanger-confirmed and segregated in 23 families, representing a complete genetic diagnostic output (70%). In 2 families, only one mutated allele (single heterozygous) was identified in known PCD genes. No hemizygous variants in X-linked PCD genes were identified. Based on the predicted impact on the encoded proteins, various types of variants were identified in known PCD genes. About 79% of the variants were high-impact truncating variants including nonsense, frameshift, mutations affecting splicing and CNVs.

Conclusion: High-throughput targeted NGS expedites PCD diagnosis, indicating significant patient benefit in its wider, earlier implementation.

Abstracts

Abstract: Mullineaux-Sanders et al.

The gut microbiota influences the in vivo lifestyle of the mouse pathogen Citrobacter rodentium

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Institute where fellowship took place: Weizmann Institute of Science, Rehovot, Israel

Background: Enteropathogenic and enterohaemorrhagic Escherichia coli (EPEC and EHEC) are human diarrheal pathogens which colonise the gut epithelium via the formation of characteristic attaching and effacing (A/E) lesions. Mice are inherently resistant to EPEC and EHEC infection. The natural mouse pathogen *Citrobacter rodentium* is widely used as a physiological small animal model of human EPEC/EHEC infection and host-pathogen-microbiota interactions. *C. rodentium* infection of mice induces diarrhea, colonic crypt hyperplasia, acute colonic inflammation and dysbiosis.

The normal gut flora (microbiota) plays a crucial role in determining the severity of *C. rodentium* infection. Many members of the microbiota provide colonisation resistance against *C. rodentium*, however the pathogen also exploits the microbiota to its own advantage, for example by using microbiota-derived cues to sense the environment and regulate expression of virulence factors.

Objectives: To investigate the effect of disrupting the microbiota at the peak of *C. rodentium* infection on pathogen-host interactions.

Method: During infection with the kanamycin (Kan)-resistant and bioluminescent strain of *C. rodentium*, ICC180, we use daily oral antibiotic treatment to induce dysbiosis from 6 days post infection (the peak of colonisation). Using in vivo bioluminescent imaging, we investigate the effect of antibiotic-induced dysbiosis in two mouse strains: the C57BL/6 model of mild infection and the C3H/HeN model of severe, lethal infection.

Results: We find that Kan, but not vancomycin or metronidazole-induced dysbiosis is sufficient to cause a re-localisation of *C. rodentium* within the host from its physiological infectious niche on the colonic mucosa to the caecal luminal contents. This also occurs with a *C. rodentium* mutant constitutively expressing virulence genes, suggesting that specific, Kan-sensitive commensals may be required for pathogen colonisation at the epithelium. In both mouse strains, *C. rodentium* persists avirulently in the caecal luminal contents under conditions of continuous Kan treatment. Interestingly, following withdrawal of Kan treatment, *C. rodentium* stably integrates into the gut microbiota of C3H/HeN, but not C57BL/6, mice, a phenomenon we term antibiotic-induced bacterial commensalisation (AIBC). *C. rodentium* in the AIBC state is non-inflammatory and C3H/HeN mice do not show signs of morbidity despite shedding 10^5-10^6 CFU/g stool *C. rodentium*. Finally, we identify a commensal Citrobacter strain as refractory to *C. rodentium* commensalisation.

Conclusion: The gut microbiota plays a key role in *C. rodentium* infection; by modulating the microbiota we can alter the physiological location of *C. rodentium* within the host and attenuate virulence.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Najajreh

Genomic Studies for the Assessment of Platinum (IV) Susceptibility to Nucleotide Excision Repair (NER)

Yousef Najajreh[1], Shuvro Nandi[2] and Simon Reed[2]

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Institute where fellowship took place: School of Medicine, Division of Cancer and Genetics, Heath Park, Cardiff, UK

Background: Platinum-based anticancer agents gained wide clinical application in treating testicular, ovarian head and neck, colon and non-small cell lung cancers. Beside Cisplatin and Carboplatin (1 and 3 in Figure-1), Oxaliplatin (4), got approved for treating advanced colorectal cancer in combination with 5-FU[5]. The clinical applicability of such drugs was hampered by their severe toxicities and by emerging resistance. One approach to reduce potential toxicity and to overcome resistance could be Pt(IV) prodrugs. Cytotoxicity of Pt drugs is correlated to the ability to induce DNA damage while the resistance was in part attributed to the efficiency of Pt-DNA adducts by Nucleotide Excision Repair (NER) pathways (both Global Genome and transcription-coupled nucleotide excision repair i.e. GG-NER and TC –NER).

Objectives: In this study we tried to address the ability of the Pt(IV) species to directly interact with global DNA without a reducing agent and exerting toxicity in a distinct mechanism.

Method:
Chemistry: a series of Oxaliplatin derivatives were synthesized (Figure 1b). While retaining the 1,2-diamminocycolexane, the equatorial ligands were modified (chlorides, or oxalate ligand, while the axial was either chloride, hydroxide or an ester derivative.

Molecular Biology: The protocol for preparation of Pt-DNA adducts using yeast DNA was applied with some modifications. Yeast DNA was incubated with Pt derivative, then fragmented using sonication. Pt adducts was removed using NaCN followed by quantification Q-PCR. For detailed procedures of the biological methods please see relevant references by Prof Reed.

Results: In contrast to current hypothesis[10], our preliminary results indicated that Pt(IV) can indeed palatinate global DNA. The resultant Pt(IV)-DNA could be detected using a novel CP 9/19 antibody developed by the Absolute Antibody company.

Networking and Meetings, Discussions and Brainstorming sessions: In addition to numerous enriching discussions that took place with Prof. Reed, several meetings and brainstorming sessions were organized while at Cardiff.

Conclusion: The fellowship was helpful in initiating a collaboration between two complementary research groups. By combining their expertise it is hoped to contribute in tackling fundamental scientific questions that has the potential to be beneficial in the treatment of cancer patients when translated at a later stage.

Abstracts

Abstract: Nasr

Exploration of the applicability of nicotinamide hot melt extrudates in treatment of acne

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Institute where fellowship took place: Centre for Pharmaceutical Engineering Science, University of Bradford, Bradford, UK

Background: Hot melt extrusion is an industrial-friendly process with wide applicability. The produced extrudates are reported to be used via several routes of administration, however, their topical applicability has not been fully explored till current date for treatment of dermatological diseases.

Objectives: The aim of the present work was to prepare and characterize hot melt extrudates using Soluplus polymer, to be loaded with nicotinamide drug, and to explore their applicability in acne treatment.

Method: The extrudates were characterized for their thermal properties using DSC, their chemical compatibility using FTIR, their crystallinity using XRD, and their water absorption potential using DVS. The extrudates were also tested for their skin adhesion potential, ability to deposit nicotinamide in different skin layers, and their clinical efficacy in acne patients.

Results: The extrudates loaded with 10% nicotinamide were found to be amorphous nature when freshly prepared and after storage, with no chemical interaction between nicotinamide and Soluplus. Upon comparing the skin adhesion and deposition of extrudates and nicotinamide gel, it was found that the extrudates displayed significantly higher adhesion and drug deposition reaching 4.8 folds, 5.3 folds, and 4.3 folds more in the stratum corneum, epidermis and dermis respectively. Furthermore, the extrudates significantly reduced the total number of acne lesions in patients by 61.3% compared to 42.14% with the nicotinamide gel.

Conclusion: Nicotinamide extrudates were found to be promising topical drug delivery means for the treatment of acne, and can be explored for applicability in other dermatological diseases.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Negev

Climate change: an emerging threat and possible opportunity for public health in the Middle East

Maya Negev[1]

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Institute where fellowship took place: London School of Hygiene and Tropical Medicine, London, UK

Background: Climate change is "the biggest global health threat of the 21st century", according to the Lancet. The Mediterranean is a climate change hotspot, where rates of climate change exceed global trends. The population in the Middle East is particularly vulnerable to climate change, due to numerous factors including conflicts, water shortage and population density.

Objectives: This presentation is an overview of current and projected climatic changes in the Middle East and their impact on public health, including recommendations for adaptation.

Method: Overview presentation.

Results: Climate change is associated with extreme events including heat waves, cold spells, droughts, floods and wildfires. In the Mediterranean, an increase in the intensity, length and frequency of heat waves, and a decrease in precipitation, have been observed. Hot temperatures are correlated with increased morbidity and mortality, especially among vulnerable populations. Climatic change has also been associated with expansion of vector-, water- and food-borne diseases, including outbreaks of West Nile Fever in the Mediterranean, and with droughts that may lead to malnutrition and migration. According to the Intergovernmental Panel on Climate Change (IPCC), temperatures will continue to increase, and extreme weather events will become more frequent. At the same time, adaptation policy can mitigate negative health impacts. Adaptation is required in the Middle East at the cross-border, national and local levels, as well as in health systems.

Conclusion: In the short-term, Middle East countries should develop resilient health systems, and prepare for more frequent and severe extreme weather events. At the community level, health systems should prepare for protecting the most vulnerable populations. In the longer-term, the health sector should work with municipalities and national governments to promote resilient communities and cities. Climate change is a global phenomenon, and its impact is cross-border including heatwaves, vector-borne diseases and droughts. Middle Eastern countries have the opportunity to work together for cross-border water, energy and health solutions, and, as also suggested by the Lancet, turn climate change into "the greatest global health opportunity of the 21st Century".

Abstracts

Abstract: Obeidat et al.

Evaluation of Matrix Tablets Based on Eudragit®E100/Carbopol®971P Combinations for Controlled Release and Improved Compaction Properties of Paracetamol

Wasfy Obeidat[1]

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Institute where fellowship took place: School of Life Sciences, University of Sussex, UK

Background: Matrix tablets fabricated by direct compression are the simplest, the most attractive and the most commonly used technology in Controlled release dosage forms (CRDF). Mixtures of polymers of various swelling, gelling, and erosion properties have gained interest in controlled matrix formulations. By optimizing of the composition of the polymeric mixtures and the total polymeric content, a range of release rates of a drug can be obtained by altering the diffusivity of the drug through the matrix tablet structure.

Objectives: To investigate the controlled release properties of matrices made of Eudragit®E100 and Carbopol®971P NF. The effects of the ratio of the two polymers, the total polymeric content, and the tablets mechanical strength on paracetamol release rates were also investigated. Paracetamol, which is a class I drug, was used as a candidate model since it has high aqueous solubility and relatively short biologic half-life of approximately 2 to 3 h in normal adults in the usual dosage range. Paracetamol has a pK of 9.51, and therefore, exhibits pH-independent release and as such its drug release would depend on the gelling and erosion properties of the polymeric matrix.

Method: For the different tablet formulations, the following procedure was followed: paracetamol was mixed with all polymeric excipients and lactose manually using the bottle method for 4 min. Then, Mg stearate and Talc were added and admixed for an additional 1 min. Accurately weighed amounts of the mixtures were manually placed into the die and were directly compressed for 30 s at different pressures (245, 490, and 735 MPa). Dissolution studies were conducted using USP XX Π rotating paddle apparatus at 50 rpm and 37°C at three different consecutive stages (pH 1.2, 4.8, and 6.8).

Results: Polymeric combination improved significantly the compaction properties of paracetamol tablets as evident by the higher crushing strengths compared to polymer-free tablets at intermediate compression pressure. When combined with Carbopol®971P NF, Eudragit®E100 was found to be capable of extending paracetamol release for more than 12 h. Korsmeyer–Peppas model was found to be the most suitable for fitting drug release data.

Conclusion: Eudragit®E100 when combined with Carbopol®971P NF was capable of improving the compaction and sustained release properties of paracetamol. The polymer combinations can potentially be used to control the release rates of highly water soluble drugs.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Oweis

Hemodynamics of aortic dissection

Ghanem Oweis[1]

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Institute where fellowship took place: Institute for Cancer Research, Surrey, UK

Background: Aortic dissection is an infrequent but fatal abnormality of the aorta. It is characterized by a tearing flap in the intimal layer of the blood vessel which lets blood flow between the layers of the vessel creating an abnormal false lumen that is parallel to the true lumen. Its diagnosis can be elusive, and treatment planning is not straightforward. The blood flow patterns in the vessel fundamentally impact the transport of the diagnostic contrast within, and the hemodynamic forcing on the tear. Improved understanding of flow dynamics can aid in improving diagnosis and prognosis.

Objectives: The aim is to understand the effect of dissection morphology on diagnostic contrast perfusion. Furthermore, identification of energetic blood flow patterns that may be associated with tear expansion may help improve prognosis and treatment planning.

Method: Eight in-vitro aortic models representing different dissection geometries were tested using a recirculating flow loop. Laser-assisted optical imaging of the flow within the transparent vessel combined with computerized image processing were used to produce the flow velocity maps. The same imaging setup was used with fluorescent dye injection to simulate the diagnostic radiographs produced by contrast-enhanced computed tomography (CT).

Results: The flow pattern in the dissection was dramatically affected by the type of false lumen, whether it was patent or non-patent (occluded). A non-patent false lumen had negligible time-averaged flow, and the fluorescent dye took longer time to appear in the images compared to it spearing in the true lumen. This suggests that a diagnostic protocol should include a time-delayed image capture to allow for the slow contrast perfusion in the false lumen. When the false lumen was patent, the dye appeared nearly at the same time in the two lumens. In the patent case, the blood velocity differential between the two lumens carried through to the non-dissected aorta producing a layer of shear vortices which rubbed against the healthy aortic wall.

Conclusion: Diagnostic imaging of a suspected aortic dissection may be improved if time delay acquisition is adopted in the protocol particularly when false lumen occlusion is probable. Shear layer vortex shedding in a patent false lumen may be one active hemodynamic tear expansion mechanism that should be factored in during treatment planning and follow up.

Abstracts

Abstract: Philippou et al.

Developing novel platforms for delivery and investigation of vascular-targeted photodynamic therapy (VTP) of pre-clinical models of prostate cancer; towards multi-modality prostate cancer therapy

Yiannis Philippou[1], Hanna Sjoberg[2], Ian Tullis[1], Sean Smart[1], Giles Mckenna[1], Ruth Muschel[1], Ian Mills[2], Avigdor Scherz[3], Boris Vojnovic[1], Freddie C. Hamdy[2], Richard Bryant[1,2]

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[3]Weizmann Institute of Science, Department of Plant Biology, Rehovot, Israel

Institute where fellowship took place: Weizmann Institute of Science, Rehovot, Israel

Background: Radiotherapy (RT) is administered for localised and locally advanced prostate cancer (PCa) and provides benefit in low metastatic burden disease. However, it can cause significant side-effects, and is not always curative. There is an unmet clinical need to develop multi-modality therapies to improve treatment outcomes for PCa. Vascular-targeted photodynamic therapy (VTP) is a novel minimally invasive surgical focal therapy technique for low-risk, low-volume PCa. However, VTP has not been investigated in combination with RT, or in higher risk disease. It is therefore necessary to develop a platform to evaluate VTP with RT in pre-clinical mouse models of PCa.

Objectives: To develop bespoke equipment to deliver VTP to flank xenograft PCa and investigate its effect on tumour growth.

Method: We developed an enclosed optical irradiation system to deliver VTP to flank tumours. A small enclosure contains a heating pad, anaesthetic tubing, and connections for physiological monitoring. The enclosure lid contains fibre-coupled excitation optics, and a positioning system to align the output beam to the target area. A guide beam is provided, and a camera is fitted to enable laser beam alignment to the target. All system functions are software controlled. A thermoelectrically-cooled semiconductor laser diode provides laser excitation, with its output launched into a multimode fibre.

TrampC1 subcutaneous flank tumours were generated in C57BL/6 mice, and treated with VTP at a volume of 80-120mm^3. The WST11 photo-sensitiser was reconstituted in sterile 5% dextrose at 2mg/mL under light-protected conditions, and aliquots stored at –20°C. On each day of treatment, an aliquot of WST-11 was thawed and filtered through a 0.2µm disc syringe filter. Mice were intravenously infused over five minutes with 7-8 mg/kg WST11 followed by a 10-minute laser transcutaneous illumination (753 nm, 120 mW/cm) of the tumour through a 1 mm frontal fibre.

Results: VTP was well tolerated and resulted in a significant tumour growth delay compared to untreated controls, similar to that achieved by 3x5 Gray RT evaluated in the same tumour model in previous experiments. Effects of VTP on the tumour immune micro-environment are being investigated.

Conclusion: We have developed a bespoke platform to deliver VTP to pre-clinical flank tumour PCa models. Preliminary experiments have established the efficacy of VTP to be broadly similar to that of RT. The results of multi-modality treatment combining VTP and RT are awaited.

Abstract: Pras et al.

Exploring Rare Genetic Variants in Age-related Macular Degeneration

Eran Pras[1,2], Nadav Shoshany[1]

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[2]Tel Aviv University, Tel Aviv, Israel

Institute where fellowship took place: London School of Hygiene and Tropical Medicine, London, UK

Background: Age-related macular degeneration (AMD) us a **multifactorial** disorder with strong genetic background.

Objectives: Our aim was to identify **rare** genetic variants in **early-AMD** cases utilizing **Whole Exome Sequencing** (WES).

Method: In our study eight non-related early-AMD families of different Jewish ethnicities were ascertained (Families 1-8). Initial mutation screening for variants (phase-1) included common (CFH p.Y402H and ARMS2 p.A69S) and rare variants (CFI p.V412M and HMCN1 c.4163delC) identified previously in our population. Four families (Families 1-3, and 7) whose initial screening did not detect carriage for the aforementioned variants underwent WES (phase-2). Bioinformatics filtering was based on functionality (variants from a panel of 234 genes with proven or presumed association to AMD); predicted severity; and frequency (rare variants with Minor Allele Frequency, MAF<1%). When applicable, further mutation screening for a specific rare variant was carried out on additional cases of similar ethnicities and phenotypes (phase-3).

Results: Phase-1 identified by mutation screening three Tunisian Jews families carrying the previously reported **CFI p.V412M** mutation. **WES analysis** has detected probable disease related rare variants in three out of the remaining four families. These included: **a novel variant in PLEKHA1** gene p.S177N in oriental Jews family (Family-2); a **previously reported variant CFH** p.R1210C in Ashkenazi Jews family (Family-1); and two other Ashkenazi Jews families (Family-3 analyzed by WES; and Family-6 discovered by screening for the specific mutation) with the **C3 p.R735W** variant.

Conclusion: We conclude that **rare, high-penetrance variants have a profound contribution to early-AMD pathogenesis. Utilization of WES in genetic research of multifactorial diseases as AMD allows a comprehensive analysis across all genes of the genome and the identification of previously unreported rare variants.**

Abstract: Sacitharan

Why does age-related arthritis occur?

Pradeep Kumar Sacitharan[1]

[1]*University of Liverpool, Institute of Ageing, Liverpool, United Kingdom*

Institute where fellowship took place: The Institute of Dental Sciences, The Hebrew University of Jerusalem, Hadassah Medical Center, Jerusalem, Israel

Background: Osteoarthritis (OA) is the most common form of arthritis worldwide and is characterized by the progressive degradation of articular cartilage. Currently, there are no effective therapeutic agents to treat or reverse this crippling disease. Advanced age is a primary risk factor for OA. SIRT1, a protein deacetylase, has been shown to control lifespan extension and promote cartilage health. My previous work on the role of SIRT1 in OA was built upon the work of the Dvir-Ginzberg group at the Hebrew University of Jerusalem.

Objectives: The objective of this fellowship was to learn new techniques and knowledge from the Dvir-Ginzberg group to help me elucidate in the future how cellular aging proteins such as SIRT1 might contribute to OA.

Method: I learnt new methods in chromatin immunoprecipitation and fluorescent assays.

Results: Due to short nature of the fellowship I only had a chance to learn new protocols and did not have enough time to generate reproducible results.

Conclusion: The fellowship allowed me to learn new techniques and experience Israeli science and culture. The techniques I experienced in Israel will be key to my future research direction and career.

Abstract: Safrai et al.

Fertility preservation for pre-pubertal boys: evaluation of controlled slow freezing of testicular prepubertal tissues

Myriam Safrai[1], Doron Kabiri[1], Michal Gropp[1], Talya Mordechai Daniel[1], Guy Hidas[1], Tal Imbar[1], Benjamin Reubinoff[1]

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Institute where fellowship took place: Nuffield Department of Obstetrics & Gynaecology, University of Oxford, Oxford, UK

Background: Fertility preservation options for cancer-affected pre-pubertal boys are very limited. Pre-pubertal testicular tissue containing spermatogonial stem cells (SSCs) can be cryopreserved for future potential use. The best method is still unknown. Controlled Slow Freezing (CSF) may be a sustainable option for cryopreserving testicular tissue.

Objectives: To assess the effect of CSF of prepubertal testicular tissues on the survival of SSCs and integrity of the testicular niche.

Method: After informed consent of the parents, we performed testicular biopsies for pre-pubertal boys, prior or after gonadotoxic treatment. One testicular fragment was immediately fixed and served as a control. The remaining fragments were cryopreserved by CSF. We thawed some of the frozen tissue and performed H&E staining and immunostaining for MAGE-A4 - marker of SSCs, and Vimentin –marker of Sertoli cells.

Results: Five prepubertal boys underwent the procedure. H&E staining did not reveal any significant differences in the number of tubules per section and structural integrity between the samples. Vimentin Immunostaining, showed similar positive staining of the Sertoli cells in all tubules. No significant difference was observed in MAGE-A4 stained SSCs after CSF. There were significantly higher MAGE-A4 positive SSCs in samples from chemotherapy naïve patients. However, prior chemotherapy treatment did not affect the survival of the Sertoli cells.

Conclusion: This study demonstrates that CSF does not damage the SSCs and sertoli cells numbers per tubule in pre-pubertal testicular tissue. It further highlights the significance of cryopreservation of the testicular tissues prior to gonadotoxic treatments. CSF appears to be a suitable option for cryopreserving pre-pubertal testicular tissues.

Abstract: Said et al.

Determination uric acid, xanthine and hypoxanthine in saliva using µSPEed and LC-MS/MS

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Institute where fellowship took place: Loughborough University, Loughborough, UK

Background: Xanthine and uric acid are playing important role in many clinically important diseases and metabolic disorders.

Objectives: The aim of this work was to explore SPEed Cartridges as a possible on-line sample preparation method in combination with tandem mass spectrometry (LC-MS/MS) for quantification of uric acid, xanthine and hypoxanthine in saliva.

Method: An autosampler connected with a LC-MS/MS instrument was set up. A C_8 sorbent was used for the µSPEed extraction. Subsequent analysis was performed with a gradient LC system.

Results: The chromatographic run time 2.5 min and the quantification ranges were 2.5×10-7 -2×10-4 M for hypoxanthine and 5.0×10-7M-5×10-4 ng/mL for xanthene and uric acid, (r2≥0.998, 0.994 and 0.993 respectively, n=6). Precision and accuracy were documented at three levels. Accuracy results were between (102-109) and precision (≤10 %).

Conclusion: This method provides an accurate, precise and automated procedure that can be applied for quantifications of oxypurine in clinical laboratories equipped with LC-MS/MS.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Sammar et al.

Placental derived extracellular vesicles express Placental Protein-13 and Levels are decreased in preeclampsia

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Background: Extracellular vesicles are important cell-derived components in communicating various physiological and pathological conditions. Preeclampsia (PE) is one of the most life threatening pregnancy complications. A hallmark of PE is elevated placental shedding of syncytiotrophoblast derived extracellular vesicles (STB-EVs) into the maternal circulation. Decreased placental expression of PP13 and its low concentrations in first trimester maternal sera are associated with elevated risk of preeclampsia. The ability of soluble PP13 to induce apoptosis and secretion of cytokines of lymphocytes suggests important immune functions.

Objectives: In this study we aimed to explore the difference in PP13 level in STB-EVs collected from PE and unaffected placentae.

Method: Placentae were obtained at caesarean section from normal and PE cases. STB-EVs were collected by the dual placental lobe perfusion using sequential centrifugation. Three populations were isolated from the maternal perfusate: a 10,000×g pellet enriched for STB microvesicles (STB-MVs), a 150,000×g pellet from the resultant supernatant enriched for STB exosomes (STB-EXs) and total STB-EVs isolated by a single 150,000 xg centrifugation. Western blot and ELISA were used to verify and quantify the respective proteomic cargo of the STB-EVs.

Results: All preparation had the STB marker placental alkaline phosphatase (PLAP), whereas ALIX and CD9 were exclusively expressed in STB-EXs. PP13 was determined for the first time in all three STB-EVs preparations, and was expressed in both their inside and on their surface. PP13 load, was significantly lower in PE compared to control in the total STB-EVs and STB-MVs, but not in STB-EXs.

Conclusion: Lower PP13 levels were observed in STB-EVs derived from PE at delivery. Circulating PP13 is therefore either soluble or associated with STB-EVs, and each may deliver distinct immunomodulatory signals associated with PE.

Abstracts

Abstract: Scott et al.

Development of a pharmacy based intervention to reduce dependence on prescribed and over-the counter medicines in Jordan: Qualitative study of experiences of people in treatment for addiction in Amman in sourcing the drugs on which they are dependent

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Institute where fellowship took place: University of Jordan, Faculty of Pharmacy, Amman, Jordan

Background: Addiction to prescription, over the counter and illicit substances is a problem in the UK and Jordan. In Jordan, regulation of medicines is similar to the UK, but enforcement is poor. In Jordan, we know medicines liable to misuse can be purchased from pharmacies, sometimes without prescription or against a previously 'spent' prescription. Previous research found that 94% (n=393) of pharmacists who completed a self-reporting questionnaire suspected some level of non-medicinal use of OTC or prescription medicines occurred amongst patients of their pharmacy (Albsoul-Younes et al. 2010). We hypothesize that there is potential for pharmacists to intervene to provide care for people who are experiencing addiction. However, before any intervention can be designed, first we need to understand how people who are addicted source their drugs of choice and therefore whether a pharmacy-based intervention may be appropriate.

Objectives: To explore the experience of people being treated for addiction in sourcing drugs, with an emphasis on pharmacy.

Method: A qualitative study of people in treatment for addiction (n=16), exploring experiences of sourcing the drugs they misused. Setting: an addiction treatment facility in Amman. All participants were male. Interviews were conducted in Arabic, recorded, transcribed then translated into English. Two were back translated into Arabic by a bilingual speaker, to validate translation. Data in English was uploaded into NVivo v11 where data analysis was undertaken by coding the transcript data and then grouping codes into sub themes and themes iteratively.

Results: Participants described experiences of obtaining prescription and OTC medicines from three main sources: drug dealers, from pharmacists (without or with a valid prescription) and from hospital stocks via hospital staff. With regard to the pharmacists theme, subthemes included greed as a motivation by pharmacists to sell medicines liable to misuse, 'going soft' on application of the regulations and sale motivated by familiarity/friendship with the patient. In some cases, the participants considered that pharmacists felt the abuse profile of the drug to be low and therefore they perceived that the pharmacist had no concerns about addiction potential.

Conclusion: Education of pharmacists on abuse potential of medicines should be an intervention component. Factors such as financial motivation and the desire to please or maintain familiar relationships may be harder to address through training. Tightening and enforcement of regulation may be needed to address these factors.

Abstract: Segev et al.

Classifying schizophrenia by patterns of drug-resistance: The role of frontal cortical glutamate

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Background: The on-going effort to develop biologically-based classification for psychotic disorders gave rise to attempts using the differential responsiveness to anti-psychotic medications as a deciphering key. Recent studies indicate two forms of treatment-resistance in schizophrenia: "early resistance" already present at illness onset, and "late-resistance" that evolves after a period of drug-responsiveness ("late resistance"). This division may represent two different clinical and biological psychotic entities.

Objectives: This study aimed to examine whether elevated glutamate levels in the anterior cingulate cortex (G-ACC), a measure previously linked to treatment-resistant psychotic states, is specific to either early or late anti-psychotics resistance.

Method: The sample was derived from three different magnetic resonance stereoscopy studies, examining G-ACC levels in patients suffering from psychotic illness. Inclusion criteria were 18-40 years of age, illness duration of below 10 years and a complete medical record from illness-onset. Clinical data was obtained via electronic health records. Patients' files were coded by Clinical Global Impression scales and the patients were classified as either responsive, early or late resistant. Comparison of the three groups G-ACC levels was performed by multinomial regression taking into account relevant demographic and clinical variables.

Results: No significant difference in G-ACC level was observed between early and late resistance. Moreover, no difference was observed between each of these groups to the responsive group nor between the unified resistant groups and the responsive group, in contrast to current literature. A trend for increased G-ACC levels was observed in patients with extensive recreational drug use, regardless of their response status.

Conclusion: G-ACC did not provide evidence that early and late resistance are distinct biological categories. The results contrasted with previous studies showing that G-ACC differs between responsive and resistant patients. This suggests that increased G-ACC levels may be a marker for a transient "state resistance" but not for long-standing "trait resistance". Future research is needed to verify the results, as well as to examine other biological markers potentially differentiating early and late resistant psychosis syndromes.

Abstract: Shenhar-Tsarfaty et al.

The cholinergic anti-inflammatory response in cardiovascular diseases - can bariatric surgery change the sympathetic prone state of obese people?

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Institute where fellowship took place: University College London Institute of Ophthalmology, London, UK

Background: My fellowship project was about retinal microvascular changes as predictors for cognitive decline in diabetic patients (Prof. Rubin, UCL Institute of Ophthalmology). Studying the long term diabetes associated complications. In the last 7 years I continue to study the cholinergic anti-inflammatory response in obese, apparently healthy and cardiovascular patients.

Accumulating evidence suggests parasympathetic dysfunction and elevated inflammation as underlying processes in multiple peripheral and neurological diseases.

Acetylcholine, the main parasympathetic neurotransmitter and inflammation regulator is part of the cholinergic signalling pathway which effect cognitive decline, stress and metabolic disorders and is continuously subjected to genetic, epigenetic and microRNA regulation. Inherited and/or acquired sympathetic prone state can lead to excessive inflammatory load and cognitive decline. To evaluate the sympathetic/parasympathetic balance we measured serum cholinesterase activities in stroke, myocardial infarction, diabetes mellitus patients and apparently healthy control. Recently we found that serum AChE activity increased with BMI in a dose-dependent manner until it reached a peak level at BMI of 30-35 kg/m^2, followed by a plateau ($p<0.001$, $n=1,450$). Similarly, AChE activity increased with waist circumference categories.

Objectives: To check if bariatric surgery can change the sympathetic prone state of obese people.

Method: Cholinesterase activities were analysed in 77 morbid obese patients before and at 3, 6, 12 and 36 months flowing bariatric laparoscopic sleeve gastrectomy (LSG) surgery-induced weight reduction. Association between metabolic outcome and AChE and the changes were evaluated.

Results: The Obesity-related AChE resistance phenotype may be reversed following LSG surgery and correlates with metabolic outcomes 36 month thereafter. (Delta BMI $r=0.315$, $p=0.015$; delta fat loss $r=0.321$, $p=0.03$; and prevalence of fatty liver, $p=0.016$).

Conclusion: Further long-term studies will be needed to validate and evaluate the beneficial effect of AChE reduction post bariatric surgery.

Abstract: Sheta

Implementing a Prenatal Fetal Echocardiography Screening in a Tertiary Fetal Medicine Unit

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Institute where fellowship took place: Cairo University, Cairo, Egypt

Background: Fetal echocardiography plays a pivotal role in identifying the congenital heart defects (CHDs) in utero. Though foetal echocardiography is mostly reserved for high risk pregnant women, its role as a routine prenatal screening tool still needs to be defined.

Objectives: To implement an early prenatal screening for detection of congenital fetal heart anomalies in first trimester scanning and confirmed by neonatal echocardiography.

Method: A prospective observational study performed at tertiary Fetal Medicine Unit, Cairo University teaching Hospitals, Kasr El Eini Medical school

Patients had a first trimester scan from 11–14 weeks which included screening for Down's syndrome by measurement of the Nuchal translucency thickness, detection of depressed Nasal bone bridge , measurement of Ductus Venosus pulsed wave doppler flow and pulsed wave doppler for tricuspid valve regurgitant flow.

Fetal screening was performed with full anatomy examination and special emphasis on the heart.

Two Dimensional echocardiography examination of the heart included; the four chamber view, intact inter-venticular septum, swipe of outflow tract and the three vessel view in the mediastinum.

Pulsed and Colour Doppler was done at level of tricuspid valve to exclude regurgitation and at the ductus venosus to detect the presence of Reversed A wave.

Follow up Neonatal echocardiography was done to confirm the early trimester echo finding.

Results: A total of 900 pregnant females were examined. The mean age of the patients was; 23.9 ± 5.2. Mean BMI was 28.5. The mean GA at the first trimester was 13.4 ± 0.7. A total of 33 congenital heart anomalies were confirmed postnatally (3.7%). Twenty one were diagnosed and 12 were missed at the first trimester and 3 were falsely diagnosed as having an anomaly giving a detection rate of 63.6%, specificity 99.7%, PPV 87.5%, NPV 98.6% and agreement reached 98.3% (kappa 0.728).

Conclusion: First trimester prenatal fetal echocardiography screening has a good early detection rate for congenital heart anomalies and should be done as a routine during first trimester screening especially for Down's syndrome. Training programs should be implemented.

Abstract: Shkedi Rafid et al.

Choice in the era of advanced genomic tests in pregnancy

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Background: Advanced genomic tests, such as Chromosomal Microarray Analysis (CMA), are becoming an integral part of pregnancy care. Such tests can identify variants of uncertain clinical significance and secondary findings (i.e. pathogenic variants not related to the condition for which testing was initiated). Unlike in the past, when people could choose between having or not having a genetic test, advanced genomic tests, at least in some countries, provide another choice- which findings are disclosed.

Objectives:
1. Assessing choices of women who underwent prenatal CMA testing regarding various types of CMA findings.
2. Evaluating whether women's choices were associated with indications for testing and with one-on-one pre-test genetic counselling.
3. Exploring attitudes towards choice by uptakers of prenatal CMA testing.

Method: Medical records of women who underwent prenatal CMA testing (n = 1070) were examined for testing indications, choices regarding CMA findings, and whether they had received individual pre-test genetic counselling. Univariable associations were analyzed using $\chi 2$ tests. Logistic regression models were used to assess independent associations with testing indication and prior genetic counselling. Women opting for prenatal CMA testing and their partners were invited to either complete a questionnaire before the test (n=194), or consent to a telephone-interview up to a week after (n=42).

Results: Approximately 56% of women chose to be informed of all types of CMA findings, and 20% chose not to be informed of any of the findings beyond standard care. Non-medical indications for testing, i.e. no abnormal findings in any of the screening/ultrasound tests, and receiving individual pre-test genetic counselling were independently associated with increased interest in a broader range of findings.

A clear majority of participants, both questionnaire respondents and interviewees, viewed the choice they were given favourably. Women were more likely to support parental choice compared to men. Arguments in favour of choice included supporting parental autonomy and preferences. Arguments against choice included trust in clinicians' judgement, and avoidance from stressful dilemmas. The most desirable findings were those perceived to be actionable, and the least desired were those perceived as non-actionable and anxiety-provoking.

Conclusion: Women were generally more likely to choose to receive additional genetic information on their fetuses than not to, albeit differences in preferences depend on testing indication and type of pre-test counselling. Most parents understand the different possible CMA findings and choose which to receive based on their moral and psychological preferences.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Stepensky et al.

Whole Exome Sequencing: a Decision-making Aid in Primary Immune Deficiency and Bone Marrow Transplantation

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Background: Sixteen years after the completion of the human genome project, use of whole exome sequencing (WES, or the sequencing of all coding exons found within the genome) has turned into a primary diagnostic tool in daily clinical use. Exome analysis is inexpensive and rapid, and is a precise and non-invasive diagnostic tool for a vast array of genetic disorders and congenital malformations. The Department of Genetics at Hadassah University Medical Center, in conjunction with the Departments of Pediatric Immunology and Bone Marrow Transplantation, was the first in Israel to introduce exome analysis as a routine diagnostic tool.

Objectives: We aim to summarize the results of all WES performed for patients with suspected primary immune deficiency (PID) in our departments and to evaluate how the availability of a genetic diagnosis impacted subsequent clinical decision making.

Method: We retrospectively analyzed the medical records of all immunodeficient patients who underwent WES between 2012 and 2019 at Hadassah University Medical Centre. Data collected included clinical presentation, results of immunological work-up, clinical course, treatment (including stem cell transplantation) and outcome.

Results: Between 2012 and 2019 230 exomes were analyzed at our institution for the patients with suspected PID. In 140 cases a precise genetic diagnosis was found. In 5 patients a new disease-causing gene was found. Based on WES findings, in 40 cases genetic diagnosis was established in siblings or additional family members. 65 patients were transplanted and 60 survived.

Conclusion: The unique composition of the population which our hospital serves (marked by a high rate of consanguinity and thus homozygosity) enabled a genetic diagnosis to be found 60% of cases referred for WES, twice the rate of medical centers worldwide. A diagnosis in the index case enabled subsequent diagnosis in affected family members for many of our patients, often prior to the onset of severe disease features. In addition, an accurate genetic diagnosis gave our team the confidence to transplant patients who otherwise may have waited several years for this curative treatment. Finally, WES helped us describe five new PID-causing genes, expanding our understanding of the biological basis of PID and hopefully leading to novel treatments in years to come.

Abstracts

Abstract: Stone et al.

Heteroresistance to fluconazole in human Cryptococcal meningitis is driven by aneuploidy

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Background: Cryptococcal meningitis (CM) causes an estimated 180,000 deaths annually, predominantly in sub-Saharan Africa, where most patients receive fluconazole (FLC) monotherapy. The mechanisms of emerging FLC resistance in CM are poorly understood. Heteroresistance (HetR) – a FLC resistant subpopulation within an otherwise susceptible strain - is a recognised in *vitro* phenomenon of *Cryptococcus spp*. The mechanism of HetR is unclear, though animal studies suggest chromosomal duplication may play a role. The clinical significance of HetR to FLC has never previously been studied.

Objectives: In serial Cryptococcal isolates cultured from fresh cerebrospinal fluid (CSF) collected using lumbar punctures within a prospective clinical observational study in Tanzanian HIV-infected patients with cryptococcal meningitis (CM):

1. To characterise for the first time the prevalence of heteroresistance to fluconazole in pre- and on-treatment Cryptococcal isolates in human CM
2. To assess the selection for resistant subpopulations during the course of induction therapy of human CM using fluconazole alone or in combination with flucytosine (5FC)
3. To determine the molecular mechanism of fluconazole resistance.

Method: The hollow fibre infection model (HFIM) was used to observe FLC resistant subpopulation dynamics at human-like drug exposures. Subsequently, a cohort of 20 patients with CM in Tanzania was prospectively observed during therapy with FLC monotherapy or in combination with flucytosine (5FC). HetR was identified by quantifying total and resistant subpopulations of *Cryptococcus* directly from patient cerebrospinal fluid (CSF). Isolates underwent whole genome sequencing (WGS). Phenotypic characterization of the clinical strains included population analysis profiling (PAP) for HetR and efflux pump activity.

Results: The hollow fibre model predicted an increase in the FLC resistant subpopulation. In the clinical study, the proportion of FLC resistant colonies in patients' CSF increased during the first two weeks of treatment with FLC monotherapy. In contrast, no resistant subpopulation was detectable in CSF by day 14 in those receiving a combination of FLC and 5FC. This same phenomenon was reproducible in *vitro* using the clinical isolates. WGS revealed high rates of aneuploidy in heteroresistant colonies as well as in relapse isolates, with Chromosome 1 (Chr1) disomy predominating. In *vitro* efflux levels positively correlated with the level of heteroresistance.

Conclusion: Our findings demonstrate the presence and emergence of aneuploidy-driven FLC heteroresistance in human CM, association of efflux levels with heteroresistance, and the suppression of heteroresistance with 5FC/FLC combination therapy.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Stott et al.

Investigating the role of Gβγ subunits in the regulation of cardiovascular Kv7 channels

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Institute where fellowship took place: Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Background: The Kv7 family of voltage gated potassium channels have important roles in the cardiovascular system where Kv7.1 channels contribute to the cardiac action potential and Kv7.4 and Kv7.5 channels are important in vascular control mechanisms. Recently it was shown that Kv7.4 channels and native vascular Kv7 channels are positively regulated by G protein βγ subunits (Gβγ), and that these subunits are essential for the basal activity of these channels. However, there are 5 different Gβ and 12 Gγ subunits and it is increasingly clear that in the regulation of other Gβγ effectors individual isoform combinations can perform specific functions. Additionally, the role of Gβγ in regulation of Kv7.1 channels is unclear. Kv7.1 channels are most commonly found in cardiac myocytes complexed with an auxiliary subunit – KCNE1. The presence of this subunit alters the biophysical properties of the channel and is important in transducing regulatory actions on Kv7.1, such as by the A-kinase Anchoring Protein.

Objectives: To determine to role of Gβγ in regulation of cardiovascular Kv7 channels, and uncover the individual subtypes involved in this regulation.

Method: Gβγ effects on Kv7.1 and Kv7.4 were studied by a combination of electrophysiology on heterologously expressed channels in Chinese Hamster Ovary cells, proximity ligation assay in overexpressed cells and native vascular myocytes, and morpholino directed knockdown of specific Gβ subunits in rat renal arteries.

Results: Strikingly, we now show that Gβγ negatively regulate Kv7.1 and Kv7.1/E1 channels which has profound implications on cardiac function and regulation. For Kv7.4 channels we show that only specific Gβ subunits (Gβ 1, 3 and 5) positively regulate channels, adding a further layer of complexity to this mechanism of regulation. We further show that it is the Gβ3 subunit which is responsible for the basal activity of Kv7 channel in vascular smooth muscle (renal artery), whereas the Gβ1 subunit appears to contribute to Kv7.4 protein synthesis or stability.

Conclusion: These findings demonstrate the critical role of Gβγ in the regulation of cardiovascular Kv7 channels and are significant in revealing the fundamental importance of Gβ specificity in ion channel regulation.

Abstract: Svetitsky et al.

Pregnancy in women with nephrotic-range proteinuria

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Institute where fellowship took place: Hammersmith Hospital, London, UK

Background: Renal disease is known to be a risk factor for complications during pregnancy, including preeclampsia, prematurity and low birth weight. Pregnancy can also accelerate long-term deterioration in renal function in women with pre existing renal disease.

Objectives: To study the effect of severe proteinuria in early pregnancy on pregnancy outcomes and long-term renal function.

Method: In this retrospective study, we assessed over 400 pregnancies in women with renal disease cared for in the Renal Obstetric Clinic in Queen Charlotte's hospital, London, between the years 2008-2018. We searched for women with severe proteinuria (uPCR >300 mg/mmol) in early pregnancy (<20 weeks.) We identified 36 pregnancies fitting these criteria.

Results: The average age of the women was 33 years (+- 5.5 years). The majority (66.7%) were diagnosed with glomerular disease as the cause of proteinuria, with the second most common diagnosis being chronic pyelonephritis/reflux nephropathy (13%). One third of the women had hypertension. Median proteinuria for the group was 616 mg/mmol, with IQ range of 522. Most of the women had reduced renal function pre-pregnancy (GFR<90ml/min) with only 27% having normal GFR. 15 women (41.7%) had been treated pre-pregnancy with an ACE inhibitor, an ARB or both.

Outcomes - 52% of births occurred prematurely (<37 weeks gestation). 19% were very preterm (28-34 weeks) and 11% were extremely preterm (<28 weeks.) There were 4 neonatal deaths (10.8% .) 56% of babies were born at a low birth weight (<2,500 grams). 36% of women had a rise in Cr of 50% or more during pregnancy. At 1 year post pregnancy, 8 women (22%) had a rise of Cr of 50% or more, or required renal replacement therapy.

Pre-pregnancy levels of proteinuria were not correlated significantly with birth weight, gestation, change in creatinine during and after pregnancy. First trimester levels of proteinuria were negatively correlated with birth weight and gestation age; however, this was not statistically significant. Women with reflux nephropathy as a cause of severe proteinuria had shorter pregnancies, babies with lower birth weight and a greater increase in creatinine after pregnancy than women with glomerular disease, however this difference was not statistically significant. Treatment with ACE pre-pregnancy was not associated with improved outcomes.

Conclusion: In conclusion, women with severe proteinuria have significant rates of adverse obstetrical events and renal function deterioration.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Vardi et al.

Preschool ADHD Guidelines

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Institute where fellowship took place: University of Cambridge, Cambridge, UK

Background: The diagnostic category of Preschool ADHD has been receiving growing attention. While treatment would clearly require multidisciplinary teams, evidence-based practices are scarce and there are no widely accepted treatment guidelines for this age group.

Objectives: To formulate a comprehensive guideline for treatment of preschool ADHD in Israel.

Method: Following the initiative of the Israeli society for ADHD, a multidisciplinary team was assembled to make recommendations regarding appropriate diagnostic questionnaires, clinical examination, occupational therapy approach, parental training, psychotherapy, pharmacology, case management, and complementary-alternative treatments. The team included child psychiatrists, developmental pediatricians, clinical and developmental psychologists, as well as occupational therapists.

Results: The team's recommendations are as follows:

1. Diagnosis of preschool ADHD should be made exclusively by a child and adolescent psychiatrist or a child neurologist/developmental pediatrician.
2. Diagnosis should follow the DC 0-5 criteria rather than DSM 5, including the Overactivity Disorder of Toddlerhood (OATD): Hyperactivity and impulsivity Cluster.
3. The use of questionnaires adapted to this specific age group is advisable.
4. Occupational therapy diagnosis could be made from the age of 3 onwards with the aim of identifying the client's profile of executive functions difficulties.
5. Interventions should be offered to both the child and the parent.
6. Parental training or Psychotherapy is first line treatment for preschoolers' ADHD and even more so in OATD.
7. Treatment plans should address: Parental mental health; Parental functioning; Family dynamics; Child-parent relationship; Environmental stressors; Personalized treatment according to social and cultural diversity.
8. There are no evidence-based recommendations regarding Complementary-Alternative treatments.
9. When pharmacological treatment is being considered, has been taken, Methylphenidate based medications are recommended as first line in preschoolers, based on the PATS study.

Conclusion: Early diagnosis and treatment of ADHD may prevent co-morbidities and may improve future outcomes. Diagnosis should be made by a multidisciplinary team, in order to offer comprehensive approach. First line treatment for preschool ADHD is parental guidance. When non-pharmacological treatment is not satisfactory, pharmacological treatment should be considered. Methylphenidate based medication is the first line of treatment for preschoolers. Working in collaboration with the educational team is crucial.

Abstract: Vinokur et al.

Neural stem cell-derived exosomes and cardioprotection

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Institute where fellowship took place: Hatter Cardiovascular Institute, University College London, London, UK

Background: Opening of mitochondrial permeability transition pore (MPTP) during the first few minutes of post-ischemic cardiac reperfusion have been reported as a critical determinant of ischemia-reperfusion injury. Activation of the "reperfusion injury salvage kinase (RISK) pathway" has potent protective effect, attenuating this process. In clinics several attempts are being undertaken to mitigate this injury, including administering of cyclosporine A (CsA), an immune-suppressant medication. Exosomes, the nano-sized vesicles, released by numerous cell types, appear to have diverse beneficial effects on the injured heart.

Objectives: The purpose of the study was to test and elucidate the cardioprotective effect of the exosomes, obtained from neural stem cells.

Method: HL-1 cells (murine cardyomyocytes) were pre-treated with exosomes, obtained from neural stem cells during their differentiation or proliferation (ExoDiff/ExoPro). The effect on MPTP opening was assessed, using confocal microscopy to measure pore opening time, employing the tetramethylrhodamine methyl ester (TMRM) fluorescent probe. Briefly, laser illumination of TMRM-loaded cells, generated oxidative stress, induced pore opening, represented by mitochondrial membrane depolarisation.

Subsequently, the mechanism of action of these exosomes was elucidated. Cells were pre-treated with specific inhibitors of various kinases, members of the (RISK) pathway (including the PI3K, MEK1/2, ERK1/2), and the protective effect on the exosomes was monitored. Furthermore, the putative message triggering the cardioprotective mechanism was investigated. The cells were pre-treated with two additional inhibitors of the extracellular signalling - SC144, suppressing the signal transduction of gp130 receptor (IL-6 superfamily), and TAK242, inhibiting TLR4-receptor-mediated cellular events.

Results: The exosomes, obtained from neural stem cells at their differentiation stage (ExoDiff), experienced a noticeably better protective effect than ExoPro or CsA. Further, ExoDiff exosomes demonstrated an impressive cardioprotection despite the presence of two inhibitors of the RISK cascade kinases - LY294002, acting against PI3K, and PD98059, inhibiting the ERK1/2 activity. Yet, SB203580, the inhibitor of p38 MAP kinase, caused a total abolishment of the protective effect of ExoDiff. Interestingly, insulin, used as an additional positive control, lost its effect when PD98059 was added. Added alone, without exosomes, none of the inhibitors had an effect on MPTP opening time.

When inhibitors of the extracellular signaling were added separately, each one reduced the protective effect of ExoDiff exosomes by 20-30%, while a combined pre-treatment resulted in its total termination.

Conclusion: Based on these findings, a hypothesis, describing the upstream events of this cardioprotective mechanism, was developed.

Abstract: Vivante et al.

History of Childhood Kidney Disease and Risk of Adult End-Stage Renal Disease

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Institute where fellowship took place: University College London, London, UK

Background: The long-term risk associated with childhood kidney disease that had not progressed to chronic kidney disease in childhood is unclear.

Objectives: We aimed to estimate the risk of future end-stage renal disease (ESRD) among adolescents who had normal renal function and a history of childhood kidney disease.

Method: We conducted a nationwide, population-based, historical cohort study of 1,521,501 Israeli adolescents who were examined before compulsory military service in 1967 through 1997; data were linked to the Israeli ESRD registry. Kidney diseases in childhood included congenital anomalies of the kidney and urinary tract, pyelonephritis, and glomerular disease; all participants included in the primary analysis had normal renal function and no hypertension in adolescence. Cox proportional-hazards models were used to estimate the hazard ratio for ESRD associated with a history of childhood kidney disease.

Results: During 30 years of follow-up, ESRD developed in 2490 persons. A history of any childhood kidney disease was associated with a hazard ratio for ESRD of 4.19 (95% confidence interval [CI], 3.52 to 4.99). The associations between each diagnosis of kidney disease in childhood (congenital anomalies of the kidney and urinary tract, pyelonephritis, and glomerular disease) and the risk of ESRD in adulthood were similar in magnitude (multivariable-adjusted hazard ratios of 5.19 [95% CI, 3.41 to 7.90], 4.03 [95% CI, 3.16 to 5.14], and 3.85 [95% CI, 2.77 to 5.36], respectively). A history of kidney disease in childhood was associated with younger age at the onset of ESRD (hazard ratio for ESRD among adults <40 years of age, 10.40 [95% CI, 7.96 to 13.59]).

Conclusion: A history of clinically evident kidney disease in childhood, even if renal function was apparently normal in adolescence, was associated with a significantly increased risk of ESRD, which suggests that kidney injury or structural abnormality in childhood has long-term consequences.

Abstract: Wefelmeyer et al.

The emergence and plasticity of synapses at the axon initial segment

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Institute where fellowship took place: Ben Gurion University of the Negev, Beersheva, Hebrew University of Jerusalem, Israel

Background: Neurons use action potentials to convey information in the brain. The site of action potential generation, the axon initial segment (AIS), is a structure at the start of the axon with a high sodium and potassium channel density. It is also the target of axo-axonic synapses formed by a specific GABAergic interneuron, the Chandelier cell.

Objectives: Previous work has shown the AIS to be a highly plastic structure, capable of changing its length and position along the axon. The synapses formed onto the AIS also undergo plastic changes. However, we know surprisingly little about how this influences action potential generation and thus communication in the brain. We therefore investigated these structural changes and their consequences for action potential generation.

Method: We visualised Chandelier cell interneurons and their boutons in somatosensory cortex at different developmental stages in *vitro* and in *vivo*. We then chemogenetically increased cortical network activity during this developmental period and assessed the resulting morphological and electrophysiological changes of the AIS and its synapses. Finally, using a genetically-encoded voltage indicator expressed in pyramidal cells, we studied the functional effect of GABAergic synapses on the AIS. In addition, we used computational modelling to understand the functional consequences of this structural plasticity.

Results: We uncovered a narrow temporal window of synapse formation at the AIS (P14-P16), which corresponds with the electrophysiological and morphological maturation of the Chandelier cell. Intriguingly, we were able to reversibly decrease AIS length and the number of synapses it receives by increasing cortical network activity during this developmental period. Specifically increasing activity in Chandelier cells mirrored the synaptic effect, suggesting this plasticity is cell-autonomous. However, when network activity was increased in adult animals (P40-P46) we saw the opposite effect: an increase in axo-axonic synapses along the AIS. This surprising switch in the direction of axo-axonic synapse plasticity may be explained in the context of homeostatic plasticity, since we find that Chandelier cell synapses transition from being depolarising at P12-P18 to inhibitory at P40-P46.

Conclusion: We propose that the switch in synapse polarity during development is paralleled by a switch in the direction of axo-axonic synapse plasticity, which acts to homeostatically stabilise network activity: decreasing axo-axonic synapse number reduces neuronal activity levels as long as they are depolarising, whereas increasing inhibitory input helps stabilise neuronal activity later during development.

Daniel Turnberg Travel Fellowship Scheme Alumni Conference 2019

Abstract: Youssef et al.

Investigation of miRNAs in Subcutaneous White Adipose Tissue During Development of Obesity

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Institute where fellowship took place: University of Liverpool, Liverpool, UK

Background: Several studies have shown the role of MicroRNAs as new mediators in the regulation of adipose tissue proliferation and differentiation. As dietary interventions dramatically affect metabolic disease and lifespan, we hypothesized that high-fat intake can impact the expression levels of micro-RNAs and thus the biological function of adipose tissue during obesity development. We also assumed that such effect may be revered by switching to normal diet.

Objectives: To study the dysregulation of some miRNAs in white adipose tissue during weight change stages, expansion\reduction; in response to a high fat diet feeding, and to evaluate their potential biomarkers and therapeutic targets.

Method: Male Westar rats of age two months were randomly divided into a normal diet group (ND), a high-fat diet group (HFD), and a switched to a normal diet group (HFD/ND). At the beginning and at intervals 2 weeks, serum lipid and hormone analysis were carried out along with total body weight and total fat mass using dual-energy X-ray absorptiometry (DEXA). The expression levels of miR 130a, miR 30a, miR 133, let 7a, miR 107, mir 125 a , and mir 195 were evaluated in inguinal subcutaneous white adipose tissue driven from HFD , HFD/ND, and ND groups using Real-time PCR. In silico analysis was performed to identify the target genes and the possible cellular pathways of the identified dysregulated miRNAs.

Results: Significant alterations were observed including total body weight, total fat mass, serum lipid, blood glucose, insulin and adipokine hormone levels during the different stages of obesity development in the HFD group while during switching to normal diet protocol , a moderate change in weight and fat mass was observed comparing to control. MicroRNAs expressions showed an alteration in let 7, mir 30, mir 133a and mir 107 levels at more than one time point in response to HFD feeding for 10 weeks. While mir 193a was up- regulated and, mir125a was down-regulated at all time points of the feeding protocol .The up regulated miRNAs in HFD group rats were down-regulated in HFD/ND group ones and vice versa .The bioinformatics results have identified a novel and most important pathways which associated with inflammatory signalling.

Conclusion: Alteration in expression levels of miRNAs could be used as potential biomarkers for adiposity changes and therapeutic targets in white adipose tissue during diet-induced obesity.

Abstracts

Abstract: Zacco et al.

Dr Jekyll or Mr Hyde? The role of RNA in the aggregation of the protein TDP 43

Elsa Zacco[1,2,3], Richardo Graña-Montes[4,5], Gian Gaetano Tartaglia[4,6], Annalisa Pastore[1,2]

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Institute where fellowship took place: Tel-Aviv University, Tel-Aviv, Israel

Background: TAR DNA-binding protein 43 (TDP43) is the major pathological protein found in toxic inclusions hallmarks of the incurable motor neuron disease amyotrophic lateral sclerosis (ALS). TDP43 is responsible for regulation and shuffling of RNA in and out of the nucleus but how interactions with nucleic acids affect its aggregation is unknown.

Objectives: Our research exploits TDP43 natural ability to recognize RNA in order to define the effect of this binding on the protein solubility and toxicity, and evaluate the possibility of exploiting TDP43-RNA interactions to stabilize TDP43 structure.

Method: We evaluated the ability of TDP43 to bind different RNA sequences and studied the consequence of this binding on its aggregation. TDP43 variants were characterized for their structural stability and conformations using circular dichroism spectroscopy; aggregation kinetics in the presence/absence of specific RNA sequences was investigated by spectrofluorometric assays; binding affinities were examined defining dissociation constants (Kd) by biolayer interferometry; electron microscopy illustrated morphological variations in TDP43 aggregates in the presence/absence of the cognate RNA.

Results: We established that, under stressful conditions, TDP-43 shifts towards a β-rich conformation, forming amyloid-like structures. The presence of short UG-rich RNAs strongly inhibits its aggregation and stabilizes native conformations. Non-UG-rich sequences show the opposite effect, accelerating the formation of aggregates in a strictly sequence-specific fashion. Although only minimal variations in Kd are observed for longer RNAs, the inhibitory/promoting effect on TDP-43 aggregation seems proportional to RNA length. In all tested conditions, the aggregates morphology does not change but the rate of formation varies with each RNA.

Conclusion: These results indicate that the type of RNA bound by TDP-43 has a leading role in dictating solubility and aggregation. The many forces determining TDP-43 structural stability include strength of RNA binding, RNA sequence and length.

This word is a proof of concept demonstrating that natural interactions between RNA and TDP43 could be exploited as a prophylactic measure to obstruct the progression of ALS.

Abstract: Zadok et al.

Ocular Magnetic Neurostimulation: A Novel Concept in the Treatment of Dry Eye Disease

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Institute where fellowship took place: Department of Ocular Biology & Therapeutics, University College London Institute of Ophthalmology, London, UK

Background: Dry eye disease (DED), a chronic disorder affecting the tear film and lacrimal functional unit, is a widely prevalent condition associated with significant burden and unmet treatment needs. Transcranial magnetic neurostimulation has been shown to be an effective tool for the treatment of major depressive disorder and other neurologic pathologies. Ocular magnetic neurostimulation (OMN) (Viveye, EpiTech mag technology, Israel) is a novel therapeutic approach for the treatment of moderate to severe DED.

Objectives: This study investigates the efficacy and safety of OMN treatment in patients with DED.

Method: This prospective, open-label, single-arm, nonrandomized pilot study included 15 patients with moderate to severe DED. In each patient the eye with the more severe corneal staining was exposed to 11 min. of ocular magnetic neurostimulation at 45% intensity, 20 Hz. The untreated eye served as a control. Follow-up assessments were scheduled before treatment application and at weeks 1, 4, 8 and 12.
The primary effectiveness endpoint was stimulation-induced change in fluorescein corneal staining score. Primary safety measure was incidence of device-related adverse events (AEs).

Results: Significant reduction of the corneal epithelial staining in treated vs. untreated eye, relative to baseline, was recorded at 1w (2.2 [SE=0.7] vs. -0.5 [SE=0.9], p=0.014), 4w (3.4 [SE=1.3], vs. 0.4 [SE=1.2], p=0.013) and 8w (7.3 [SE=1.6] vs. 2.1 [SE=1.7], p=0.019) after magnetic neurostimulation treatment. Significant reduction in symptoms scores was recorded in both eyes at 8w vs. baseline (31.3 [SE=4.7] vs. 47.3 [SE=2.2], p<0.01). Patients reported substantial reduction in overall lubricants consumption. No treatment related adverse events were reported.

Conclusion: The ocular magnetic neurostimulation treatment has demonstrated substantial reduction of symptoms and promoted healing of the corneal epithelium in moderate to severe dry eye disease patients. This innovative treatment may serve as an effective tool to treat DED.

Abstract: Ziv et al.

Identification of Adverse Childhood Experiences (ACEs) by Child and Adolescent Mental Health (CAMH) professionals

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Background: Adverse childhood experiences (ACEs) are stressful early life events that harm children or negatively affect the environment in which they live. The different types of ACEs include Mental illness in family, Parental separation, Drug abuse in family, Physical abuse, Domestic Violence, Alcohol abuse in family, Verbal abuse, Sexual abuse and Incarceration in family. ACEs are common and are linked with significant mental and physical health illnesses. Early detection of ACEs by health professionals enables initiation of appropriate trauma informed interventions and may reduce the harmful outcome of ACEs. Despite the high prevalence of ACEs and their negative lasting effect, ACEs are under-detected by health professionals, emphasising the need to improve the current identification methods.

Objectives: Here we evaluate the rate of ACEs detection among children admitted to Child and Adolescent Mental Health Services in the United Kingdom and explore the barriers for ACEs enquiry during the initial mental health assessment.

Method: We carried out semi-qualitive interviews with Child and Adolescent Mental Health (CAMH) professionals, as well as a case audit designed to evaluate the rate of detection of ACEs on admission and discharge from an inpatient children's mental health unit.

Results: We showed that whereas the vast majority of the professionals do enquire about illnesses and parental separation, only minority of the professionals enquire about abuse and violence. The main barrier reported was clinician's discomfort to enquire about ACEs due to lack of training.

Conclusion: ACEs are under-detected by CAMH professionals in the United Kingdom. Staff training is urgently required to improve early identification techniques of ACEs by professionals, to enable early intervention, and to reduce the negative physical and mental health consequences of ACEs.

#MedSciLife

#MedSciLife is a campaign created by the Academy of Medical Sciences to share the life experiences of those working in biomedical and health research, to celebrate diversity and provide advice and support to medical researchers at all stages of their career.

Our aim is to create opportunities for researchers at all levels to share the different ways they work, allowing them to pass on advice and practical tips to the next generation of scientists.

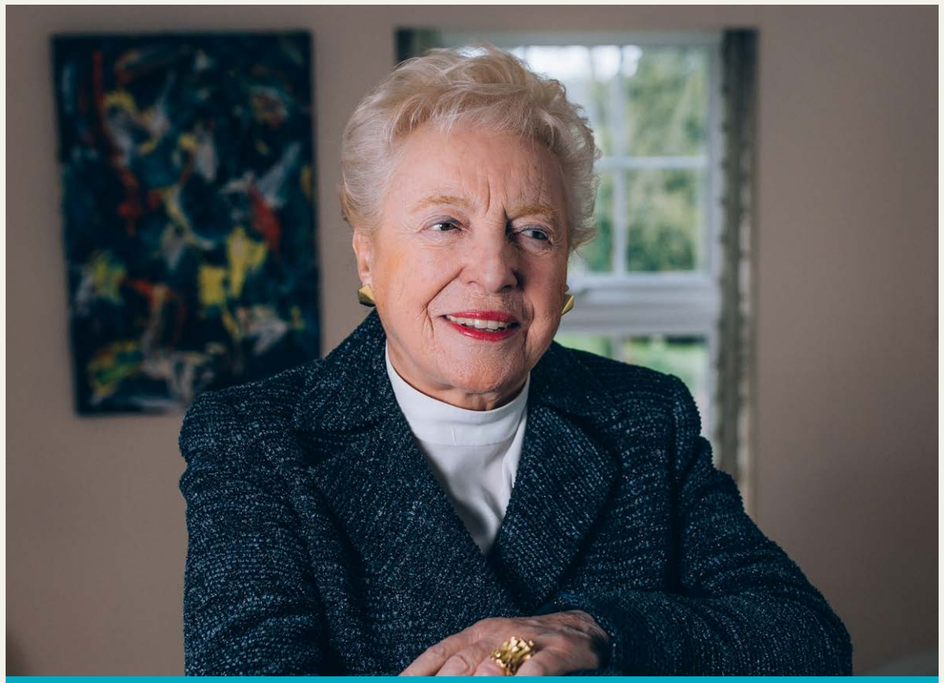
Striving for work-life balance does not mean you have to compromise. You can be a great clinician and an accomplished researcher without sacrificing your home life. Be ambitious and aim to achieve both.

Collaborate – rather than compete – with your colleagues and look for inventive mutually-beneficial solutions to manage responsibilities, time, commitments and goals.

Mr Kourosh Saeb Parsy

University Lecturer and Honorary Consultant Transplant Surgeon, University of Cambridge

#MedSciLife



Much that other people find important is just “stuff”. I focus on ideas, on learning and on innovation generally – the things that I know and care about.

I work hard, recover from the many blind alleys and am motivated to succeed. My success was found at the edge of failure.

Dame Stephanie ‘Steve’ Shirley

Entrepreneur and philanthropist

Reflecting on their personal journey also affords researchers the opportunity to explore and share the way their passions and achievements outside of work have influenced their careers.

We believe that time outside of work has the potential to nourish creativity, build resilience, and give fresh perspectives on existing problems, precisely the skills that result in the best quality research. A life outside science is not an extra, but an integral part of who we are as scientists.

Our campaign provides a hub for biomedical and health researchers to describe their personal journeys and their attempts to blend their work and home lives. We hope this will provide a valuable resource for those currently working in the field and those considering medical science as a career.

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Making it happen

The Daniel Turnberg Memorial Fund was established by Edna and Leslie Turnberg following the loss of their son Daniel in a plane crash in Africa at the age of 37. Daniel had already made a mark as a bright young doctor and as a medical researcher and was destined for a future full of promise. A graduate of Leeds University, he trained first in hospitals in Yorkshire before starting his specialist training in renal medicine in a series of London teaching hospitals. He went on to obtain his PhD for his research into the role of the immune system in kidney disease at Imperial College and the Hammersmith Hospital before taking up a lectureship in renal medicine at the Royal Free Hospital in 2006.

But above all his academic achievements it was the universal view of his kind and gentle nature, his compassion for others and his sense of fun and enthusiasm for everything that life had to offer that earned him the love, respect and admiration of his patients, colleagues and wide circle of friends. In setting up this fund his parents hope to continue a keen interest he had in international medicine and in encouraging greater understanding between Israel, the Middle East and the UK.

Our thanks must go to our exceptional supporters. We would like to thank the following for their continuing major donations:

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