Beyond Sciences Initiative

1st International Remote Conference: Science & Society

January 23 & 24, 2016.

PARTICIPANT BOOKLET

CANCER

CHRONIC DISEASES

EDUCATION & TECHNOLOGY

GLOBAL HEALTH

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Beyond Sciences Initiative

Contents

Welcome Address

Dear Colleagues and Friends,

It is our pleasure to extend a warm-hearted welcome to all presenters and participants of the 1st International Remote Conference: Science and Society, hosted by the Beyond Sciences Initiative (BSI).

This meeting will connect students, community specialists, researchers, professors and medical specialists around the globe - representatives from over 20 different countries. We look forward to learning about scientific advances from our local and international colleagues, including the social, cultural and political contexts in which they conduct their academic activities.

Our scientific program is exceptionally rich, with specific foci on cancer, chronic diseases, education & technology and global health. Our goal is to enable high caliber discussions surrounding research and community activities in order to foster international collaboration.

On behalf of the members of the Organizing Committee from BSI chapters across the globe, we thank you for your participation in our 1st International Remote Conference. We anticipate that this meeting will be the impetus for many more fruitful global discussions in the future.

Sincerely Yours,
The Beyond Sciences Initiative Executive Team

Welcome to Our Global Participants

Europe
Germany
Norway
Poland
Portugal
Russia
Sweden
Switzerland
Turkey
Ukraine

Americas
Brazil
Canada
USA

Asia
India
Iran
Japan

Africa
Egypt
Ethiopia
Kenya
South Africa
Sudan
Uganda

Oceania
New Zealand

Conference Program: Day 1

Saturday, January 23, 2016.

Time (EST)	Topic	Speaker
7:00 – 7:15am	**Opening Ceremony –** Introduction and Welcome from BSI	**Dr. Eleanor Fish**
Scientific Session 1: Cancer		
7:15 – 7:45am	**Keynote – Harnessing the Power of Networks for Global Good**	**Dr. Fredrick Chite Asirwa** Kenya
7:45 – 8:00am	**Wrestling with Warburg: Restoring Normal Cellular Metabolism in GBM Through PINK1 Reactivation**	**Brian Golbourn** Canada
8:00 – 8:15am	**Anti-tumour Activities of a Novel Diterpene Derivative Against Liver Cancer**	**Ahmed Elsharkawy** Egypt
8:15 – 8:30am	**Oxysterols and Adrenocortical Carcinoma: Proliferation and Steroidogenesis**	**Sarah Lawless** Poland
8:30 – 8:45am	**Evaluation of Repigmentation with Cultured Melanocyte Transplantation (CMT) Compared with Non-Cultured Epidermal Cell Transplantation in Vitiligo at 12th Week Reveals Better Repigmentation with CMT**	**Suraj Varkhande** India
8:45 – 9:00am	**BREAK**	
9:00 – 9:20am	**Cross-Cultural Experience – Determinants of Health in Ghana (Humans of Ghana)**	**Shannon Wong** Canada
Scientific Session 2: Global Health		
9:20 – 9:50am	**Keynote - From Bench to Bedside: Bringing a Treatment for Ebola to Guinea**	**Dr. Eleanor Fish** Canada
9:50 – 10:05am	**Pregnant Dichotomies: Reproductive Justice and Women in Poverty**	**Joanna Dowdell** Canada
10:05–10:20am	**A Study on Challenges Facing Implementation of Free Maternal Services in Webuye Sub-County Hospital**	**Charles Mwembu** Kenya
10:20–10:35am	**Happy Pensioners: Psychological Model of Subjective Well-Being in Late Adulthood**	**Iryna Horbal** Ukraine
10:35–10:50am	**Building Sustainable Research Capacity in Sub-Saharan Africa**	**Vineet Joag** Kenya/Canada
10:50–11:05am	**Beneficial Off-Target Effect of the BCG Vaccine on Newborn Mortality**	**Nelly Amenyogbe** Canada
11:05 – 11:15am	**BREAK**	
11:15 – 11:45am	**Cross-cultural Experience – Art and Social Determinants of Health in Congo**	**Nadia Farzal** Canada

Conference Program: Day 2

Sunday, January 24, 2016.

Time (EST)	Topic	Speaker
Scientific Session 3: Chronic Diseases		
7:00 – 7:30am	**Keynote – New Medicines for Malaria Eradication**	**Dr. Timothy Wells** Switzerland
7:30 – 7:45am	**Management Outcomes of Type 1 Diabetes Mellitus in Under Fourteen Years Clients Receiving Care in the Home Glucose Monitoring Program at the Moi Teaching and Referral (MTRH) in Eldoret, Kenya**	**Dr. Nicholas Muema** Kenya
7:45 – 8:00am	**CD4: A Surrogate Marker for T-Cell Aging**	**Dr. Sanket Rane** India
8:00 – 8:15am	**Incidence and Severity of Burns in Two Hospitals in Nairobi and Nakaru, Kenya**	**Elise Fryml** Canada
8:15 – 8:30am	**Knowledge, Attitude and Mental Health Practices in Western Kenya**	**Ruth Anyango** Kenya
8:30 – 8:45am	**Regulation of Neural Stem/Progenitor Cells by Known and Novel Centrosomal Proteins**	**Germán Camargo Ortega** Germany
8:45 – 9:00am	**BREAK**	
9:00 – 9:15am	**Cross-Cultural Experience – Environment and Outreach activities** **Cross-Cultural Experience – Graduate and Outreach activities**	**Moi** **NII BSI Chapter**
Scientific Session 4: Education and Technology		
9:15 – 9:45am	**Keynote – Industry or Academia: A Personal Journey in Developing Innovative Medicines**	**Dr. Kuldeep Neote** USA
9:45 – 10:00 am	**Selecting the Right Candidate: An Examination of Current Admissions Processes and Tools Used by Graduate and Professional Programs**	**Dr. Behrouz Moemeni** Canada
10:00 – 10:15 am	**From Bench to Shelf: Creating Life Sciences Products as a Graduate Student**	**Payam Zarin** Canada
10:15 – 10:30am	**Psychiatric and Neurocognitive Implications of Cannabis Dependence in Young Adults**	**Peter Fettes** Canada
10:30 – 10:45am	**BREAK**	
10:45 – 11:00am	**Cross-cultural Experience – Video on Educational Outreach**	**CCEx Cultural and Extension Committee of ICB, USP** Brazil
11:00 – 11:30am	**Closing Ceremony –** Awards and Acknowledgements	

Instructions for Conference Participants

Step 1. To participate in the conference, all attendees and presenters must visit the links below to register for the day they would like to attend. If you plan to attend a single day, please visit the respective link and register. If you plan to attend both days of the conference, **you will need to visit both links and register**. Registration simply requires you to input your name and email address.

Registration for January 23rd (Day 1)
https://attendee.gotowebinar.com/register/7827016830603625474

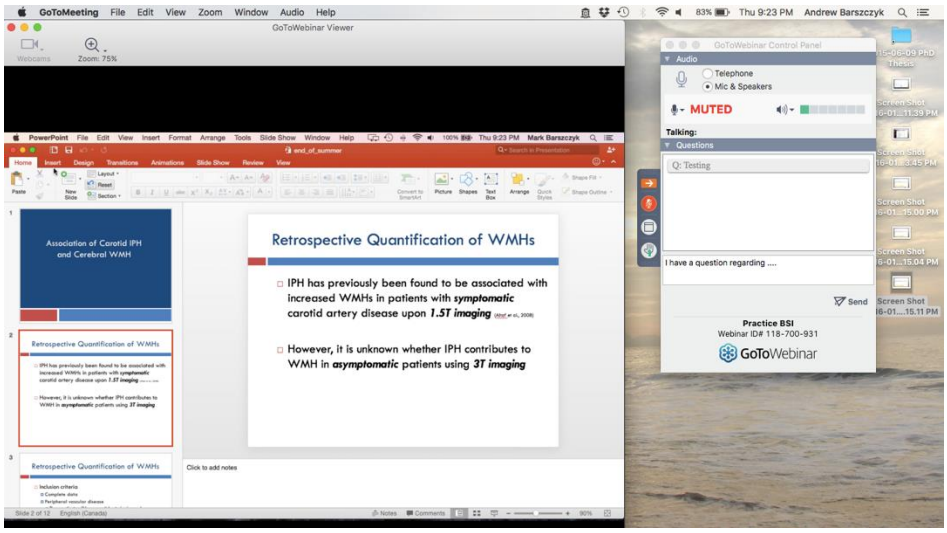
Registration for January 24th (Day 2)
https://attendee.gotowebinar.com/register/3279100287564005634

Step 2. You will be immediately emailed a personalized link to join the conference. The link will become active one hour prior to the start of the conference on both days to allow participants to log on early and test their setup.

- If you have never used GoToWebinar software before, you will be prompted to download a small file (Citrix Online Launcher, 21Mb) upon visiting the personalized link. **This is required to attend and present and should be done as early as possible before your presentation timeslot to prevent delay**!

Instructions for Conference Participants

Step 3. Once installation is complete, you will automatically join the conference as an attendee. A Control Panel will appear that provides you with the option to share your microphone, webcam and screen if you are given presenter status. A Viewer window will also appear allowing you to view what is currently being shown by the current presenter. Attendee status grants you the ability to see and hear other participants of the conference but you cannot be heard yourself, share your webcam or share your screen. However, you may type questions throughout the conference, which will be read by moderators to the current presenter.

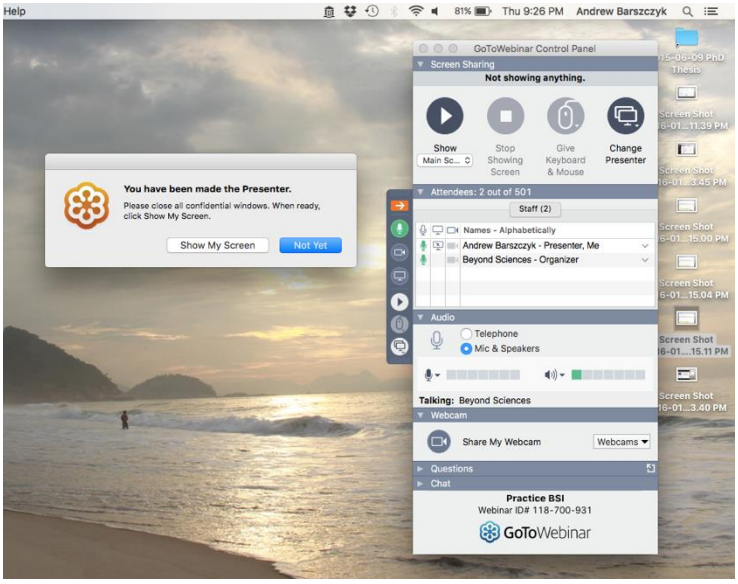


Step 4. If you are a presenter and it is your time to present, the conference organizer will automatically assign you presenter status. You will be notified you are being made the presenter, and when ready, click Show My Screen on the prompt. Presenter status will change your Control Panel to a more advanced style and by default share your screen and enable your microphone. If you wish (and it is recommended!), click the icon enabling the option to share webcam so that attendees may see you speak.

Instructions for Conference Participants

Once you are a presenter:

- ✓ Minimize the GotoWebinar Control Panel prior to opening up your presentation program (ie. PowerPoint) so that it does not float over your slides and start presenting!
- ✓ Once your presentation is complete, a moderator will appear on the screen and ask the presenter any questions that were typed by conference attendees.
- ✓ Finally, the next presenter will be given presenter status.
- ✓ To leave the conference, simply close the GoToWebinar Control Panel. You will be able to rejoin the conference at any point by visiting your personalized conference link.



We will hold at least 1 test run for any attendees or presenters who wish to familiarize themselves with the software or test their hardware! We highly encourage presenters to attend the test run held on Jan 19th, 9-10:30am EST. Register at: https://attendee.gotowebinar.com/register/2334296542975918849

If any issues are encountered prior to or during the conference, please email *beyondsciencesinitiative@gmail.com* and we will respond immediately!

BEYOND SCIENCES INITIATIVE
1ST INTERNATIONAL REMOTE CONFERENCE: SCIENCE & SOCIETY

PRESENTER ABSTRACTS

SS1-1: Cancer

Timeslot: 7:45-8:00am

Presenter: Brian Golbourn
Institution: University of Toronto, Canada
Co-Author: Sameer Agnihotri

Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada

Wrestling with Warburg: Restoring Normal Cellular Metabolism in GBM Through PINK1 Reactivation

Glioblastoma multiforme (GBM) is the most malignant primary brain tumor affecting both children and adults. According to the World Health Organization, GBM is designated a high grade or Grade IV tumor with an average survival of approximately 12-16 months. The molecular underpinnings of GBM have been well characterized and additional genetic lesions have been identified through The Cancer Genome Atlas (TCGA) project of human GBMs. However, the genetic complexity of GBM makes it challenging to determine the contribution of individual genes during tumour formation. One of the defining hallmarks of GBM is altered tumour cell metabolism. This process is referred to as the Warburg effect and is defined by a shift from oxygen dependent energy production, or oxidative phosphorylation, to oxygen independent energy production, or glycolysis. Genes that regulate cellular metabolism and drive biological processes such as proliferation and invasion represent therapeutically relevant targets and candidates for novel drug design. Thus, to identify major genetic drivers from within large genomic datasets, functional genomic strategies must be used to understand precisely where, when and how genes promote initiation, progression, and therapeutic resistance of GBM.

Well-characterized GBM mouse models offer an opportunity to test the impact of glioma-specific genetic alterations, using viral and non-viral random mutagenesis strategies. We have previously employed a retroviral gene trap strategy directed against brain cells harbouring alterations that predispose them to GBM formation to identify genes involved in tumour initiation or progression. Using this screen, we identified PTEN Induced Kinase 1 (PINK1) which is a mitochondrial serine/threonine kinase that normally regulates reactive oxygen species (ROS) production and oxidative phosphorylation and is often mutated in patients with familial Parkinson disease. Our preliminary results show that reduced levels of PINK1 are able to reprogram metabolism in normal brain cells through ROS dependent stabilization of hypoxia-inducible factor-1α (HIF1 α), a transcription factor implicated in the Warburg effect. Conversely, we demonstrate that overexpression of PINK1 in GBM cells suppresses ROS, HIF1α and lactate production and favorably increases oxidative phosphorylation over glycolysis. This data suggests that reactivation of PINK1 in GBM cells may restore normal cell metabolism, resulting in tumour regression. Additionally, reduced PINK1 expression correlates with worse overall survival for glioma patients and may serve as a useful prognostic marker for these diseases.

SS1-2: Cancer

Timeslot: 8:00-8:15am

Presenter: Ahmed Elsharkawy
Institution: University of Alexandria, Egypt
Co-Authors: Ahmed M El-Sharkawy[1], Ahmed Malki[1,2], Stephen C Bergmeier[3]

[1]Biochemistry Department, Faculty of Science, Alexandria University, Alexandria, Egypt
[2]Department of Health Sciences, Biomedical Sciences Program, Faculty of Science, College of Arts and Sciences, Qatar University, Doha, Qatar
[3]Chemistry and Biochemistry department, Ohio University, Athens, USA

Anti-tumour Activities of a Novel Diterpene Derivative Against Liver Cancer

Hepatocellular carcinoma (HCC) is the fifth most common primary malignancy worldwide with increasing incidence. Previously, our laboratory reported on novel isosteviol derivative that cause cytotoxicity in human non-small lung carcinoma epithelial cells null for p53 (H1299). The current study aims to investigate the effect of novel isosteviol derivative on cytotoxicity towards human HepG2 hepatocellular cancer cells and in animal model of HCC. isosteviol derivative induced growth inhibition mainly through apoptosis in Hepatocellular carcinoma cell line HepG2. Our novel isosteviol derivative increased expression of ERK1, p53 and BAX and reduced expression levels of Bcl-2 and Akt. Additionally, isosteviol derivative induced G1 phase arrest presumably sensitizing liver cancer cells to apoptosis by increasing expression of p21 and cyclin-E. Additionally isosteviol significantly increased sphingomyelinase activity and increased formation of ceramide as well as increased expression levels of JNK phoshorylation, caspase-8 and caspase-9. In vivo studies were performed to assess the anticancer effect of isosteviol derivative on Diethyl Nitrosamine - induced liver cancer in female rats by evaluating physiological processes and the expression levels of β catenin and E cadherin. The approximate lethal dose of isosteviol derivative was determined to be 90mg/kg and it led to significant reduction in tumor size compared to the untreated group. In vivo studies revealed that isosteviol derivative does not induce any apparent toxicity towards the treated hosts which is a feature not present in most chemotherapeutic drugs. Isosteviol derivative induced growth inhibition in HepG2 cell line mainly through mitochondrial apoptosis possibly via sphingomyelinase pathway. In vivo studies revealed that Isosteviol derivative does not induce any apparent toxicity towards the treated hosts, which are a feature not present in most chemotherapeutic drugs. These results indicate that Isosteviol derivative may be a promising candidate for the development of antitumor drug.

SS1-3: Cancer

Timeslot: 8:15-8:30am

Presenter: Sarah Lawless
Institution: Poznan University of Medical Sciences, Poland

Oxysterols and Adrenocortical Carcinoma: Proliferation and Steroidogenesis

Background: Adrenocortical carcinoma (ACC) is a rare and aggressive malignancy with a very high recurrence rate. Currently, the only treatments for this cancer are suboptimal. These tumours tend to be highly functional undergoing ACTH-independent steroidogenesis, however, the molecular pathogenesis is incompletely understood (Fassnacht et al., 2013 & Powell et al., 2008). ACC is associated with rapidly developing Cushing's syndrome, virilisation and hypermineralocorticoidism (Gazdar et al., 1990). The mechanisms by which adrenocortical carcinoma proliferates is still unclear, one possible mechanism is by the Liver X receptor (LXR) which is responsible for cholesterol metabolism and reverse cholesterol transport. Oxysterols are the natural ligands of LXR (Cummins and Mangelsdorf, 2006). They are oxidized cholesterol derivatives known to play a role in cholesterol regulation (Assmann et al., 1975). Previously shown to induce steroidogenesis and cell proliferation, oxysterols provide a suitable candidate for ACC instigation and progression.

Aims: In this study, we investigated the effects of a natural oxysterol, 27-hydroxycholesterol and a synthetic LXRα agonist, T0901317, on cell cycle pattern and on gene expression of key regulators involved in the steroidogenic pathway (ABCA-1, LXRα, SR-B1, ERα, StAR, CYP11A1, CYP17A1. CYP11B1 and CYP11B2).

Methodology: Adrenocortical carcinoma cells (H295R) were treated with varying concentrations of 27-Hydroxycholesterol and T0901317, in a both stimulated and unstimulated setting using forskolin, to mimic ACTH, for 24 hours. BrdU/PI staining was used for cell cycle analysis by flow cytometry. RT-PCR was used to measure the expression of ABCA-1, LXR α, SR-B1, ERα, StAR CYP11A1, CYP17A1. CYP11B1 and CYP11B2.

Results: We found that both 27-Hydroxycholesterol and T0901317 exerted a proliferative effect on these cells after treatment for 24 hours, however, 27-hydroxycholesterol exerted a much more pronounced effect. We have concluded that this occurs through a mechanism which is not LXRα mediated alone, most likely Estrogen Receptor-alpha (ERα) plays a major role also. H295R cells oxysterol responsive following induction of ABCA-1 and decreased expression of CYP27A1, two known targets of oxysterols. Steroidogenic enzymes showed a variable response with an overall increased effect. Genes involved in steroidogenesis all exhibited upregulation in the presence of 27-Hydroxycholesterol. T0901317 results showed steroidogenic gene expression was increased following similar patterns shown by 27-Hydroxycholesterol results. Overall, 27-Hydroxycholesterol has been shown to play a role in upregulation of the steroidogenic pathway which is shown to be LXR-alpha mediated.

Conclusion and Implications: In Conclusion, LXR-alpha and ER-alpha were shown to play a role in proliferation and steroidogenesis in ACC. In the future, it may be possible to develop a strong antagonist to inhibit the proliferation of this aggressive cancer. Furthermore, identifying and targeting more oxysterol-associated molecular pathways, will offer novel therapeutic targets for ACC.

SS1-4: Cancer

Timeslot: 8:30-8:45am

Presenter: Suraj Varkhande
Institution: National Institute of Immunology, India

Evaluation of Repigmentation with Cultured Melanocyte Transplantation (CMT) Compared with Non-Cultured Epidermal Cell Transplantation in Vitiligo at 12th Week Reveals Better Repigmentation with CMT

Background: Vitiligo is a multifactorial depigmenting disorder of the skin leading to severe psychological trauma and low self esteem resulting in impaired quality of life. We have evaluated the outcome of non-cultured epidermal cell transplant (NCES) and culture melanocyte transplant (CMT) on the bilateral lesions of the same patients to minimise inter-individual differences.

Methods: Thirty individuals with bilateral lesions were treated with autologous NCES on one side and CMT on the other side after dermabrasion and followed up at 4th, 8th and 12th week to evaluate the extent of repigmentation. Repigmentation was evaluated by three methods visual, graph paper (3D) and image analysis (2D). Paired student's t-test and Fisher's exact test were used to study the statistical significance.

Results: Both NCES and CMT resulted in diffused pigmentation. In the visual analysis, excellent pigmentation was observed in significantly higher number of cases with CMT as compared to NCES group as early as 8th week ($p<1.23 \times 10^{-6}$) and this trend continued for the 12th week as well. Good repigmentation was observed in significantly higher number of patients on CMT as compared to NCES group as early as 4th week after transplantation ($p<9.32 \times 10^{-8}$). Graph paper (3D) and image analysis (2D) showed similar results, where significantly higher percent repigmentation ($P<0.0001$) was observed in CMT sites (mean±SEM 80.59±2.8% with 3-D and 81.66±2.86% with 2-D analysis) compared with NCES sites (28.39±3.5% with 3-D and 27.73±4.19% with 2-D analysis).

Conclusions: CMT results in better coverage and faster repigmentation in vitiligo and needs to be included in standard care for stable vitiligo after proper training in growing and enriching autologous melanocytes. However, to be able to use it clinically, approval from the regulatory bodies in different countries, like FDA in USA, would be required.

SS2-1: Global Health

Timeslot: 9:50-10:05am

Presenter: Joanna Dowdell
Institution: University of Toronto, Canada

Pregnant Dichotomies: Reproductive Justice and Women in Poverty

Background: In evaluating accessibility of reproductive healthcare programs for women in poverty, a dichotomy of the reproductive services offered that are deemed "useful" versus that which are defined as "wasteful" for particular groups is easily established. In the late 20th century, particularly invasive population control methods began to take hold due to misconceptions regarding environmentalism, as well as discourse that portrayed women in poverty in the Global South as having hoards of resource-hungry children, and the conception of such children as being wasteful. This view was an environmentally based distraction from necessary dialogue around first-world overconsumption, however the distraction was enough for some countries to begin harsh forms of population control, including forced sterilizations. In contrast, in more recent years since reproductive technologies such as in vitro fertilization (IVF) became available for affluent individuals, many of these countries have opened employment through the labour of surrogacy.

Aims: This research seeks to understand the way that the politics of wasteful reproduction versus useful reproduction controls the accessibility of reproductive healthcare for women in poverty in low-income countries. By exploring community research models that exemplify the perspectives of the communities of women in poverty facing constrained choices regarding personal reproductive health, we hope to open discussion around the topic of inequitable healthcare access and reproductive justice.

Methods: This study consisted of examining and juxtaposing published records regarding sterilization procedures and surrogacy procedures on women from marginalized communities in South Asia.

Results: The analysis shows that forced sterilization and surrogacy have been introduced to similar populations of marginalized women, often in a forced or constrained manner. This means that the same groups of women in South Asia who bore the brunt of sterilization procedures have also been targeted for surrogacy transactions, which place a very specific value on their wombs, but only for the purpose of bearing children that are not their own.

Conclusion: Thus, sterilization is enforced onto groups of women whose children are deemed excessive or wasteful, however this same group is then told that the use of their bodies to reproduce for more affluent individuals is useful and valuable. This dichotomy of wasteful versus useful reproduction extends from neoliberal politics deep into the types of reproductive health services that are accessible to - or forced upon -marginalized groups of women.

Implications: When healthcare accessibility, or access to free, prior, and informed consent of healthcare, is examined in the context of reproductive justice, these backgrounds must be understood in order to ensure equity and ethical regulations

SS2-2: Global Health

Timeslot: 10:05-10:20am

Presenter: Charles Mwembu
Institution: Moi University School of Medicine, Kenya

A Study on Challenges Facing Implementation of Free Maternal Services in Webuye Sub-County Hospital

Introduction/Background information: The concept of maternal mortality has become an everyday phenomenon of the contemporary world. Women of childbearing age face the agony of pregnancy's possibility leading to death. Due to the high maternal mortality rates, the government in 2013 introduced free maternity services as a social security measure. The implementation of free maternal health service has faced unforeseen challenges. The purpose of the study is to identify the challenges facing its delivery. Moreover, suggest recommendations that would ensure effectiveness of the whole process.

Study objectives: The broad objective is to identify the challenges facing the implementation of free maternal services in Webuye Sub-County Hospital. The specific objectives are: To identify the challenges facing the workforce of the maternity section of the hospital, to identify challenges facing the delivery of free maternity service in terms of equipment's and supplies required and to identify challenges encountered in re-imbursement of funds from the national government.

Methodology: Study Design: Cross-sectional study to conduct the interviews and a retrospective study look at the records concerning free maternity services. Sampling method: Convenience sampling. Data collection and presentation: Primary data from interviews and secondary data through review of records. Data was presented in prose, bar charts and tables.

Findings: The challenges found were workforce shortage, poor working conditions, inadequate equipment and supplies, inadequate space for expansion and cumbersome procurement. Moreover, challenges due to re-imbursement of funds included inadequate funds to run the program and irregularity on when it's distributed.

Conclusion: Free maternity care has been very beneficial to our country. However; the delivery of free maternity care is highly challenged by shortage of staff. The current equipment and infrastructure is not enough to run this scheme to its full potential and there is no clear protocol guiding the Ministry of Health on re-imbursement of funds back to the facilities.

SS2-3: Global Health

Timeslot: 10:20-10:35am

Presenter: Iryna Horbal
Institution: Ivan Franko National University of Lviv, Ukraine

Happy Pensioners: Psychological Model of Subjective Well-Being in Late Adulthood

As a quantitative indicator, "primary index" (Ryan, Deci 2001) of happiness subjective well-being (SWB) is widely studied nowadays, together with objective facts taken into account while defining life quality index. Experiencing happiness is connected with "flow" activity (Csikszentmihalyi 1990) that accords person's abilities, delights and leads to personal potential realization. However, for moving on the way of personal growth one needs to have enough resource which likewise uncloses through SWB experiencing. SWB is handled as an attitude to life composed of both cognitive and affective components. It is a predisposition and a result of this attitude's behavioral fulfillment through self-growth and self-realization. In late adulthood this fulfillment is somewhat specific due to many changes – health, interaction, financial, changes of social roles, activity changes etc. On the one hand, the changes may be thought to be negative and to cause low life quality. On the other hand, late adulthood period is not scarce – this is the highest stage of maturity where special moral resource appears and uncloses a perspective of highest forms of personal realization – Ego-integration. Thus, happiness has no age limits but among pensioners it is connected to somewhat different characteristics than before and the aim of the study was to define those peculiarities. 260 pensioners (age 60-88, N=260) were involved in the study of their content of SWB experiencing (measured with E. Diener Satisfaction with Life Scale and N. Bradburn Affective Balance Scale) and its correlations with amount of personal traits and social functioning characteristics. Discriminant analysis has shown that the most important factors for the differences in SWB level are such traits as high emotional intelligence (N. Hall EQ Self-evaluation Test) and low depression level (W. Zung Depression Scale). Thus, SWB in late adulthood is mainly dependent on the personal peculiarities that ensure inner harmony, understanding of person's feelings and other people's emotions. For being happy, pensioner needs to be emotionally mature and ready for social interaction. Using factor analysis 5-factor model of SWB determination was created. Besides described emotional maturity, hardiness (S. Maddi Hardiness Test) is very important. It mainly works through emotional component of SWB and correlates with frequent communication with relatives. According to C. Ryff (1989) interaction with the closest is the main factor of happiness among elderly people. One more serious factor was found to be physical health but not a passport age. Pensioners also pay big attention to their social status (education level, amount of social benefit) that mainly influences on cognitive aspect of SWB. Finally, financial independence is important: if a person has an opportunity to avoid material support of relatives, this makes him/her feel younger. On the other hand, such identification with late age stereotypes reduces both cognitive and affective well-being. Such finding should be used while developing socio-psychological accompaniment programs for pensioners and for prevention of undesirable psychological difficulties of adaptation to retirement for those who soon will reach old age.

SS2-4: Global Health

Timeslot: 10:35-10:50am

Presenter: Vineet R Joag
Institution: Department of Immunology, University of Toronto, Canada and University of Nairobi, Kenya
Co-Authors: Rupert Kaul

Department of Immunology, University of Toronto, Canada

Building Sustainable Research Capacity in Sub-Saharan Africa

This talk will explore some of the causes of poor biomedical research capacity in Sub-Saharan Africa (SSA) and novel funding mechanisms to address capacity gaps. Increased research spending in SSA in the past decade has resulted in a concomitant rise in North-South partnerships. Equity and participatory approaches are critical for enabling and productive partnerships and I present a tool generated primarily by African and Canadian researchers intended to help foster just and sustainable collaborations among researchers worldwide.

SS2-5: Global Health

Timeslot: 10:50-11:05am

Presenter: Nelly Amenyogbe
Institution: University of British Columbia, Canada
Co-Authors: Morten Bjerregaard-Andersen[1], Kristina Lindberg Larsen[2], Christine Stabell Benn[2], Peter Aaby[2], Scott Tebbutt[3]

[1]Statens Serum Institute, Copenhagen, Denmark
[2]Bandim Health Project, Guinea-Bissau and Statens Serum Institute, Copenhagen, Denmark
[3]University of British Columbia, British Columbia, Canada

Beneficial Off-Target Effect of the BCG Vaccine on Newborn Mortality

Background: Epidemiological studies have shown that BCG immunization at birth is associated with a 50% reduction in mortality rate in the first week of life independent of tuberculosis disease. As the underlying mechanisms of these non-specific effects (NSEs) remain unknown, BCG is not optimally exploited to prevent early neonatal death.

Aims: Identify signatures of BCG NSE in human newborns and dissect mechanisms in animal models.

Methods: The 'BCG-Immediate' trial is being conducted at the National Hospital in Guinea-Bissau, comparing in-hospital survival of low-birth-weight infants given BCG at birth or at hospital discharge. Whole blood transcriptomic, metabolomic, and proteomic signatures will be compared 24 hours after randomization in association with early neonatal survival outcomes. In parallel, we have shown that BCG reduces mortality from polymicrobial sepsis by 46% in our newborn mouse model, used to study mechanisms of NSE.

Results: Immunized animals have a reduced bacterial burden compared to naive counterparts. Preliminary findings from the BCG- Immediate cohort reveal an enrichment in neutrophil-associated RNA transcripts, correlating with transcriptional responses in immunized newborn mice.

Conclusion: BCG may protect newborns from sepsis by altering innate immune function.

Implications: Furthering our understanding of NSEs will allow us to use targeted immune modulation as a means to combat neonatal death.

SS3-1: Chronic Diseases

Timeslot: 7:30-7:45am

Presenter: Dr. Nicholas Muema
Institution: Moi University School of Medicine, Kenya
Co-Authors: Phinehas Omondi, Jemimah Akinyi , Aisha Mohamed

Moi University, School of Medicine, Eldoret, Kenya

Management Outcomes of Type 1 Diabetes Mellitus in Under Fourteen Years Clients Receiving Care in the Home Glucose Monitoring Program at the Moi Teaching and Referral (MTRH) in Eldoret, Kenya

Background: This study evaluates the impact of home glucose monitoring program in under fourteen years clients receiving care in the diabetes clinic at MTRH. The program is one of a kind in Sub-Sahara Africa. The clients are enrolled into the program after meeting the criteria then issued with a glucometer for blood sugar testing at home. They are then phoned weekly for results and insulin dose adjusted as per the results. The impact of the program on pediatric population with type I diabetes mellitus however has never been evaluated since its commencement in 2011. Most of the Type I diabetes mellitus diagnosis in Kenya is incidental, thus clients do not know whether they have it until when they present to a health facility. It is associated with low survival rates in sub Saharan Africa with about 1% surviving beyond six years. After three months of follow up, most clients show improvement which is reflected by drop in HbA1c levels. Effective management of type I diabetes in the early years of life has been shown to slow down the progression of the disease and increases survival into late years of adulthood.

Methodology: The study period was two years between 2011-2013. It addressed the following question: what is the outcome of management of type I diabetes clients under the age of 14 years receiving care in the HGM program in MTRH in Eldoret, Kenya? The Inclusion criteria was all type 1 diabetes clients under the age of fourteen years being followed up in the HGM program at MTRH. All clients who did not meet the inclusion criteria were excluded. The study involved retrospective chart review of medical records of all the participants and recording of the data in forms. A univariate analysis of the data collected was done and the results obtained recorded.

Results and discussion: The average age of clients in the program is 10.7 years with majority being male. The HbA1c level dropped by18.3%in first three months, number of episodes of severe hypoglycemia reduced by 33.7%, hospitalizations due to DKA also declined by 83.3% within six months and only three case fatalities were reported in the two year period of study. There is marked improvement within the first three months of follow up which maybe attributed to intense follow up.

Conclusion and recommendation: According to these statistics we conclude that the clients are doing well under the program and therefore we recommend that more research should be exploited in this field as improvement is largely influenced by several parameters pertaining to quality of life of clients. Improvement is not guaranteed based on adequate treatment alone but rather food security, exercise and adherence to medication comprise some of the parameters.

SS3-2: Chronic Diseases

Timeslot: 7:45-8:00am

Presenter: Dr. Sanket Rane
Institution: National Institute of Immunology, India
Co-Authors: Rituparna Das[1], Arundhoti Das[2], Jenine Durdik[3], Anna George[2], Satyajit Rath[2], Vineeta Bal[2]

[1]Yale Cancer Center, Sterling Hall of Medicine, New Haven, USA,
[2]National Institute of Immunology, New Delhi, India
[3]Department of biological sciences, University of Arkansas, Fayetteville, USA

CD4: A Surrogate Marker for T-Cell Aging

Dynamics of cognate and non-cognate interactions during post-thymic survival of naïve CD4 (NCD4) T lymphocytes in periphery may have distinct consequences on their function. It is not clear if there is any association between duration of peripheral residence of NCD4 T cells and their activation, proliferation and Effector functions. Alteration in phenotypic properties of NCD4 T cells owing to longer or shorter duration of peripheral residence also remains possible. Through our study, we are trying to understand the correlation between duration of peripheral residence and variations in phenotypic (CD4 levels) and functional properties of NCD4 T cells. We examined separated NCD4hi and NCD4lo subsets of mouse NCD4 cells. NCD4lo cells were smaller, had higher CD5 levels, responded poorly, were more Th2-skewed, with lower levels of the dual-specific phosphatase (DUSP)6-suppressing micro-RNA miR181a. Thymic NCD4lo and NCD4hi subsets did not show differences. Adoptive transfer-mediated parking in vivo lowered CD4 levels, increased CD5 and ROS levels and induced hypo-responsiveness in NCD4 cells, dependent at least in part on MHC class II availability. ROS scavenging or DUSP inhibition ameliorated hypo-responsiveness. These data indicate complex roles for microenvironmental signaling governing phenotypic and functional heterogeneity of peripheral T cells, and suggest potential therapeutic interventions for successful vaccination in the elderly.

SS3-3: Chronic Diseases

Timeslot: 8:00-8:15am

Presenter: Elise Fryml
Institution: University of Toronto, Canada
Co-Authors: Shahla Yekta[1], Elise Fryml[2], Jennifer Gatebi[3], Joseph Wanjeri[4], Peter Oduor[5], Asrat Mengiste[3], Leila Kasrai[1]

[1]Division of Plastic and Reconstructive Surgery, University of Toronto, Toronto, Canada
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[4]Kenyatta National Hospital and University of Nairobi, Nairobi, Kenya
[5]Rift Valley Regional Hospital and Egerton University, Kenya

Incidence and Severity of Burns in Two Hospitals in Nairobi and Nakaru, Kenya

Introduction: Worldwide, burns are the 4th most common injury. Burns severe enough to require medical attention have a worldwide incidence close to 11 million. Burns from fires account for 310 000 deaths each year, with 95% of injuries occurring in low- and middle-income countries (LMICs). In these countries, the quality of acute care varies and prevention programs are not common. Children under 5 years of age have the highest risk of burn injuries. In Kenya, about 60-80% of urban dwellers live in slums, so socioeconomic status is an important consideration when investigating burn injuries. However, there is a paucity of data about the demographics of burn injuries in Kenya.

Objective: This study aimed to better understand the demographics and socioeconomic factors of burn victims at hospitals in Nairobi and Nakuru, Kenya.

Methods: We recruited 359 burn victims who presented to either Kenyatta National Hospital/ U of Nairobi in Nairobi, or Rift Valley Provincial General Hospital (RVPGH)/ Egerton U in Nakuru, Kenya. We administered a comprehensive questionnaire to assess the incidence and severity of the burns.

Results: The burns patients ranged in age from 5 weeks to 80 years. The majority (50.7%) of patients were young children below the age of five. Burns were caused predominantly by either scalds (55.2%) or flames (37.7%). The majority of patients reported 2nd degree burns (57.2%). Burns from flames were more likely to be associated with greater severity relative to burns from scalds. Adult patients were seen to have significantly higher proportion of more severe burns in comparison to pediatric patients under age 5.

Conclusion: This study provides new demographic and etiologic data on Kenyan burn injuries, which can serve to guide prevention and treatment efforts. In particular it underscores the importance of our current cookstove barrier project in the rural slum of Kibera.

SS3-4: Chronic Diseases

Timeslot: 8:15-8:30am

Presenter: Ruth Anyango
Institution: Moi University School of Medicine, Kenya

Knowledge, Attitude and Mental Health Practices in Western Kenya

Introduction: Mental disorders contribute to 14% of the global burden of disease. Future projections show a 15% significant increase in the mental health disorders by the year 2020 of the global burden disease. Approximately 10-15% of the population suffers from common mental health problems and from substance related disorders including alcohol dependence. In Kenya, the current burden of disease for mental health is high and continues to rise amid the high poverty levels and scarcity of mental health specialist in the country. Resource allocation and the dearth of mental health specialists are possibly the major contributors to the current status of mental health. Of the annual health budget only 0.5% is allocated to mental health. Most of the funds are spent on treatment in hospitals to severe mental health disorders and there are few resources available for early interventions and preventions through educating the community.

Methods: We carried out a community based cross sectional study among communities in western Kenya. Five Villages were purposively selected and mapping done with the help of the village elders. A total of 600 households leaders were interviewed but only 140 respondents who answered questions on mental health were included in the final analysis. Data collection was done through semi structured interview schedules. Analysis was done using SPSS Version 21 where descriptive statistics and the inferential statistics were reported. Inferential statistics assumed a 95% confidence interval and a test significance value at ≤0.05.

Results: Out of the 140 respondents, 48.5% were not aware of mental illnesses and their causes. Of the respondents not aware, 60.3% attributed the cause of mental health to be diseases not capable of causing mental illness and 29.3% attributed it to witchcraft and cultural malpractices. However 61.1% of the respondents said that most people suffering from mental illness were taken to a rehabilitation facility, 31.3% were taken to witchcrafts and traditional healers, 19.1% were neglected and 19.8% were taken for prayers or a form of spiritual intervention. The association between demographic characteristics (age, sex, marital status, religion) and mental illness awareness were not statistically significant ($p>0.05$).

Conclusion: There is a significant gap in the knowledge of mental illnesses among the communities in western Kenya. This delays seeking of appropriate intervention hence prolonging the duration of the illness.

Key words: Mental health, awareness.

SS3-5: Chronic Diseases

Timeslot: 8:30-8:45am

Presenter: Germán Camargo Ortega
Institution: Ludwig-Maximiliams Universität München, Germany
Co-Author: Magdalena Götz

Helmholtz Zentrum München, Institute of Stem Cell Research, Neuherberg, Germany

Regulation of Neural Stem/Progenitor Cells by Known and Novel Centrosomal Proteins

Understanding mechanisms controlling neural stem cell (NSC) homeostasis and commitment to specific fates is fundamental for their efficient manipulation and future use in regenerative medicine. Given that the regulation of NSCs first, at different stages of development and second, between different species is by no means totally overlapping but rather has its own specific requirements (see for instance Ninkovic & Goetz, 2013 and Taverna et al., 2014), it is of prime importance to analyze the similarities and differences. To contribute to this goal, our laboratory interrogates novel neurogenic molecular pathways by identifying common regulators of NSCs in different contexts including the developing and adult murine brain, the devolping human brain and models of neurodegeneration and repair (Pinto et al., 2008; Beckervordersandforth et al., 2010). This approach has proved successful for the identification of new factors essential for neurogenesis (Agoston et al., 2013; Brill et al., 2008, Pinto et al., 2009; Stahl et al., 2013) and key in direct neuronal reprogramming (Masserdotti et al., 2015). Here, I will discuss about the current understanding of the role of known and new centrosomal proteins in the regulation of neural stem cells.

SS4-1: Education & Technology

Timeslot: 9:45-10:00am

Presenter: Dr. Behrouz Moemeni
Institution: BeMo Academic Consulting Inc., Canada

Selecting the Right Candidate: An Examination of Current Admissions Processes and Tools Used by Graduate and Professional Programs

One of the biggest challenges facing professional and graduate programs is the ability to select the most appropriate candidates for the profession. Every year, graduate and professional programs such as medicine, dentistry, pharmacy, and law utilize a combination of assessment tools to narrow down their large pool of applicants. These candidates are not only selected based on their didactic capacities (i.e. grades and aptitude scores), but more importantly, their emotional intelligence (EI) and non-cognitive skills (NCS). To demonstrate their EI & NCS, applicants are currently asked to write essays, construct autobiographical sketches, perform situational judgment tests (e.g. CASPer Test), and conduct in person interviews. However, most of the current assessment tools are ineffective, and for example in medicine, lack of professionalism of doctors is the number one complaint by patients costing billions of dollars every year. There are both advantages and disadvantages to all of these admission tools, and their reliability and efficacy is still under investigation. Yet, the importance of admissions tools cannot be overstated in selecting the most knowledgeable, compassionate, mature and professional of applicants, as the selection of an inappropriate candidate will not only have a negative impact on those under the care of the professional, but also the greater profession and society as a whole. We will review the efficacy of the most popular assessment tools during this presentation and in the process we will propose alternative admission tools that can be introduced to test not only EI and NCS but also an important variable that has been connected with professional excellence, namely Intrinsic Motivation (IM).

SS4-2: Education & Technology

Timeslot: 10:00-10:15am

Presenter: Payam Zarin
Institution: University of Toronto, Canada

From Bench to Shelf: Creating Life Sciences Products as a Graduate Student

Background: Basic research in the medical sciences often yields little more than publication of the results in peer reviewed journals. One may argue that there is a disconnect between this final product and the public's image of medical research yielding immediate improvements in health practice.

Aims:
1. To discuss some of the elements involved in translating basic research into life sciences products.
2. To provide an overview of technology entrepreneurship from a graduate student perspective.

Results: We will discuss various obstacles faced by many life sciences start-up companies including regulatory, intellectual property, and legal issues. We will also discuss strategies for creative marketing, building a customer base, and attracting private funding.

Conclusions: Creating a start-up is a difficult but rewarding process!

Possible Applications or Implications: Students will be motivated to start their own company.

SS4-3: Education & Technology

Timeslot: 10:15-10:30am

Presenter: Peter Fettes
Institution: Institute of Medical Sciences, University of Toronto

Psychiatric and Neurocognitive Implications of Cannabis Dependence in Young Adults

Background: The incidence of cannabis dependence and abuse among adolescents and young adults has been on the rise in the last 10 years, and 9% of those who use cannabis will develop psychological dependence. Heavy cannabis use has been linked to impairments in working and episodic memory, as well as deficits in attention and executive functioning. The development of mood disorders such as depression and anxiety, as well as psychotic disorders such as schizophrenia, has been associated with chronic cannabis abuse. Prolonged heavy use and a younger age of onset of cannabis dependency are associated with more severe impairments in executive function domains.

Method: Twenty young adults 18-24 years of age with cannabis dependency (10 female; M THC UDS=97.9; M g/day=1.4), and twenty healthy peers (12 female), completed questionnaires assessing psychiatric symptomatology, perseverance, and overall well-being, and behavioral measures of executive functioning (abstraction, inhibition, working memory, reasoning, mental flexibility). Participants were requested to submit a urine sample for biomarker testing of quantitative levels of: THC, ETG, cocaine, opioids, opiates, and benzodiazepines.

Results: Results showed that there were no significant differences between the clinical group (cannabis dependent) and their healthy peers on anxiety, depression, psychoticism, global psychiatric symptomatology, overall wellbeing, and perseverance. No significant correlations were found between overall marijuana consumption (g/day)/age of onset of dependency and self-reported psychiatric health and wellbeing. Additionally, no significant differences were found in behavioral measures of concept formation, working memory, abstraction, logical reasoning, mental flexibility, and efficiency. However, a more severe working memory deficit was significantly correlated with an earlier onset of cannabis dependency (r=.478, p=.033).

Conclusions: No evidence of neurocognitive impairments or psychiatric symptomatology were found to be associated with psychological cannabis dependence. A significantly greater working memory deficit, however, was found in those who became dependent at a younger age.

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PRE-RECORDED PRESENTER ABSTRACTS

To Access: http://www.beyondsciences.org/video/

Session Topic: Global Health

Presenter: Nafiseh Talaei
Institution: University of Toronto, Canada
Co-Authors: Tao Yu[1], Kieran Manion[2], Rod Bremner[1], and Joan E. Wither[2]

[1]Lunenfeld Tanenbaum Research Institute, Toronto, Canada
[2]Toronto Western Research Institute, Toronto, Canada

Identification of the slam adapter molecule eat-2 as a lupus susceptibility gene that acts through impaired negative regulation of dendritic cell signaling

Background: Systemic lupus erythematosus (SLE) is a generalized autoimmune disease characterized by production of autoantibodies directed against nuclear antigens that deposit in various organs causing tissue damage. There is a strong gender imbalance in the prevalence of SLE as it mainly affects women of childbearing age, with the highest incidence of disease occurring between the ages of 15 and 50 years. The New Zealand Black (NZB) mouse strain spontaneously develops a lupus-like autoimmune phenotype. Genetic loci on chromosome (c) 1 have an important role in development of disease in NZB mice. B6 mice with an introgressed homozygous NZB (c) 1 interval (70 to 100 cM) develop high titres of antinuclear antibodies and severe glomerulonephritis (GN). Using subcongenic mice with shorter intervals in this region we demonstrate that T cell and dendritic cell (DC) defects, derived from several genetic loci, synergize to convert preclinical disease to fatal GN by leading to expansion of pro-inflammatory T cells. EAT-2, an adapter molecule in the SLAM signaling pathway that is located in the 70-96 cM region, has a promoter polymorphism in NZB mice that is predicted to lead to decreased expression. In this study, we examine whether altered expression of this molecule leads to the abnormal DC function observed in these mice.
Methods: Expression levels of EAT-2 were evaluated in bone marrow derived DC from c1 congenic and B6 mice using qRT-PCR and Western blots. EAT-2 promoter activity was investigated using a luciferase reporter assay. siRNAs targeting the EAT-2 gene were introduced into B6 and c1 congenic DC. Subsequently, naïve OVA-specific TCR transgenic (OTII) T cells from B6 and c1 congenic mice were isolated and co-cultured with EAT-2 silenced- or scrambled control-treated DC in the presence of OVA peptide. In parallel, DC were stimulated with anti-CD40 before and after knock-down of EAT-2. Production of cytokines (IL-12, IL-6, IFN-g) by DC and T cells was analyzed by flow cytometry. p38 MAP Kinase and JNK phosphorylation levels were evaluated by flow cytometry after stimulation of DC with anti-CD40 in the presence or absence of SLAM crosslinking.
Results: Silencing of the EAT-2 gene in DC that lacked this polymorphism led to increased production of IL-12 and enhanced differentiation of T cells to a Th1 phenotype in T cell-DC co-cultures, reproducing the phenotype observed for c1(70-100) DC. SLAM signaling has been previously shown to inhibit production of IL-12 by CD40L-activated DCs. Consistent with a role for EAT-2 in this inhibition, knock-down of EAT-2 resulted in increased production of IL-12 by CD40-stimulated DC. Assessment of downstream signaling following CD40 crosslinking in the presence or absence of SLAM crosslinking revealed that SLAM co-engagement blocked activation of p MAP Kinase signaling pathways in DC, which was reversed in DC with the NZB EAT-2 allele.
Conclusion: We conclude that EAT-2 negatively regulates cytokine production in DC downstream of SLAM engagement and that a genetic polymorphism that disturbs this process promotes the development of lupus.
Implication: Our study suggests that drugs that negatively regulate DC function may be effective for treatment of Lupus.

Session Topic: Global Health

Presenter: Aphlyne Ouma
Institution: Moi University School of Medicine, Kenya
Co-Author: V.C Kosgei

Moi University, School of Medicine, Eldoret, Kenya

Assessing the level of mental health awareness and public health interventions in mental health care in western Kenya.

Introduction: Statistics show that mental illness account for up to 14% of the global burden of disease. In Africa 5% of the population suffer from mental illness and despite the increased prevalence rate, it remains ignored even as much attention is directed towards other illnesses.

Objectives: To determine the level of mental health awareness and the available public health interventions

Methodology: We systematically reviewed reports by the Community Based Education and Service (COBESII) program by the students from the college of health sciences -Moi University. Five of the stations were randomly selected and analyzed with focus on mental health awareness and public health interventions.

Findings: The alarming figures were at 50% associated with depression, 9% schizophrenia, 5% bipolar and 5% dementia. The respondents reported challenges in detection, access to mental health services and treatment. 37% were aware of causative factors living out 52%. In some study areas there were no psychiatric facilities and even personnel available. A wide variation on management included 37.5 % visiting the health centers, 12% seeking divine intervention and using herbs, at 50.5% were other methods.

Conclusion: The mismatch between the global burden of mental disorders and the availability of mental health resources is alarming. Thus, the apparent lack of mental health issues leads to a grim conclusion. How do people seek help for what they don't understand? This calls for improved awareness campaigns.

Session Topic: Global Health

Presenter: Oluoch Emmanuel Benge
Institution: Moi University School of Medicine, Kenya
Co-Authors: Kate Mandere ,Clara Laibuch, Jemimah Aumah, Mary Sala, Gabriel Kigen

Moi University, School of Medicine, Eldoret, Kenya

Adherence to Antiretroviral Therapy Amongst Adolescents Enrolled at AMPATH Center, Eldoret-Kenya.

Background: Although much headway has been made by many researchers on the subject of adherence to Antiretrovirals (ARV), gray areas still overlie the distribution amongst the various age groups. The research aims at shedding light on the level of adherence to ARV therapy amongst adolescents.

Aims: 1.To determine the level of adherence to ARV Therapy amongst adolescents enrolled in AMPATH-Eldoret .2.To identify the challenges facing adherence to anti-retroviral therapy amongst adolescents in AMPATH- Eldoret, Kenya. 3.To find out how adherent adolescents ensure compliance.

Methodology: A cross- sectional study design was undertaken to provide at a glance, data on adherence to ARV Therapy amongst adolescents. Data was collected using detailed questionnaires, and semi-structured interviews.

Results: The level of adherence amongst adolescents aged between 9-19 years at AMPATH Eldoret is 97.65%. The modal category of duration of missed medication was less than a week representing 46.44% of the participants. The challenges involved in taking ART amongst adolescents though varied in nature could be easily related to factors significant for their age; high pill load, stigma especially at school, side effects of the ARVs, inadequate social support and poor nutritional support.

Conclusion: The level of adherence currently amongst adolescents enrolled at AMPATH Eldoret of 97.65% is commendable having bypassed the WHO recommendations of 95%. Establishment of an adolescent friendly clinic where adolescent are closely followed up with thorough counseling has been key in achieving such a high level of adherence. A heavy pill burden is the greatest challenge in adherence amongst adolescents. Most find the drugs cumbersome to take because they are many pills taken at least twice with strict timing. Stigma comes a close second as most adolescents are unwilling to let their peers know their HIV status for fear of desertion. A reduction in pill burden was recommended as the best means of improving adherence. Others include improvement in family and peer support to be achieved through mass education.

Implications: The gains in achieving the levels of adherence of 97.65% is commendable hence, we must continue to ensuring support to this unique age group. Similar organizations tasked with provision of Antiretroviral Therapy and allied services to adolescents can adopt AMPATH model of care. Pill burden still remains a challenge that needs to be addressed.

Session Topic: Cancer

Presenter: Swarnendra Singh
Institution: Cancer Microarray Genes and Proteins Laboratory, National Institute of Immunology, India
Co-Author: Anil Suri

Cancer Microarray, Genes and Proteins Laboratory, National Institute of Immunology, New Delhi, India

Testis specific heat-shock protein 70-2 (hsp70-2); a novel potential therapeutic target for renal cell carcinoma

Background: Renal cell carcinoma (RCC) represents one of the most resistant tumors to radiotherapy and chemotherapy. Current treatment options for RCC patients are limited because of the lack of therapeutic targets. Testis specific heat-shock protein 70-2 (HSP70-2), a member of HSP70 chaperone family, has been shown to be involved in various cancers. In the present study, we investigated the association of HSP70-2 with various malignant features of cancer cells, in order to develop a novel target for RCC.

Aims: To delineate the putative association of HSP70-2 with RCC malignant properties; the study was divided into two major objectives.

1. HSP70-2 gene and protein expression in RCC cells.
2. HSP70-2 knockdown and its effects on various cancer malignant properties

Material and methods:HSP70-2 mRNA and protein expression was investigated in A704, ACHN and Caki-1 cells derived from RCC patients by reverse transcription-polymerase chain reaction (RT-PCR) and by Western blotting. Validation of HSP70-2 protein expression was carried out by indirect immunofluorescence (IIF) and flow cytometry for cytoplasmic localization, colocalization in various subcellular compartments and surface localization respectively. The gene silencing approach employing plasmid driven shRNA targets was used to examine the involvement of HSP70-2 in cancer cell viability, cell growth, colony formation, migration, invasion and wound healing assays in high grade invasive A704 and Caki-1 cells.

Results: Our RT-PCR and Western blotting data showed HSP70-2 expression in all RCC cells. Our results showed that HSP70-2 was predominantly expressed in cytoplasm and colocalized with endoplasmic reticulum, mitochondria, Golgi body and plasma membrane but not with the nuclear envelope. Knockdown of HSP70-2 expression in RCC cells with specific shRNA demonstrated significant reduction in cellular proliferation, colony formation, migration, invasion and wound healing properties.

Conclusion: Our findings demonstrate that HSP70-2 is expressed in various RCC cell line models. HSP70-2 colocalization with vital cell organelles indicate its possible involvement in networking pathways operating there. For the first time, we have put forth an evidence of potential role of HSP70-2 in various malignant properties of RCC cells indicating that HSP70-2 could serve as a novel potential therapeutic target for the RCC.

Session Topic: Cancer

Presenter: Jonathan Chan
Institution: University of Toronto, Canada
Co-Author: Rahul Pal

National Institute of Immunology, New Delhi, India

Biological Validation of Human Chorionic Gonadotropin

Human Chorionic Gonadotropin (hCG) is a hormone produced during pregnancy that acts on the corpus luteum to stimulate the secretion of progesterone, a steroid responsible for maintaining the uterus in a receptive state. In recent years, hCG has also been shown to be produced by a wide variety of cancers. In many cases, its presence is associated with poor patient prognosis. The preparation of hCG was determined to exhibit a high degree of purity as assessed by SDS-PAGE analysis. The preparation bound both polyclonal and monoclonal anti-hCG antibodies as assessed by ELISA and radio-immunoassay. As determined by the binding of Annexin-V, hCG reduced chemotherapeutic drug-induced apoptosis in cancer cells.

DIGITAL POSTER ABSTRACTS

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Session Topic: Global Health

Presenter: Amrita Jha Kumar
Institution: Institute of Biomedical Sciences, University of Sao-Paulo, Brazil

Neonatal Anoxia in Rats: Evaluation of its Effects on Spatial Memory in Adolescence

Background: Neonatal anoxia, has been reported as a world wide clinical problem, it results in brain injury in new-born as cognitive and behavioural deficits, cerebral palsy, epilepsy, hearing and visual impairment (Dell'Anna et al., 1997). Our laboratory has observed in the rats submitted to neonatal anoxia hypocampal cell death, by necrosis and apoptosis, and altered neurogenesis what corroborates with defects in learning and anxious behavior.

Aim: To amplify the comprehension of the effects of neonatal anoxia in rats by evaluating the consequences on anxiety and spatial memory in adolescence and also evaluate eventual gender differences using a non-invasive and global model of anoxia.

Method: Wistar rats 30 hours old (6-8 grams), male and female, will be exposed to 25 minutes to 100% nitrogen gas flow of 3L/min, pressure 101.7 kPa at a temperature between 35 and 37°C in a semi- in hermetic chamber polycarbonate. The animals were subjected to anxiolytic behavior measured by elevated plus maze test at P33. Spatial memory was assessed at P35 by using Morris water maze over 6 days, 3 trials per day.

Result: Anoxia effect on female rats showed more anxiolytic behavior than males as she spends more time in open arm, and her frequency of entering the open arm is bigger. Spatial memory is impaired more in anoxia male group than in the female group, as they take more time to reach critical quadrants and path length.

Conclusion: Neonatal anoxia, affects at behavioral level, the reference spatial memory and anxiety. Gender difference was observed in this study, since the effects are different between males and females.

Implication: The observed results are evidence of the damaging effects of neonatal anoxia on behavior: anxiety and spatial memory. In addition it shows gender differences, what indicates that strategies or treatments should be developed to minimize them, but also that the gender difference should be considered for a more effective result.

Acknowledgments: this research is developed in partnership with Aline Vilar Machado Nils, Kelly Patricia Nery Borges, Vitor Yonamine Leee, Livia Clemente Motta Teixeira, Silvia Honda Takada, Gilberto Fernando Xavier and Maria Inês Nogueira.

Session Topic: Global Health

Presenters: Shannon A. Wong[1,2*], Lauren Y. Chan[1,2*]
Institution: [1]School of Medicine, Queens University, Kingston, [2]Canada Social Medicine Network, British Columbia, Canada, *Equal contribution
Co-Author: Michael Stein[2]

[2]Social Medicine Network, British Columbia, Canada

The Social Medicine Network: Promoting Social Accountability Among Healthcare Workers and Trainees

The Social Medicine Network is an interdisciplinary group of healthcare professionals, trainees and community-based organizations that work to enhance understanding of the broad range of social factors that affect health and well-being, and to foster health from multidimensional perspectives. Founded on principles of social justice and human dignity, we work to improve health outcomes and reduce health inequities in our communities. As a community of practice, we facilitate opportunities for healthcare, advocacy, research, education and community-engaged initiatives.

The Social Medicine Network website allows healthcare students and professionals to search for information on community engagement, advocacy, research, clinical elective, and other learning opportunities, and discuss and advocate for health societies and foster social accountability. The categories of interest include access to services, aboriginal health, mental health, addictions, advocacy, food security, maternal and child health, and LGBTQ health, to name a few.

Our vision is to be more effective in responding to the social determinants of health and to help mitigate the disparities that act as barriers to health. We work to promote social accountability among healthcare workers by establishing a network uniting individuals and organizations passionate about health and human dignity.

Session Topic: Global Health

Presenters: Mile Stanojčić[1]
Institution: [1]SunnybrookResearch Institute, Ross Tilley Burn Centre, Department of Surgery, University of Toronto
Co-Author: Marc G. Jeschke[1]

THERMAL INJURY PLUS PSEUDOMONAS AERUGINOSA INFECTION INDUCES ACTIVATION OF THE NLRP3 INFLAMMASOME AND ALTERATIONS IN IMMUNE CELLS

Background: Severe burn injury is a catastrophic event that forces patients to endure a life long battle recovering both physically and psychologically. Thermal injury produces a wide array of stress-associated inflammatory and metabolic changes aimed at restoring systemic homeostasis. *Pseudomonas aeruginosa* is a gram-negative bacterium that causes serious infections in immune-compromised patients and is particularly common during critical illness and thermal injury. The proliferation of *P. aeruginosa* infection in the wounds of burn patients in combination with its antibiotic resistant properties contributes towards skin graft failure, increases risk of sepsis, multi-organ dysfunction and mortality. The mechanism for this sequence of events is not well understood; however, recent studies of stress-induced diabetes have brought into question the role of the NLRP3 inflammasome. Using white adipose tissue from burn patients, preliminary data from our lab suggests that there is increased NLRP3 activity in patients after severe burn injury. The specific mechanism of pathogen-induced activation is still under debate. The purpose of this study was to use a two-hit mouse model of infectious thermal injury to determine the role of NLRP3 inflammasome during the development of burn-induced inflammatory response and subsequent infection-induced complications.

Hypothesis: Severe burn with *pseudomonas aeruginosa* infection induces NLRP3 inflammasome activation in various tissues including lung, liver and adipose. Collectively, this activation will promote the inflammatory cascade that directly contributes to pathology and mortality.

Methods: C57BL/6 mice (6-8 weeks old) were divided into three groups: sham(n=5), burn (n=30) and burn+PA (n=30) infection. Burn and burn+PA were exposed to a 30-40% scald injury and the later group received a topical infection of *Pseudomonas aeruginosa* 72-hours later. All burn and burn+PA mice were sacrificed at 1-, 3-, 6-, 12-, 24- and 48-hours after experimental condition. Flow Cytometry was conducted to characterize the proportions of monocytes, macrophage, neutrophils, B-, T-, NK- and NK-T cells in the skin, bone marrow, spleen, liver, adipose tissue and lung.

Results: Infectious burn resulted in a decrease in weight accompanied by an enlarged spleen. No significant fluctuations in blood glucose were noted between the three groups. The skin of infectious burn+PA had increased neutrophils compared to burn alone and sham, one day after insult. Reduced monocytes were observed in both the bone marrow and spleen at the same time point. In contrast, the liver showed increased presence of monocytes with decrease B-, T- and NK-T cells in contrast to both burn and sham groups. Collectively, this suggests that infection causes the activation of innate immune cells towards the site of infection early preceded by declines with corresponding increases in the organs suggests systemic infiltration and migration.

Conclusion: This project is the first study to describe the relationship between infectious complications and NLRP3 inflammasome activation after severe burn. These studies will provide insight about the upstream and downstream factors that are inducing inflammasome activation and largely, the degree of diminished metabolic response.

Session Topic: Global Health

Presenters: Vineet R. Joag[1,2]
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Identification of Specific Cellular Targets of HIV Infection in the Cervix

A better understanding of the cellular targets of HIV infection in the female genital tract may inform HIV prevention efforts. Proposed correlates of cellular susceptibility include the HIV co-receptor CCR5, peripheral homing integrins, and immune activation. We used a CCR5-tropic pseudovirus to quantify HIV entry into unstimulated endocervical CD4+ T cells collected by cytobrush. Virus entry was threefold higher into cervix-derived CD4+ T cells than blood, but was strongly correlated between these two compartments. Cervix-derived CD4+ T cells expressing CD69, α4β7, or α4 β1 were preferential HIV targets; this enhanced susceptibility was strongly correlated with increased CCR5 expression in α4 β7+ and CD69+ CD4+ T cells, and to a lesser extent in α4 β1+ CD4 T cells. Direct binding of gp140 to integrins was not observed, integrin inhibitors had no effect on virus entry, and pseudotypes with an env that preferentially binds α4 β7 still demonstrated enhanced entry into α4 β1+ cells. In summary, a rapid and sensitive HIV entry assay demonstrated enhanced susceptibility of activated endocervical CD4+ T cells, and those expressing α4 β7 or α4 β1. This may relate to increased CCR5 expression by these cell subsets, but did not appear to be due to direct interaction of α4 β7 or α4 β1 with HIV envelope.

Session Topic: Global Health

Presenters: Luana Angélica J. De Carvalho
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Neonatal Anoxia: Evaluation in Rats of Its Effects on Somatic and Sensory-motor Development.

Background: The neonatal anoxia is characterized by a significant reduction in the availability of oxygen during birth, is one of major causes of infant mortality and the emergence of long lasting neurological sequels including cerebral palsy, epilepsy, learning disabilities, hyperactivity, cognitive and sensorimotor deficits, among others.

Aim: To investigate whether neonatal anoxia impacts somatic and sensory motor development, as well as the onset of some ontogenetic reflexes in male rats.

Method: Wistar rats 30 hours old (6-8 grams), male, were exposed for 25 minutes to 100% nitrogen gas flow of 3L/min, pressure 101.7 kPa at a temperature between 35 and 37°C in a semi-hermetic chamber polycarbonate. After that the animals were returned to the cages with their mothers, where they remained until P21. Their physical and somatic growth and ontogenesis of reflexes were daily evaluated. A control group of animals were subjected to the same experimental conditions but the chamber was opened to atmospheric air rather than nitrogen stream.

Results: The results showed that animals submitted to anoxia showed, compared to the control, significant delay in the appearance of the opening of the ear canal (control: 14 ± 0.01; anoxia: 14.83 ± 0.40), in the outburst of the upper incisors (control: 9.75 ± 0.16; anoxia: 10.66 ± 0.42) and lower (control: 9.62 ± 0.26; anoxia: 10.66 ± 0.42) and in the maturation of ontogenetic reflex: like negative geotaxis (control: 9.75 ± 0.31; anoxia: 12 ± 0.96). In addition, the anoxic animals exhibited an advance in the onset of placing vibrissae (control: 10.87 ± 0.35; anoxia: 9.16 ± 0.70). Skull morphometric measurements of the body, body weight, eyes and pinna opening and decubitus recovery reflexes, aversion cliff, response to shock, acceleration and palmar pressure were also were evaluated, but not significantly different was observed. The delay in the negative geotaxis reflex during puerile phase indicates a non-functional integrity of motor and muscular system, these changes can be reflected in locomotor activity these animals as well as in their behavior.

Conclusion: Neonatal anoxia in rats exerts damaging effects on their morphofunctional characteristics, sensory-motor and reflex parameters. Regarding the maturation of physical characteristics, there was a delay on the unfolding of the pinna and opening of ear and eruption of lower and upper incisors in anoxic animals compared with control. The anoxic insult at P2 day causes delayed sensorimotor development of the rats which lasted until weaning.

Implications: The results point that the treatments or strategies to cure or minimize the effects of neonatal anoxia should be taken as early as possible in order to avoid physical and behavioral defects.

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Session Topic: Cancer

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Telomerase inhibition induces growth arrest in paediatric ependymoma

BACKGROUND: Ependymomas represent the third most common paediatric brain tumour, yet effective therapeutics are lacking and 5-year survival rates remain poor at approximately 50%. Previous studies have shown that over 50% of paediatric ependymomas possess active telomerase, an enzyme that permits a limitless growth potential through the prevention of telomere erosion and subsequent senescence. Since telomerase is present in the majority of ependymomas and absent in the majority of somatic cells, telomerase inhibition represents an ideal therapeutic strategy for telomerase-positive paediatric ependymomas. We hypothesize that inhibiting telomerase will induce growth arrest in paediatric ependymoma cell and animal models.

METHODS: Paediatric ependymoma cell lines (R254, BXD-1425EPN) and tumour initiating cells (TICs) (E520) were treated with the telomerase inhibitor Imetelstat in parallel with untreated and mismatch control until growth arrest was observed. Throughout treatment, a number of parameters were assessed including senescence (beta-galactosidase), apoptosis (TUNEL), telomerase activity (telomere repeat amplification protocol) and telomere length (telomere restriction fragment assay). To study telomerase inhibition *in vivo*, subcutaneous injections of 50,000 E520 cells were performed and mice were treated with either PBS, mismatch control or Imetelstat (3x/week) for 4 weeks (N=6 mice/group). Tumour growth was measured with calipers and tumours were weighed upon sacrifice.

RESULTS: Imetelstat treated R254 cells showed a reduced proliferative rate following 6 weeks of treatment and total growth arrest following 15 weeks of treatment. This observed growth arrest was associated with a marked inhibition of telomerase activity, shortened telomeres, an 80% increase in senescence and 20% increase in apoptosis. BXD-1425EPN cells treated with Imetelstat exhibited drastically reduced growth associated with telomerase inhibition and a 50% increase in senescence, while E520 TICs have thus far shown a reduced growth rate. *In vivo*, Imetelstat reduced tumour volume by 40% and tumour mass by 35% compared to PBS controls following 4 weeks of treatment.

CONCLUSIONS: These findings demonstrate that telomerase inhibition can effectively reduce paediatric ependymoma growth both *in vitro* and *in vivo*. Since children harboring telomerase-positive ependymomas exhibit a significantly worse prognosis than those lacking telomerase, telomerase inhibition may serve as a promising therapeutic approach for paediatric ependymoma.

Session Topic: Cancer

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Enhancement of human hematopoietic stem cell-derived T-lymphopoiesis by human progenitor T-cells generated *in vitro*

Hematopoietic stem cell transplantation (HSCT) is a cornerstone for the treatment of hematological malignancies. Although it can restore a functional immune system, profound immune deficiency still exists due to the impaired recovery of the T-cell compartment in both cell number and function. Underlying causes are a defective thymic microenvironment and impaired production of thymus-seeding progenitors in the host. Our group has previously demonstrated that human umbilical cord blood hematopoietic stem cells (HSCs; $CD34^{+}CD38^{-/lo}$) co-cultured on OP9-DL4 cells give rise to $CD34^{+}CD7^{++}$ human progenitor T-cells (proTs). These *in vitro*-generated proT cells have thymus colonizing potential in NOD/SCID/γc (NSG) mice, and can additionally enhance HSC-derived engraftment in the thymus *in vivo* when transferred together with HSCs. Furthermore, proT cells are able to induce phenotypic changes in the thymic microenvironment of hosts compared to non-injected littermate controls. These changes are supported by higher thymic transcript levels of *Ccl19*, *Ccl21*, and *Ccl25* in hosts injected with proT cells compared to controls. To better understand a mechanism underlying these observations, we now reveal that proT cells express the receptor activator of NF-κB ligand (RANKL), which likely plays a role in the maturation of the thymic microenvironment. We are currently examining the mechanistic importance of RANKL expression in proT-mediated effects in the thymus through use of protein-mediated inhibition and gene modification approaches. These findings will provide significant insights into human T-cell regenerative approaches, and support the use of *in vitro*-derived proT-cells for potential adoptive cell transfer in the clinical setting during periods of immunodeficiency following HSCT.

Session Topic: Cancer

Presenter: Charles W. Tran
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Cellular pathways modulating the activity of the E3 ubiquitin ligase Cbl-b in regulating T cell function

Casitas B lymphoma b (Cbl-b) is a master regulator of immune function in T cells, and represents a promising target for the immunotherapy of many diseases including cancer and chronic viral infection. Cbl-b was identified as an important regulator of T cell immunity. Cbl-b functions as an E3 ubiquitin ligase, and has been shown to have many target substrates including PLC-γ, TCR-ζ, and Vav. Cbl-b is important for the maintenance of peripheral tolerance and the loss of Cbl-b results in the development of systemic autoimmunity.
We have identified a putative regulatory axis for Cbl-b that involves the PI3K/Akt(PKB) pathway signaling through glycogen synthase kinase 3 (GSK-3). Using mass spectrometry and chemical inhibitors of GSK-3, we have found that the phosphorylation of Cbl-b is significantly reduced when GSK-3 activity is inhibited. Additionally, GSK-3 conditional knockout mice have reduced levels of Cbl-b in CD4+ and CD8+ Tcells. Our data suggest that GSK-3 regulates Cbl-b in T cells, and that these signaling events occur downstream of the PI3K/Akt signaling pathway.

Session Topic: Cancer

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Role of Notch Signaling in anto-Tumor-Associated Antigen T Cell Activation with Artificial Antigen Presenting Cells

Adoptive cell transfer of ex vivo-expanded tumor infiltrating lymphocytes (TILs) is currently an effective tool in the treatment of metastatic melanoma. While promising, it is not a widely applicable immunotherapy due to limitations in proliferative potential and access to TILs and endogenous antigen presenting cells (APCs) that are required for TIL expansion. Unlike patient-derived natural APCs, such as dendritic cells, “artificial” APCs (aAPCs) are a readily accessible and easily manipulated cell source that has been shown to support priming and activation of tumor-associated antigen (TAA)-specific $CD8^+$ cytotoxic T lymphocytes (CTLs). Here we addressed whether Notch signaling would influence the expansion and lead to enhanced cytotoxic function of TAA-specific CTLs obtained from human naïve peripheral blood $CD8^+$ CTLs. K562 erythroleukemia-derived cells (aAPCs) expressing costimulatory ligands and presenting a TAA peptide (Mart-1) were modified to express Delta-like-4 (DLL4), a member of the family of ligands for Notch receptors. We hypothesize that provision of Notch signaling during priming and early activation will generate an increased pool of Mart-1- specific CTLs with enhanced effector function. Our preliminary results using $DLL4^+$ aAPCs point to an important role for adopting Notch-driven CTL expansion strategies, and earlier polyclonal stimulations suggest the effect of DLL4 may manifest at the effector cell stage. Others have shown that provision of DLL4 to mouse $CD4^+$ T lymphocytes during priming generates lymphocytes with greater anti-tumor activity, thus induction of this phenomenon in lymphocytes capable of inducing direct lysis of tumor cells, such as CTLs, is an attractive therapeutic avenue. An important goal of our work is to address the current practical limitations in cancer immunotherapy and generate a translatable strategy to render all patients eligible for immunotherapy.

Session Topic: Chronic Diseases

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Can probiotics promote stress resilience?

Stressful life events may contribute to the evolution of mood and anxiety states. A growing body of evidence suggests that microorganisms inhabiting the gastrointestinal tract, referred to as gut microbiota, may interact with the evolution of stress-related disorders. We examined in mice whether administration of probiotic bacteria would modulate social disturbances normally elicited by a naturalistic stressor in the form of social defeat. Male C57BL/6 mice were defeated by a male CD-1 mouse (Defeat condition) or put in sensory contact with a male C57BL/6 mouse (No stressor condition) on each of 10 consecutive days. Non stressed and defeated mice were then administered a probiotic formulation (1 x 109 colony forming units/day) or a placebo on each of 21 consecutive days, after which their behaviors were assessed in a social interaction test. Probiotic treatment limited social avoidance behaviors towards a social target in mice that had experienced social defeat but did not affect social interactions among mice that had not been stressed. These results suggest that targeting gut microbiota with beneficial bacteria may promote resilience to the depressive-like effects of social stressors in male mice.

Session Topic: Chronic Diseases

Presenter: Magar Ghazarian
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Type I interferon responses drive intrahepatic CD8 T cells to promote metabolic syndrome

Insulin resistance (IR) precedes type II diabetes and is a key feature of obesity-related metabolic syndrome. Multiple factors contribute to obesity-induced IR, but low-grade chronic inflammation of metabolic tissues is central in its development. Immune mechanisms leading to IR in visceral adipose tissue (VAT) have been the focus of intensive research. However, the means by which immune cells impact the liver to control glucose homeostasis remains poorly understood. We assessed adaptive immune cells within livers of C57BL/6 mice fed a high fat diet (HFD) for 16 weeks by flow cytometry. Compared with normal chow diet (NCD)-fed controls, HFD-fed mice had increased hepatic CD8 T cells, which were primarily T effector memory (Tem) and pro-inflammatory IFNg+ and TNFa+ cells. HFD-fed CD8-/- mice were protected from hepatic IR, as indicated by improved pyruvate tolerance test and reduced expression of hepatic gluconeogenic enzymes. Consistently, transfer of hepatic CD8 T cells into HFD-fed CD8-/- mice worsened disease. Additionally, we found an aberrant increase in type I interferon (IFN) gene expression in livers of HFD-fed mice. Importantly, total CD8 T cell and CD8 Tem populations were reduced in the livers of IFNaR1-/- HFD-fed mice, and IFNaR1-/- HFD-fed mice were protected from IR. Consistently, treatment of WT HFD-fed mice with IFNaR1 blocking antibody reversed glucose intolerance. Mixed bone marrow chimeras generating CD8 T cell specific IFNaR1-/- mice were also protected from disease. Thus, we hypothesize that obesity induces a type I IFN response in the liver that drives hepatic CD8 T cells to promote local inflammation and whole-body glucose intolerance.

Session Topic: Chronic Diseases

Presenter: Edward Chen
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Shaping the Peripheral γδ T-Cell Repertoire and IL-17 Effector Subset through Temporal Induction of Notch Signaling in vivo.

γδ T-cells have emerged as important innate cells implicated in both protective and destructive immunity. The tissue and functional specificity associated with different Vγ-expressing T-cell subsets makes it important to gain better understanding of how the temporal development of these subsets is regulated. In mice, Vγ5+ and Vγ6+ cells are known to develop exclusively in utero. Still unknown is the contribution of in utero, neonatal, and adult periods to the generation of Vγ1+ and Vγ4+ cells, and whether there is restricted temporal development of IL-17 producing γδ T-cells (γδ T17). Through bone marrow reconstitution of adult mice, different groups show that γδ T17 cells either can or cannot be generated. Thus, it remains unresolved as to whether the generation of this effector subset is restricted to in utero life. To address these questions, we utilized a novel mouse model whereby Notch signaling can be temporally controlled. This allows us to restrict the induction of T-cell development during *in utero*, neonatal, and adult periods, determining the contribution of these developmental windows to the generation of $Vγ1^+$ and $Vγ4^+$ subsets, and γδT17 cells. Our results show that $Vγ1^+$ and $Vγ4^+$ cells can be generated in all three periods, but greater propensity to generate Vγ4 versus Vγ1 occurs earlier versus later in life, respectively. γδ T 17 cells were generated from all three periods, although at lower frequencies after birth and their tissue distribution was differentially regulated. Our ability to regulate the appearance of γδ T-cells will serve to address the unique temporal requirements for their differentiation.

Session Topic: Chronic Diseases

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Enforcement of γδ T-Cell Lineage Commitment by pre-TCR in Precursors With Weak γδ TCR Signals.

Developing thymocytes bifurcate from a bipotent precursor into αβ or γδ lineage T cells. Considering this common origin and the fact that the T cell receptor (TCR) β, γ and δ chains simultaneously rearrange at the double negative (DN) stage of development, the possibility exists that a given DN cell can express and transmit signals through both the pre-TCR and γδ-TCR. We have tested this scenario by defining the differentiation outcomes and criteria for lineage choice when both TCRβ and γδ-TCR are simultaneously expressed in Rag2-/- DN cells via retroviral transduction. Our results show that Rag2-/- DN cells expressing both TCRs developed along the γδ-lineage, up-regulated CD73 expression, showed a γδ-biased gene expression profile, and are competent producers of interferon (IFN)-γ in response to stimulation. However, in the absence of Id3 expression and/or strong γδ-TCR ligand, γδ-expressing cells showed a lower propensity to differentiate along the γδ -lineage. Importantly, differentiation along the γδ-lineage was restored by pre-TCR co-expression, which induced greater up-regulation of CD73, higher levels of γδ-biased genes, and recovery of functional competence to produce IFNγ. These results cement the signal strength hypothesis as they confirm a requirement for strong γδ TCR ligand engagement to promote maturation along the γδ T-cell lineage, while additional signals from the pre-TCR can serve to enforce a γδ-lineage choice in the case of weaker γδ-TCR signals.

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