**Abstracts**

**LB1475**

The immune-phenotype of small plaque psoriasis

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Small plaque psoriasis (SPP) presents as a unique morphology that resemble guttate psoriasis but lesions are larger, are chronic, and are not associated with streptococcal infection. We have observed SPP develop in four different population groups: patients under TNFa-inhibitor therapy, patients with concurrent SLE or ANA positivity and psoriasis. The pathogenesis of TNFa-induced lesions is dominated by the type-1 interferon (IFN) pathway, increased expression of LL37 and IL6 by keratinocytes, activated plasmacytoid dendritic cells and release of type-1 IFN. These lessons express fewer epidermal CD8 T cells. We hypothesize that SPP develops as a result of increased expression of cytokines and antimicrobial peptides involved in the type-1 IFN pathway. Skin biopsies were obtained from patients with TNFa-induced psoriasis, SLE and psoriasis, positive ANA and psoriasis, IC1-induced psoriasis (n=12) and chronic plaque psoriasis as control (n=3). Immunohistochemistry was performed using antibodies against MXA, LL37, IL6 and CD8 T cells. Immunohistochemical evaluation revealed an increased expression of MXA (p<0.05), LL37 (p<0.05), IL6(p<0.05) in the keratinocytes of all clinical scenarios of SPP. There was a decreased CD8 T cell migration to the epidermis in SPP. This is the first study to describe the immune phenotype of SPP to extend the phenotype observed in TNFa-induced psoriasis to varying clinical scenarios. There was an increased expression of cytokines in the type-1 IFN pathway as well as fewer epidermal CD8 T cell migration in SPP than in chronic plaque psoriasis. This immune-phenotypic analysis may suggest tailored therapy for this form of psoriasis.

**LB1477**

IQGAP3 could be a promising target link for breaking the vicious circle of psoriasis

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The IQGAP family is a group of scaffold proteins coordinating signaling by facilitating the physical interactions between the effector proteins and localizing them to specific areas of a cell. They seem to be promising therapeutic targets capable for altering of various signaling cascades without direct influence on the key regulators of the pathways. IQGAP proteins are involved in the regulation of the cell cycle, MAPK cascades, EGF cascades, cadherin signaling and other pathways important for psoriasis. IQGAP1 is present in all layers of the epidermis, whereas IQGAP3 accumulates in proliferating basal keratinocytes. We have carried out the analysis of the RNA-seq data from the GEO database (GSE67785, GSE66511, GSE44745, 40 skin biopsies) and found IQGAP3 expression was significantly upregulated in the psoriatic lesions and in the lesional skin of patients with psoriasis. Our qPCR analysis of the HaCaT keratinocytes stimulated with proinflammatory cytokines as well as mitogens. The results obtained suggest that IQGAP3 could be a promising target link for breaking the vicious circle of psoriasis. We will perform the further experimental verification of this hypothesis. The research is supported by funding AAAA-A16-1161110175-9.

**LB1478**

MC1R variants and cutaneous melanoma risk in the Southern Brazil population

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Background: Melanocortin 1 receptor (MC1R) gene variants have been associated to fair skin and may independently cause an increase risk for the development of cutaneous melanoma. Objectives: To analyze the coding region of the MC1R gene in patients with cutaneous melanoma and controls from Southern Brazil and the relationship of gene variants with melanoma risk factors. Methods: We evaluated 72 patients with melanoma and 66 controls. Genotyping of the MC1R coding region was performed by sequencing in all individuals. Results: Of the 138 patients studied, 63 (45.65%) carried at least one MC1R variant. Variants were more common in the melanoma group, with 45 cases carrying at least one variant (62.5%), while only 18 controls (27.27%). Presence of MC1R variant conferred an increase of melanoma risk, OR 5.05 (95% CI: 1.68 - 15.21, P=0.004) for carriers of at least one MC1R variant and 11.55 (95% CI: 1.74 - 76.62, P=0.011) in individuals with one or two or more MC1R sequence variants, respectively. The risk of melanoma was not modified significantly by skin phenotype and hair color. Conclusions: Being a carrier of one MC1R variant is associated with an increased melanoma risk, if the individual has two or more, the risk is even higher. This predisposition is independent of phenotypic characteristics.

**LB1479**

Identifying intratumor heterogeneity in mycosis fungoides using high throughput DNA sequencing

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Mycosis fungoides (MF) is a common extranodal T-cell lymphoma primarily arising in the skin. In early disease stages, MF presents as skin patches and plaques that in some cases may progress to tumour and disseminate to lymph nodes and other internal organs. Early diagnosis is difficult as the histology overlaps with features of inflammatory skin diseases. Even when the diagnosis is established there are no prognostic markers that predict whether the disease will be aggressive or indolent. Lastly, there are no curative treatments and MF will invariably relapse even after aggressive chemotherapy. The disease is a diagnostic, prognostic and therapeutic challenge. The main objective of this study is to address the question of tumour heterogeneity in MF. To date, MF is considered to be monoclonal, derived from a transformed, mature memory T-cell. However, clinical observations and preliminary data suggest that MF comprises multiple subclones, which may be of importance for understanding tumour evolution and resistance to therapy. We plan to address this objective using Whole Exome Sequencing (WES) of MF tissue prepared by laser microdissection (LMD). Patients with MF usually present with multiple lesions and it is not clear whether these lesions develop by evolution from plaques or rather emerge from lymphoma precursor cells. Comparison of plaques and tumors based on genetic abnormalities (somatic mutations and copy number variations) revealed that except a single parental clone, tumors and plaques have an independent genetic origin. This result provides us the first evidence intratumor heterogeneity at genomic level in MF.

**LB1480**

Systemic platelet-activating factor receptor agonist augments non-melanoma skin cancer growth

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Platelet-activating factor receptor (PAF-R) agonists are pleiotropic phospholipid mediators that influence multiple biological processes including the induction and resolution of inflammation, tissue repair, and tumor growth. PAF-R agonists have been shown to modulate tumorigenesis and tumor growth in various cancer models by suppressing either cutaneous inflammation and/or anti-tumoral adaptive immunity. Notably, we have shown that systemic administration of a PAF-R agonist augments the growth of subcutaneously engrafted human cutaneous melanoma tumors in a PAF-R-dependent manner. However, its topical applications suppressed tumor incidence/multiplicity and growth of non-melanoma skin cancer (NMSC) induced by the topical applications of two-stage chemical carcinogenesis (DMBA/PMA). The present study was aimed to determine the systemic effects of a PAF-R agonist on a recently characterized model of 25 weeks of topical DMBA/PMA induced melanocytic nevus formation and their progression into malignant melanoma as well as on NMSC. Our studies demonstrate that systemic administration of a PAF-R agonist for 30 weeks improved survival and delayed tumor growth. The acute application of a PAF-R agonist led to a diminished skin thickness and growth of NMSC compared to DMBA/PMA alone-treated group. These effects were mediated via mechanism in-part associated with increased chronic inflammation and decreased numbers of intra-tumoral CD1+ T cells. These findings highlight the importance of systemic PAF-R agonist in modulating cutaneous carcinogenesis in response to diverse stimuli.

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**Note:** The above abstracts are a selection from the Journal of Investigative Dermatology (2018), Volume 138. Each abstract is a summary of a research article focusing on various dermatological conditions, their mechanisms, and potential therapeutic approaches.