POSTER #1

IDENTIFICATION AND CHARACTERIZATION OF PROTEINS INTERACTING WITH THE TUMOR SUPPRESSOR PROTEIN, p16. Akbari E[1], Allan L[2], Demetrick DJ[3]. [1]Department of Undergraduate Medical Education, Faculty of Medicine, University of Calgary. [2]Department of Medical Biochemistry, Faculty of Medicine, University of Calgary. [3]Departments of Pathology, Oncology and Medical Biochemistry, Faculty of Medicine, University of Calgary.

The p16 gene is located in chromosome 9p21, a region that is linked to familial melanoma. Molecular analyses of melanoma and squamous cell carcinoma (SCC) *in situ*, show that loss of p16 plays a critical role in carcinogenesis. In addition, p16 expression in primary malignant melanoma has been associated with prognosis and lymph node status. p16 is a member of cyclin dependent kinase inhibitors (INK4), a group of proteins that are involved in the G1/S transition of the cell cycle. The four members of the INK4 family (p15, p16, p18, and p19) are biochemically indistinguishable in their ability to bind CDK4/CDK6, and cause pRb dependent cell cycle arrest in G1. Interestingly, only p15 and p16 are known tumor suppressors that are often deregulated or inactivated in many cancers. We hypothesize that p16 has distinct and specific functions from those of p18 and p19, in addition to cell cycle arrest in G1. These functions are likely mediated through the interactions of p16 with its specific binding partners. A cDNA library was screened using a yeast two-hybrid system for detecting specific binding partners of full-length p16. Identified interactions are currently being confirmed in an *in vivo* expression system using co-immunoprecipitation technique. Over forty possible p16 binding partners were identified in our initial screen. Importin 4 and transcription factor AP-2γ were chosen for further investigation based on the biological likelihood of their interaction with p16. Such proteins may confer specific function to certain INK4 proteins and not to others. If true, this finding would help to explain how the deregulation of this particular INK4 protein, p16, leads to cancer development.

POSTER #2

EXPRESSION OF αVβ6 INTEGRIN IN SCARLESS AND SCAR FORMING WOUND HEALING. Eslami A[1], Gallant-Behm CL[2], Wiebe C[1], Hart DA[2], Hakkinen L[1], Larjava H[1]. [1]Faculty of Dentistry, University of British Columbia; [2]Faculty of Medicine, University of Calgary.

The critical event in scar formation is accumulation of collagen-rich extracellular matrix as a response to excessive activity of transforming growth factor-β1 (TGF-β1). However, very little is known about the mechanisms that activate the latent TGF-β during scar formation. Interestingly, lung fibrosis can be mediated by activation of TGF-β1 by αvβ6 integrin expressed by the lung epithelial cells. We hypothesized that αvβ6 integrin expressed by wound keratinocytes participates in TGF-β activation during wound healing. In the present study, we compared the expression and localization of αvβ6 integrin and TGF-β in scar-free oral mucosal and scar-forming skin wound healing. Standardized, full-thickness excisional wounds were created in the skin (heals by scar formation) and gingiva (heals with minimal scar formation) of red Duroc pigs. Frozen sections from wound biopsies collected from unwounded tissue and from 3-49 days after wounding were used for immunostaining of αvβ6 integrin, TGF-β1, TGF-β3, and latent TGF-β binding protein (LTBP; involved in αvβ6 integrin-mediated activation of TGF-β). Integrin

αvβ6 was not expressed by unwounded tissue. However, its expression was induced in both gingiva and skin three days after wounding and it co-localized with TGF-β1, TGF-β3 and LTPB in the wound keratinocytes. In skin wounds, expression of αvβ6 integrin was strongly down-regulated after 21 days. However, in gingival wounds, αvβ6 integrin was still expressed 49 days after wounding in parallel with strong expression of TGF-β3. Colocalization of αvβ6 integrin and TGF-β1, TGF-β3 and LTPB in wound keratinocytes suggests that αvβ6 integrin may interact with TGF-βs and participate in their activation during wound healing. Prolonged expression of αvβ6 integrin in scarless gingival wounds may provide a mechanism to prolong the increased level of anti-fibrogenic TGF-β3.

POSTER #3

MICE LACKING β6 INTEGRIN IN SKIN SHOW ACCELERATED WOUND REPAIR IN IMPAIRED WOUND HEALING MODEL. Yanshuang Xie, Lari Häkkinen and Hannu Larjava. Laboratory of Periodontal Biology, Department of Oral Biological and Medical Sciences, Faculty of Dentistry, University of British Columbia, Vancouver, BC, Canada.

Integrins are a family of cell adhesion molecules that mediate cell-cell and cell-extracellular matrix (ECM) interactions. Integrin αvβ6 is an epithelial-specific integrin that is not constitutively expressed by healthy epidermis but its expression is induced during wound healing. Studies have suggested that αvβ6 integrin promotes cell migration and proliferation, activates TGFβs and modulates protease activity *in vitro*. The role of αvβ6 integrin in wound healing is still, however, poorly defined. We have previously reported that αvβ6 integrin is highly expressed in poorly healing human wounds and its overexpression is associated with chronic wounds in a mouse model. The objective of this study was to investigate the *in vivo* role of αvβ6 integrin in an impaired wound healing model using β6 integrin-null (β6-/-) mice exposed to dexamethasone. Wound area measurement and hydrogen peroxide test showed an accelerated wound closure in treated β6-/- mice compared with wild-type (WT) controls. Granulation tissue formation, re-epithelialization and regeneration of basement membrane proceeded faster in treated β6-/- mice than WT controls. The differential recruitment of inflammatory cells and the expression of key wound healing cytokines in the wounds demonstrated differences in molecular healing between treated β6-/- and WT mice. These findings suggest that delayed wound repair that occurs in dexamethasone-immunosuppressed mice can be at least in part reversed by suppressing αvβ6 integrin expression in the epidermis and may provide a specific target for future therapeutic intervention in impaired wound healing.

POSTER #4

EXPRESSION OF SMALL LEUCINE-RICH PROTEOGLYCANS AND TRANSFORMING GROWTH FACTOR-β IN HUMAN ORAL MUCOSAL WOUND REGENERATION. Honardoust D, Eslami A, Larjava H, Hakkinen L., University of British Columbia, Faculty of Dentistry, Department of Oral Biological and Medical Sciences, Vancouver, BC, Canada.

The hallmark of scar formation is excessive accumulation of abnormally organized collagen in response to increased activity of transforming growth factor-β (TGF-β). Remarkably, wound healing in human oral mucosa rarely results to scar formation. Thus,

understanding the mechanisms involved in oral wound healing may provide important information about the biological processes that regulate scar formation. The small leucine-rich proteoglycans (SLRPs), decorin, biglycan, fibromodulin, and lumican, are extracellular matrix (ECM) molecules that interact with type I collagen and regulate collagen fibrillogenesis. SLRPs also bind to TGF-β inhibiting its biological activity. Our aim was to analyze the expression of SLRPs and TGF-β during human gingival wound regeneration. Expression of SLRPs, TGF-β1, TGF-β3 and collagen deposition and organization were analyzed in frozen sections from full-thickness, excisional human gingival wounds (collected 3-60 days after wounding) by immunohistochemical and histochemical techniques. Expression of the studied molecules were spatio-temporally regulated in distinct wound cells and ECM. Strongest upregulation for all of the molecules except lumican occurred from day 7 to 28 after wounding. After 60 days, expression of lumican remained still reduced while the expression of decorin, fibromodulin and TGF-β3 were still upregulated. Gradual increase in expression of SLRPs correlated with maturation of collagen in the wound ECM. Expression of fibromodulin, lumican and TGF-β1 and -3 were spatio-temporally upregulated also in the wound epithelium. Expression of SLRPs is spatio-temporally regulated in parallel with increased expression of TGF-β and collagen maturation at different stages of wound healing suggesting that SLRPs collaborate to regulate collagen organization and TGF-β activity in wound regeneration.

POSTER #5

ELASTOSIS PERFORANS SERPIGNOSA: TREATMENT WITH LIQUID NITROGEN CRYOTHERAPY. Roop Randhawa BSc[1], Shannon Humphrey MD[2], Chih-ho Hong MD FRCPC[2]. 1. Faculty of Medicine, University of British Columbia. 2. Department of Dermatology and Skin Science, University of British Columbia.

Background: Elastosis perforans serpiginosa (EPS) is an uncommon dermatosis affecting children and young adults, which presents with hyperkeratotic papules in an arcuate or serpiginous arrangement. Histologically EPS is characterized by transepidermal elimination of altered elastic fibers. Most reported treatment modalities have limited success in EPS. Reported ablative treatments include cryotherapy, cellophane tape stripping, electro-desiccation and curettage, cryotherapy, glycolic acid, salicylic acid, flashlamp pulsed-dye laser, Er:YAG laser, and carbon dioxide laser. Other methods include oral and topical retinoids, intralesional and topical steroids, and topical calcipotriene. **Objective:** EPS is generally regarded as difficult to treat, and many treatments have been reported with modest efficacy. We report a case with complete clearance using liquid nitrogen cryotherapy to treat EPS and we review the relevant literature. CASE: A 13-year-old boy presented with a 1-year history of facial lesions that were unresponsive to topical therapy with betamethasone valerate 0.1% cream. The clinical and histopathological findings were consistent with EPS. The patient was treated with liquid nitrogen spray 10 times over 15-month period. During that time, he developed new lesions, which were also treated. **Results:** The treatment was well-tolerated, and no complications were encountered. The treated areas showed marked improvement. There was less erythema and thickness, and the patient remains virtually clear without recurrence, or new lesions, with 4 months follow-up. **Conclusion:** We report complete resolution of EPS in a 13-year-old boy following successive treatments with cryotherapy. Liquid nitrogen cryotherapy may be an effective treatment method, and should be considered in the management of EPS.

POSTER #6

CLINICAL TRIALS AT THE UBC DEPARTMENT OF DERMATOLOGY AND SKIN SCIENCE: 2006 IN REVIEW. Rayone Christante, Sherry Phillips, Anna Daly, Jennifer Briggs, Anne Lee-Fraizer, Stuart Maddin. Clinical Trials Unit, UBC Department of Dermatology and Skin Science, The Skin Care Centre.

Building upon the expertise of the members of the Department of Dermatology and Skin Science at UBC, the Clinical Trials Unit at the Skin Care Centre has been investigating novel therapeutics for a wide range of dermatological conditions for nearly 40 years. A review of the activity of the Clinical Trials Unit over the past year was conducted. Extension studies and studies prematurely terminated by the study sponsor were not included in the analysis. From January to December 2006, over 149 subjects participated in 13 Phase II, III & IV trials. The indications included plaque and scalp psoriasis, atopic dermatitis, and venous leg ulcers. Therapeutics studied included topical agents and intramuscular and subcutaneous injection therapies. Treatment strategies for adults and children were studied. Recruitment targets were met or exceeded in more than half of the trials. A variety of pharmaceutical sponsors, faculty members and clinic staff have partnered with the Clinical Trials Unit to make each of these studies possible.

POSTER #7

PRIMARY HUMAN KERATINOCYTES EXTERNALIZE SEVEN 14-3-3 ISOFORMS VIA EXOSOMES. Claudia Chavez-Munoz M.D., Jennifer Morse, Runhangiz Kilani PhD, Aziz Ghahary PhD. Burn and Wound Healing Research Lab, Jack Bell Research Centre. Department of Surgery, UBC.

Different isoforms of 14-3-3 protein have been involved in a wide range of vital regulatory processes. Our group for the first time, showed that, 14-3-3 proteins are released to the extracellular environment and were found to be a potent Matrix Metallo Proteinases (MMP's) stimulators in fibroblasts. The mechanism by which 14-3-3 proteins are externalized is unknown. Here we hypothesized that the pathway of releasing these proteins are due to exosome-dependent secretion. To test this hypothesis, primary human keratinocytes and primary human fibroblasts were isolated from human foreskin. Exosomes were purified from Keratinocyte Condition Medium. Exosomal preparations and keratinocyte lysates were analyzed by several techniques, including Western Blot, Transmission Electron Microscopy (TEM) and immunogold labeling. In order to prove the mechanism, fibroblasts were treated with condition medium from keratinocytes before and after exosome purification. Biochemical analyses of the exosome preparation indicate that this fraction contains all seven mammalian 14-3-3 isoforms. Furthermore, TEM revealed small vesicles under 100nm in diameter with its distinctive saucer-like shape that are salient features of exosomes. The immunogold labeling confirmed that the purified vesicles were indeed exosomes. MMP-1 expression confirmed the release mechanism of 14-3-3 protein to the extracellular environment and also explains the expression when fibroblasts are co-cultured with keratinocytes. This study unravels the possible mechanism by which 14-3-3 proteins are released to the extracellular space.

POSTER #8

RESEARCH PROPOSAL: EFFECT OF INTERFERON GENES IN ALOPECIA AREATA. Wen-Yu Wu, Andreas M. Finner, Nina Otberg, Jerry Shapiro, Kevin McElwee. Department of Dermatology and Skin Science, University of British Columbia.

Background: Alopecia areata (AA) is a common skin disease characterized by a rapid onset of non-scarring hair loss in defined patches. The pathogenesis of AA is unclear, but it is thought to be mainly due to an autoimmune process. An increase in the expression of helper and cytotoxic T-cells and hair follicle reactive autoantibodies has been reported in AA patients. Interferons (IFNs) are important immune system mediators that could impact the initiation or amplification of autoimmunity and tissue damage through their diverse action on dendritic cells, T and B lymphocytes, NK cells and mononuclear phagocytes. **Objective:** To explore the potential contribution of IFN-α, INF-β and INF-γ gene expression in patients with AA. **Methods:** Extract RNA from the peripheral white blood cells in 16 patients with AA and 8 normal controls, then conduct cDNA synthesis. Quantitative real-time PCR analysis will be used to determine cDNA expression of IFN associated target genes, including IFN-γ, IFN-γ R1, IFN-γ R2; IFN-α , IFN-α R1, IFN-α R2; IFN-β1; MX1, IFIT1, IFI44 (IFN-α induced genes); IRF1, GBP, CXCL9 (IFN-γ induced genes); TLR7, TLR9, DDX58, and MDA5 (IFN-α inducing genes). **Proposal/Presupposition:** IFN-γ may be a critical factor in mechanisms of adaptive immune responses. IFN-α and IFN-β expression may reflect the potential involvement of the innate immune system and possibly disease mechanisms associated with bacterial or viral infections agents.

POSTER #9

RESEARCH PROPOSAL: ETHNIC VARIATIONS IN SCALP HAIR SIZE AND DENSITY. Nina Otberg, William Wu, Jianhuan Zhao, Harvey Lui, Jerry Shapiro.
Department of Dermatology and Skin Science, University of British Columbia.

Hair follicles have been shown to form conduits and reservoirs for topically applied substances and therefore play an important role in transcutaneous drug delivery. Previous studies have shown ethnic differences in vellus hair size and distribution. Little data on scalp hair follicles can be found in literature. These data vary and suggest great variations in different ethnic groups and different hair colors. The aim of this study is to provide the first data on the impact of hair color and ethnic background on hair density and hair follicular characteristics using macro photography in combination with a special software program, Trichoscan®, as well as near-infrared in-vivo confocal reflectance microscopy. The hair density will be measured in a dime sized spot in the occipital area with the Trichoscan® technique. The same are then will be measured with confocal microscopy. The diameter of the follicular orifice, hair shaft diameter and surface area, taken by the follicular orifice, will be calculated by an image analyzing computer program (analysis®). A ratio of diameter of the orifice and hair shaft diameter will be calculated. A total of 100 volunteers will be enrolled. The proposed study will help to establish normal values for hair density in different ethnic groups, which is a prerequisite for the assessment of hair loss conditions. Moreover it provides information on a potential follicular reservoir in scalp skin which is crucial for the development of topical drugs and scalp cosmetics.

POSTER #10

THE EFFECTS OF PHOTOPHERESIS ON DENDRITIC CELL FUNCTION IN PATIENTS WITH CHRONIC GRAFT VERSUS HOST DISEASE. Raewyn Broady, Jessie Yu, Megan Levings*. Immunity and Infection Research Centre, Vancouver Coastal Health Research Institute and Departments of Medicine and *Surgery, University of British Columbia.

Extracorporeal photopheresis (ECP) is a novel immunomodulatory therapy that has been used successfully for the treatment of chronic graft versus host disease (cGVHD) of the skin. Treatment of cGVHD patients with ECP results in a remarkable improvement in cutaneous manifestations with a reduction in erythematous and lichenoid skin changes. ECP induces apoptosis in mononuclear cells and when these cells are reinfused into the patient they produce a suppressor response that targets non-exposed T cells via a mechanism that is not yet understood. We hypothesise that phagocytosis of these apoptotic cells results in the development of T regulatory cells that actively suppress pathogenic T effector cells. Using an in vitro model, we investigated whether DCs that have phagocytosed ECP-treated cells develop a tolerogenic phenotype. Immature DCs were generated from monocytes and subsequently exposed to ECP treated cells, necrotic cells or induced to mature with CD40 ligand (L). After 24 hours of co-culture DCs exposed to ECP treated PBMCs expressed relatively low levels of co-stimulatory molecules. DCs exposed to ECP treated cells also had a reduced capacity to stimulate T cell proliferation in comparison to immature or CD40L matured DCs. Future experiments will investigate whether T cells primed with DCs previously exposed to ECP-treated cells develop a regulatory phenotype. We aim to develop the skin explant assay as a platform to study the T cells in skin samples from patients with cGVHD pre and post ECP as this model provides an in situ histopathologic readout for studying the interaction of T cells with skin tissue.

POSTER #11

CYTOKINES IN ALOPECIA AREATA: A STUDY OF KEY CYTOKINES IN THE C3H/HEJ ALOPECIA AREATA MOUSE MODEL. Armin Barekatain, Jerry Shapiro, Kevin McElwee. Department of Dermatology and Skin Science, University of British Columbia.

Alopecia areata (AA) is a chronic hair loss disease involving peri- and intra-follicular infiltration by mononuclear cells. Several studies suggest immunomodulatory cytokines expressed by the inflammatory infiltrate not only act as mediators of immunity and inflammation but also regulate cell proliferation and differentiation and, as such, may play an important part in regulating hair growth and AA development. We examined in vivo levels of mRNA of 13 cytokines and chemokines in the skin, draining lymph nodes, spleen, and thymus of C3H/HeJ mice with AA and normal haired littermates using quantitative RT-PCR techniques. The levels of IFN-γ and IL10 were statistically significantly higher in the skin and lymph nodes of AA-affected mice than in healthy controls while that of IL18 was lower. No statistically significant changes were found for the mRNA expression levels of IL17, IL21 and GM-CSF. Three main subfamilies of chemokines studied were CC chemokines, including RANTES, macrophage inflammatory proteins α and β (MIP-1 α and β), CXC chemokines, including CXCL1 and CXCL10, and CX3C chemokines represented by CX3CL1; all of which were found highly expressed in skin draining lymph nodes and/or the skin of mice with AA. Chemokines

are involved in chemoattraction and activation of leukocytes to the site of inflammation and in the induction of cytokine production and are thus key determinants of inflammatory reactions and immunity. The fact that all the studied chemokines were expressed at significantly higher levels in AA-affected mice than in controls suggests they may play an important role in AA pathogenesis.

POSTER #12

NUCLEAR FACTOR-KAPPAB SUBUNIT p50 PROMOTES ANGIOGENESIS THROUGH REGULATING IL-6 EXPRESSION IN MELANOMA. Kai Gao[1], Colleen C. Nelson [2] and Gang Li[1]. [1]Department of Dermatology and Skin Science, [2]Prostate Centre, Vancouver Coastal Health Research Institute, University of British Columbia, Vancouver, BC, Canada.

Angiogenesis is one of critical steps during melanoma development. However, its molecular mechanism is not clear. Using cDNA microarray technology, we found expression of IL-6, a pro-angiogenic factor in other types of cancer, is significantly increased in melanoma cells stably overexpressing NF-kB subunit p50 (designated as "p50 stable clone") comparing with the vector. Real time RT-PCR confirmed that expression of IL-6 is 99±3.1 folds higher in p50 stable clone than in vector. Therefore, we hypothesized that NF-kB subunit p50 may promote angiogenesis in melanoma through upregulating IL-6 expression. Indeed, conditioned medium from melanoma cells transfected with p50 increased HUVEC proliferation. Taken together, our data suggest that NF-κB p50 may play an important role in melanoma angiogenesis and blocking NF-κB activity may be used as a potential therapeutic regime for human melanoma.

POSTER #13

PROGNOSTIC SIGNIFICANCE OF ING3 SUBCELLULAR LOCALIZATION IN HUMAN CUTANEOUS MELANOMA AND ITS ROLE IN MELANOMA CELL GROWTH. Yemin Wang[1], Derek L. Dai[1], Magdalena Martinka[2] and Gang Li[1]. [1]Department of Dermatology and Skin Science, [2]Department of Pathology, Vancouver Coastal Health Research Institute, University of British Columbia, Vancouver, BC, Canada.

The novel tumor suppressor ING3 has been shown to modulate transcription, cell cycle control and apoptosis. Our previous study demonstrated that ING3 promotes UV-induced apoptosis via the Fas/caspase-8 dependent pathway in melanoma cells. To investigate the putative role of ING3 in melanoma development, we examined ING3 expression with tissue microarray and immunohistochemistry in 57 dysplastic nevi, 114 primary melanomas, and 50 metastatic melanomas. Our results showed that nuclear ING3 expression was remarkably reduced with the progression from dysplastic nevi to primary and metastatic melanomas (P<0.05), apparently correlated with the shift of ING3 from nuclear to cytoplasm (P<0.001). This translocation was associated with the decreased disease-specific 5-year survival of patients with primary melanoma (P=0.0028). The multivariate Cox regression analysis revealed that nuclear-to-cytoplasm shift of ING3 is an independent prognostic factor in primary melanomas (relative risk, 4.29; P=0.032). The role of ING3 in cell cycle progression and cell growth of melanoma cells were also investigated. In MMRU cells, the highest level of nuclear ING3 is in G_1-phase, which declined in S-phase and was barely detectable in G_2/M phase. Overexpression of ING3 inhibited the colony formation efficiency in four melanoma cell lines. The stable overexpression of ING3 inhibited MMRU cell growth rate and arrested

cells at G_1-phase. The expression of p21 was significantly increased in ING3-overexpressing cells. Taken together, our data indicate that ING3 may be an important marker for human melanoma progression and prognosis as well as a potentially selective therapeutic target.

POSTER #14

THE INFLAMMATORY RESPONSE TO BASAL CELL CARCINOMAS. Blanche K.K. Lo, Mei Yu, Bryce Cowan, David Zloty**,** Larry Warshawski**,** Jerry Shapiro, and Kevin J. McElwee. Department of Dermatology and Skin Science, University of British Columbia, Canada.

Basal cell carcinoma (BCC) is the most common cutaneous skin malignancy amongst the Caucasian population. Although BCCs rarely metastasize and cause death, they can behave aggressively with deep invasive properties resulting in significant morbidity for the patient. While the fundamental mechanism of BCC growth initiation requires genetic mutation in one or more genes of the sonic hedgehog pathway, knowledge of the molecular basis of BCC development is incomplete. Using microarray analysis, we previously identified differentially expressed gene patterns associated with BCC growth, with known function from other biological contexts (e.g. host immune response, proinflammation). In this study, in order to further elucidate the complex alterations in BCC-associated gene expression, we defined a panel of 35 immune function-associated genes and applied the technique of real-time RT-PCR to determine differential gene expression in three major BCC subtypes: 1) nodular 2) superficial and 3) morpheiform, as compared with normal skin epithelium. Based on the data analysis, chemokines of the C-X-C subfamily, particularly CXCL9, CXCL10, and CXCL11 were upregulated significantly in BCCs as compared to normal skin epithelium (27.35 fold, 11.20 fold and 32.28 fold respectively), while expression of cytokines such as IL6, IL7, and IL12α were significantly reduced in the tumors (65.49 fold, 3.39 fold, and 3.89 fold respectively). The differential gene expression in BCCs as compared to normal skin may provide some insights into the role of the intrinsic factors and inflammation in the etiopathogenesis of BCCs. The identified genes may be active participants in an inflammatory response against BCCs.

POSTER #15

A PILOT STUDY OF DIFFERENTIATING MALIGNANT MELANOMA FROM SEBORRHEIC KERATOSES USING LASER SPECKLE IMAGING. T.K. Lee, L. Tchvialeva, D.I. McLean, H. Lui, H. Zeng. BC Cancer Research Centre and Dermatology and Skin Science, University of British Columbia, Vancouver, Canada.

Background: The incidence of malignant melanoma has been increasing steadily for the last four decades. It is desirable to develop automated diagnostic devices to facilitate early detection of the disease. Such devices should ideally be able to differentiate melanoma from all skin conditions including seborrheic keratosis, which is a common benign skin lesion that may resemble a melanoma according to the well known clinical ABCD rule. Skin surface roughness is the key diagnostic feature for differentiating melanoma from seborrheic keratoses. **Objective**: To investigate whether a new laser speckle imaging technique that measures *in vivo* skin surface roughness based on the contrast of a laser speckle image can be used to differentiate between melanoma and seborrheic keratoses or melanocytic nevi. **Materials**: A laser speckle imaging prototype

was constructed using a fiber-coupled diode laser (λ=670nm, Lc=0.154 mm) and was used to measure the surface roughness of four seborrheic keratoses, seven nevi, two melanomas, and nine normal skin surfaces. **Results**: The mean root-mean-square roughness for seborrheic keratoses (46μm) was slightly higher, but not statistically significant, than nevi (39μm); similarly, the mean roughness for melanoma (23μm) and normal skin (19μm) were similar. However, the mean root-mean-square roughness for seborrheic keratoses was significantly larger than melanoma (t-test; p=0.049). **Conclusion**: Our laser speckle imaging prototype showed potential in differentiating seborrheic keratosis from melanoma. Integrating the prototype with a reflectance colour imaging device, which analyzes melanomas, nevi and normal skin based on clinical ABCD rule, may result a useful diagnostic tool for evaluating suspicious pigmented skin lesions.

POSTER #16

TUMOR SUPPRESSOR ING1B COOPERATES WITH p53 AS CHROMATIN ACCESSIBILITY FACTORS FOR NUCLEOTIDE EXCISION REPAIR IN DNA DAMAGE. Ronald P.C. Wong and Gang Li. Department of Dermatology and Skin Science, The University of British Columbia, Vancouver, BC, Canada.

DNA damaging agents such as ultraviolet radiation which generates bulky DNA adducts. Failure to repair DNA damage produces mutation which is important in carcinogenesis. The highly compact chromatin structure is an obstacle for DNA repair. We have shown that tumor suppressor ING1b enhanced nucleotide excision repair (NER). To further elucidate the mechanism by which ING1b regulates NER, we investigated the accessibility of different factors to chromatin after ING1b overexpression. We found that ING1b increased triton-insoluble proliferating cell nuclear antigen (PCNA) in MMRU cells which represents the chromatin bound form of the protein. PCNA is an essential factor in NER and has previously been shown to interact with ING1b. UV irradiation increased triton-insoluble PCNA. ING1b knockdown by siRNA decreased triton-insoluble PCNA which was restored by histone deacetylase inhibitor treatment. This suggests that ING1b is essential for PCNA recruitment to chromatin after UV irradiation through chromatin relaxation as histone hyperacetylation and chromatin relaxation induced by histone deacetylatase inhibitor treatment bypassed the requirement of ING1b for PCNA to access chromatin after UV irradiation. Furthermore, p300 overexpression increased PCNA binding to chromatin which was abrogated by ING1b siRNA treatment, implicating that ING1b may cooperate with p300 as chromatin accessibility factor for NER. These data suggest that ING1b may enhance nucleotide excision repair through enhancing chromatin accessibility of PCNA to chromatin by chromatin remodeling. This sheds light on the role of tumor suppressor ING1b in nucleotide excision repair which is an essential mechanism to protect cells from genotoxic events.

POSTER #17

WHY SKIN DOESN'T LEAK: 2007. Neil Kitson[1] and Jenifer Thewalt[2]. [1]Department. of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada, [2]Departmentsartments. of Molecular Biology & Biochemistry and Physics, Simon Fraser University, Burnaby, BC, Canada .

We summarize our view of the formation and nature of the intercellular component of the stratum corneum permeability barrier. First, solid (crystalline) lipid domains are essential

to stratum corneum barrier function. Second, such domains must form through lipid crystallization and phase separation at physiological temperatures. We cannot conceive how such crystallization could occur within a biological membrane capable of normal functions such as fusion and exocytosis. Third, although crystallization could perhaps begin within the membrane contents, but not the outer membrane, of the lamellar body (lamellar granule), larger domains could logically only occur following extrusion from the keratinocyte, and therefore within the intercellular spaces of cell layers entering the SC compartment. The rate and extent of lipid crystallization during epidermal differentiation must be determined by local physical conditions of course, but we presume the crystallization will begin to occur at some reasonably predictable point in epidermal differentiation, when lipid modifications result in inevitable phase separation. We presume also that the entire crystallization process, and resultant barrier formation, would be altered by ambient physical and pathological conditions, inflammation being an obvious example. Epidermal differentiation is accelerated in inflammatory conditions such as psoriasis, and one might expect that the extent of lipid crystallization would be reduced as a result. The physiological consequence of reduced SC lipid crystallization might be impaired barrier function.