5184 - The acceleration of melanoma in situ – Trends in melanoma incidence from 1995-2015 from Victoria, Australia/Victoria Harris, LLB, MD

Objective 1: Determine the trend in melanoma in situ incidence from 1995-2015

Objective 2: Explore patient characteristic (age, gender, site, etc) in melanoma in situ incidence

Objective 3: Compare the trend in incidence over time of melanoma in situ and invasive melanoma

ABSTRACT

Background Early detection of melanoma is a positive prognostic factor. Therefore, monitoring melanoma incidence has clinical significance [1]. National registries routinely report only the incidence of invasive melanoma (MMinv) with less attention to incidence of melanoma in situ (MMis) despite increases in both [2, 3]. Methods All melanoma records from 1995-2015 at the Victorian Cancer Registry, Australia were reviewed. Adjustments for multiple primary tumours followed international standard practice. Age standardised incidences and five-year age groups incidences were calculated. Trend analyses of incidences were performed by Poisson regression and Joinpoint analyses. Results A substantial acceleration in MMis incidence from 2012 is observed with annual percentage changes of 14.7% and 17.7% for men and women. The fastest annual increases from the 2012 joinpoint are seen in women aged 70-74 years (23.6%) and men aged 65-69 years (17.6%). In contrast, MMinv incidence growth remains steady with males demonstrating a 0.9% annual growth rate and females close to zero. Discussion MMis incidence is increasing at a much faster rate than MMinv incidence, particularly since 2012. This result could be masking increases in MMinv through earlier detection. Therefore, public reporting of both MMis and MMinv rates has significant public health implications.

5159 - Content Based Image Retrieval using Deep Learning as a Decision Support Tool for Dermoscopy/Jordan Yap, BSc

Objective 1: Create a system to perform query-by-example image retrieval to aid doctors in diagnosing skin lesion images

Objective 2: To evaluate the system’s performance on retrieving visually similar skin lesion images

Objective 3: None

ABSTRACT

Content based image retrieval (CBIR) is useful in medical applications to support physicians’ decision making on suspicious cases by displaying visually similar images. We have built a CBIR tool that when given a dermoscopy image as a query, finds similar images from a database containing thousands of previously validated images. This tool can also be useful for non-expert physicians, medical students and researchers. We use a deep neural network trained for segmenting skin lesions to extract image features for our CBIR system. We find that using the image features from the neural network to generate a candidate set of similar images gives superior performance over using standard image colour histograms and texture descriptors. Our CBIR system performance is further improved by refining the images in the candidate set using features calculated from only the predicted lesion region which excludes normal skin. Performance is evaluated qualitatively by an expert dermatologist to determine the relevance of the retrieved image’s size, colour, shape and texture to the query image. Quantitatively we evaluate our method on a dataset with 6036 benign or malignant skin-lesion images. In the top 15 most similar images retrieved, 80.1% are of the same class as the query image.
3:50 PM - 4:00 PM

5290 - Assessment of Sun-Protective Attitudes and Behaviours of parents and the impact on their children/Victoria Harris, LLB, MD

Objective 1: To determine whether parent’s knowledge and attitude to sun protection impacted their child’s UV exposure

Objective 2: Assess the sun burn risk and frequency of children

Objective 3: Assess the change in sun protection behaviour with age in children

ABSTRACT

Background: Prolonged UV exposure increases the risk of non-melanoma skin cancer (NMSC). Despite health campaigns to minimize UV exposure in Australia, NMSC increased by 86% between 1997 and 2010. Parent’s attitudes to sun protection may influence children’s exposure.

Objective: We sought to determine whether parent’s knowledge and attitude to sun protection impacted their child’s UV exposure.

Methods: A cross-sectional study was conducted of parent’s behaviours and attitudes toward sun protection. Surveys completed by parents attending dermatology clinics in Sydney and Gosford. Basic descriptive statistics applied with SPSS statistics software.

Results: Parents with a lower level education were strongly correlated with higher rates of experiencing serious sunburn (p<0.0001). There was strong evidence that the child is more likely to have been seriously burnt when the parent didn’t apply sunscreen to the child (p<0.01). There is evidence (p<0.05) of an association between parent burning in the past 12 months and whether their child had also been burnt in that time. There was strong evidence for a relationship between more sunburns and older age in children (p<0.001).

Conclusion: Older generations of Australians with high incidence of melanoma and NMSC may be transferring negative messages to younger generations in regards to UV exposure behaviours.

4:00 PM - 4:10 PM

5289 - Risk Factors Associated with a Recent Change in Mole(s) Size, Shape, or Color among American Academy of Dermatology SPOTme® Program Participants (2009-2010)/Derek Beaulieu, BS

Objective 1: Identify the factors associated with a recent change in mole(s) morphology among first-time AAD SPOTme® program screening participants (2009-2010)

Objective 2: Determine if indoor tanning behaviors were independently associated with a recent change in mole(s) morphology in this population

Objective 3: None

ABSTRACT

In one study of melanoma patients, changes in mole size (50%) and color (40%) were commonly reported at the initial medical visit, with a change in size found to be an independent predictor of increased Breslow depth.1 Using 2009-2010 American Academy of Dermatology SPOTme® program data, we performed multivariable logistic regression analysis to identify the factors associated with reporting a recent change in mole morphology among first-time screening participants. Unique to these two years, screening questions focused on recency of the exposure and recency of the outcome (changing mole). Records for 118,085 first-time participants were analyzed. Thirty-three percent of participants reported a recent change in mole(s) size, shape, or color. Regression analysis revealed positive associations with higher mole counts (50+ moles adjusted OR 1.78 [95% CI: 1.68-1.88]), uninsured status (aOR 1.56 [1.50-1.62]), non-Caucasian race (e.g. Black aOR 1.40 [1.30-1.51]), infrequent sunscreen use (e.g. Never use aOR 1.36 [1.28-1.44]), higher numbers of blistering sunburns before age 20 (10+ burns aOR 1.26 [1.21-1.32]), female sex (aOR 1.24 [1.20-1.27]), a personal history of melanoma (aOR 1.23 [1.11-1.37]), and chronic indoor tanning bed use (7-10 times aOR 1.30 [1.18-1.43]) but not the number of times indoor tanning in the past year.
**4:10 PM - 4:20 PM**

**5049 - A Survey Based Study of Management of Longitudinal Melanonychia Amongst Attending and Resident Dermatologists/ Shari Lipner, MD, PhD**

**Objective 1:** To assess management of longitudinal melanonychia amongst dermatologists.

**Objective 2:** To assess nail examinations amongst dermatologists.

**Objective 3:** To assess knowledge of the ABC mnemonic for subungual melanoma amongst dermatologists.

**ABSTRACT**

Subungual melanoma (SM) represents 0.7-3.5% of melanoma cases, but often carries a worse prognosis than similarly staged cutaneous melanomas. While longitudinal melanonychia (LM), is the most common presenting sign of SM, it is not specific for SM. A nationwide survey-based study was performed to assess nail examinations, management of LM, and knowledge of the ABC mnemonic for SM amongst dermatologists. Surprisingly, most dermatologists did not ask patients to remove nail polish during all physical examinations or examine the nails at each visit. In addition, many physicians were “not confident” in managing patients with LM and were not familiar with the ABC mnemonic. Our data reinforce the need for increased efforts in educating dermatologists, particularly residents, about nail examinations, LM, and warning signs for SM.

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**4:20 PM - 4:30 PM**

**5078 - TRPV4 CHANNEL MEDIATES DERMAL FIBROBLAST DIFFERENTIATION AND IS ASSOCIATED WITH SCLERODERMA/Rishov Goswami, MSc**

**Objective 1:** TRPV4 channel mediated fibrogenesis in SSc

**Objective 2:** Successful manipulation of the TRPV4 activity may be a targeted therapeutic approach to the SSc treatment

**Objective 3:** None

**ABSTRACT**

Scleroderma (SSc) is a multisystem idiopathic connective tissue disease with high morbidity and mortality. Exact cause for SSc is still remain unknown and there are no effective medical treatments available. Emerging data support a role for both a mechanical signal, e.g., matrix stiffness, and a chemical signal, e.g., transforming growth factor (TGF) beta1, in fibroblast activation, migration, and differentiation. Published work showed that TRPV4, an ion channel in the transient receptor potential vanilloid family, is activated by a range of mechanical and chemical stimuli. We obtained evidence that: 1) increased numbers of TRPV4 positive myofibroblasts are present in skin tissues of patients with SSc compared to controls, 2) Trpv4-/- mice prevented skin fibrosis development as assessed by dermal thickness, subcutaneous fat deposition, macrophage accumulation, myofibroblast abundance, and collagen deposition in skin in a bleomycin model of SSc, 3) genetic ablation or pharmacologic antagonism of TRPV4 abrogates both matrix stiffness and TGFbeta1-induced normal dermal fibroblast differentiation, and 4) TRPV4 modulates profibrotic TGFbeta1 actions in a Smad-independent but PI3K-AKT-dependent manner. Altogether, these results, for the first time, showed that TRPV4 channel mediates fibrogenesis in SSc. Successful manipulation of the TRPV4 activity may be a targeted therapeutic approach to the treatment of SSc.
4:30 PM - 4:40 PM

5046 - A novel approach to keloid and hypertrophic scar therapy: sustained release of proteases from PLGA microparticles/Jillian Tengood Hillman, PhD

Objective 1: To encapsulate collagenase, elastase and papain, into PLGA microparticles

Objective 2: To evaluate the efficacy of protease microspheres compared to protease solutions

Objective 3: None

ABSTRACT

Hypertrophic and keloid scarring is the result of aberrant healing and often associated with physical, psychological and social impairments, with treatment resulting in varying degrees of recurrence (50-70%).1–8 New research reveals limited efficacy of direct collagenase injections; however, the reduction was not sustained beyond 6 months.9 Because proteases have a short half-life and are self-digesting, protease solution activity is limited for scar treatment, which requires long-term intervention. Encapsulating these protease enzymes in poly(lactic-co-glycolic acid) (PLGA) microparticles can preserve their activity, creating a protease reservoir to allow for sustained delivery and prolonged activity.10,11 We have developed PLGA microparticles encapsulating collagenase, elastase and papain, individually, which can be combined for the treatment of keloids and hypertrophic scars. We hypothesized that sustained release of collagenase, elastase and papain, from PLGA microparticles would prolong the activity of these proteases when compared to a solution of the same proteases. Our studies revealed that collagenase, elastase and papain, can be encapsulated in PLGA microparticles and released over at least 30 days. Strikingly, sustained delivery of proteases ex vivo was achieved with up to a 26-fold increase in activity. These results demonstrate the potential of an intralesional injection for the treatment of keloids and hypertrophic scars.

4:40 PM - 4:50 PM

5091 - Live Mycobacterium leprae inhibits autophagy and apoptosis of infected macrophages and prevents engulfment of host cell by phagocytes/Degang Yang, MD

Objective 1: To investigate how live, but not dead, M. leprae promoted M2 macrophage skewing.

Objective 2: To investigate how whether there were strain differences between L-lep and T-lep patients.

Objective 3: None

ABSTRACT

Previous studies demonstrated that live Mycobacterium leprae (M. leprae) infection promoted macrophage differentiation toward the M2 type, with elevated interleukin (IL)-10 production. The underlying mechanism is not entirely clear. In this study, we treated macrophages with primary M. leprae strains isolated from both lepromatous leprosy (L-lep) and tuberculoid leprosy (T-lep) patients. We found that infection by live M. leprae, regardless of the primary strain, resulted in M2 skewing in the infected macrophage. This skewing was associated with downregulated IRGM expression, a core organizer protein in the autophagy assembly and reduced autophagosome formation, and with lower annexin V staining and lower caspase 3 and caspase 9 activity. Moreover, live M. leprae-infected macrophages prevented efficient phagocytosis by uninfected bystander macrophages. As a result, the phagocytes secreted less pro-inflammatory cytokines, and preferentially primed anti-inflammatory T cell responses. Together, these results suggested that live M. leprae could employ a strain-independent mechanism to suppress inflammation, possibly involving the inhibition of autophagy and apoptosis in the infected macrophages.
5310 - Role of IL-32 in the autophagy and antimicrobial activity during M. leprae infection/Gabriella Marvizi, BA

Objective 1: Identify the LC3 autophagy marker in the skin lesions of leprosy patients presenting with different clinical forms.

Objective 2: Determine whether autophagy and phagolysosomal fusion is dependent on vitamin D, and whether this pathway is IL-32 dependent.

Objective 3: None

ABSTRACT

Leprosy, a disease caused by the intracellular pathogen Mycobacterium leprae (mLepr), offers a model for investigating immune responses to infection as the disease represents a spectrum, where the clinical manifestations correlate with the immune response. By investigating leprosy, we discovered a pathway involving induction of IL-32, triggering the differentiation of monocytes into dendritic cells with antigen presenting function. Il-32 derived dendritic cells have the ability to cross-present antigen via MHC class I to CD8+ T cells for host defense against infection. This study determined if autophagy and phagolysosomal fusion occur in mLepr-infected macrophages, whether this is dependent on vitamin D, and whether this is IL-32 dependent. As demonstrated by immunohistochemistry, LC3 autophagy protein expression was greater in the tuberculoid form versus the lepromatous form of leprosy, indicating that more autophagy occurs in the tuberculoid form. Through imaging by confocal microscopy, we did not find a significant difference in the colocalization of M. leprae and autophagosome in macrophages between the vitamin D-sufficient serum (VDSS) and -insufficient serum (VDIS); thus, no conclusion can be drawn about the dependence of autophagy on vitamin D. However, IL-32 induces autophagy and phagolysosomal fusion in both the VDSS and VDIS. These results pose significant relevance to therapeutic intervention in infectious diseases such as leprosy.

5:00 PM - 5:10 PM

5114 - Biomechanics & Periorbital Aging: Impact of constant skin micro-movements on cellular responses/Nadine Pernodet, PhD

Objective 1: skin aging around the eye has been attributed to chronological, hormonal and lifestyles factors. for the first time, we will show the 4th factor of aging and involvement of biomechanics: understanding how constant micromovements such as blinking, acceler

Objective 2: Cellular biomechanics has become a growing research area and is seen as a strong contributor to determining many cellular functions (good or bad)

Objective 3: None

ABSTRACT

Periorbital skin is more vulnerable than the surrounding facial skin. Not only it is much thinner but it is also under constant movement due to daily facial expressions, including blinking, smiling, laughing and crying. As a result, the periorbital skin cells are under constant mechanical stress due to continuous stretching and contracting. The cells sense the strain (deformation) in the extracellular matrix (ECM) caused by mechanical stresses and translate this information into very specific cellular responses. Although the molecular signaling and regulatory mechanisms are not fully understood, this constant feedback and cellular response mechanism between external and internal forces have been demonstrated to have a strong impact on cellular behavior. In this study, we analyzed how skin cells from different aged donors respond to constant movement by mimicking the eye blinking rate (15 times/min) with a small skin stretch (~7%). Using confocal microscopy, we identified changes in skin cell orientation as a function of age. Inflammation and collagen levels were also affected by these micromovements, as well as energy production in the form of ATP. We show for the first time how aged-derived cells do not respond as well as young-derived cells to constant micro-movements although both types of cells accumulated damage due to this constant mechanical stress. These results provide new insight into the impact of biomechanics on the cellular responses of young and old skin cells, and the problem of why periorbital skin appears to age more rapidly than other areas of facial skin.
5:10 PM - 5:20 PM

5153 - Diet-sensitive PKCbeta signaling and development inflammation in skin microenvironment/Kamal Mehta, MD

Objective 1: Diet and dermal inflammation

Objective 2: Signal transduction and adipocyte inflammation

Objective 3: None

ABSTRACT

Obesity aggravates many skin diseases, including psoriasis, cellulitis, and fungal infection. Despite knowledge that dermal adipocytes are intimately associated with the skin microenvironment, diet- or obesity-induced signaling changes in adipocytes and their impact on cutaneous pathophysiology are not well understood. We previously reported that a systemic PKCbeta deficiency protects from high-fat diet-induced adipose hypertrophy at various anatomical locations (1-6). We now report that the PKCbeta deficiency is also associated with an improvement in the dermal adipocyte inflammation as well as texture and density of the skin hair. To understand the molecular basis of PKCbeta action, we determined the high-fat diet-PKCbeta interaction and the impact of PKCbeta deficiency on adipocyte signaling and metabolism. We found that dietary fat strongly induces expression of adipose PKCbeta and inflammatory markers in a time-dependent manner. The impact of diet-PKCbeta signaling on downstream adipocyte inflammatory mediators, mitochondrial dysfunction, and autophagy levels were also assessed. To dissect adipose-specific contribution of diet-adipocyte PKCbeta/inflammation axis on immune responses, wound healing and scarring, and hair-follicle growth, we have generated a floxed PKCbeta mouse model which will allow us to generate an adipocyte-specific PKCbeta deficiency. The results presented suggest that PKCbeta is a physiological transducer of dietary lipids and plays a critical role in modulating dermal inflammatory microenvironment.

5:20 PM - 5:30 PM

5306 - Efficacy of ROR gamma Inverse Agonists in Imiquimod induced Psoriasis Model with both Oral and Topical Administration/Kavitha Nellore, PhD

Objective 1: To develop novel ROR? inverse agonists for the treatment of Th17 mediated autoimmune disorders

Objective 2: To evaluate lead compounds in Imiquimod induced psoriasis model with oral and topical administration

Objective 3: To compare efficacy of ROR? inverse agonists with IL-17 antibody in psoriasis model

ABSTRACT

The nuclear hormone receptor ROR? controls the differentiation of Th17 cells that play a key pro-inflammatory role in a variety of autoimmune diseases including psoriasis. Aurigene has identified potent inhibitors of ROR? with >100 fold selectivity against ROR?/ROR? as well as other nuclear receptors. Lead compounds inhibit differentiation of primary mouse/human CD4+ve T cells to Th17 cells without affecting Th1, Th2, or Treg cell differentiation. Lead compounds have shown optimal physicochemical profile including good solubility and high free fraction, leading to excellent pharmacokinetic profile in mice and rats. Clean in-vitro safety profile has been demonstrated in hERG patch clamp assay, CERE88 safety panel and Ames test. Inhibition of IL-17 production has been observed in CytoStim™ stimulated psoriasis patient blood samples. In Imiquimod (IMQ) induced model of psoriasis in mice, oral administration of lead compound has shown efficacy comparable to murine anti IL-17 antibody administration. Upon topical application, lead compound has shown significant improvement in skin histopathology and reduction in IL-17 levels with 30-fold higher exposure in skin compared to plasma. In 28 days rodent toxicity study, compound was well tolerated at several fold of the efficacious exposure. Advanced safety studies are now in progress to enable IND filing.