**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 different population groups, patients under TNFα-inhibitor therapy, immune checkpoint inhibitor (ICIII) therapy, and patients with concurrent SLE or ANA positivity and psoriasis. The pathogenesis of TNFα-induced lesions are dominated by the type-1 interferon (IFN) pathway. Increased expression of LL37 and IL36 by keratinocytes, activated plasmacytid dendritic cells and release of type-1 IFN. These lesions 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 TNFα-inhibited psoriasis, SLE and psoriasis, positive ANA and psoriasis, IC-1 induced psoriasis (n=12) and chronic plaque psoriasis as control (n=3). Immunohistochemistry was performed using antibodies against MxA, LL37, IL36 and CD8 T cells. Immunohistochemical evaluation revealed an increased expression of MxA (p<0.05), LL37 (p<0.05), IL36(p<0.05) in the keratinocytes of all clinical scenarios of SPP. There was decreased CD8 T cell migration to the epidermis in SPP. This is the first study to describe the immune phenotype of SPP. We extend the phenotype observed in TNFα-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.

**LB1476**

Long-lived cells surviving myelosuppressive treatment provide proof for T cell tissue-residency in human skin

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Due to lack of appropriate model systems, little is known about human T cell longevity and resistance to radiation. Myelosuppressive conditioning and subsequent allogeneic hematopoietic stem cell transplantation (HSCT) represent unique situations in the human body to study residency of skin T cells. Therefore, we profiled immune cell abundance and recovery dynamics in 45 patients in the process of HSCT. Skin biopsies and peripheral blood were taken at up to 5 time points before and after HSCT and analyzed for immune cell subtypes using flow cytometry, tissue immunohistochemistry and low-input RNA sequencing. Upon myelosuppressive treatment (chemotherapy and total body irradiation), recirculating immune cells declined in skin and peripheral blood, while a subset of dermal CD8 T cells expressing residency markers and lacking expression of genes associated with tissue egress remained stable throughout all time points analyzed. This skin-resident subset displayed high proliferative potential after TCR stimulation and was enriched in patients who later developed acute graft-versus-host disease of the skin. Furthermore, chimerism analysis after transplantation revealed that, unlike in peripheral blood, skin-resident T cells of the recipient constituted a third of dermal T cells at time of full immunological recovery (14 weeks post-transplant) and coexisted with donor T cells years after engraftment. We have thus identified a long-lived and remarkably resistant population of dermal T cells in the skin of HSCT recipients, which is likely insufficiently targeted by current therapies for chronic inflammatory skin conditions.

**LB1477**

IQGAP1 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, GPCR cascades, F-actin 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 (GSE41745, 40 psoriatic biopsy pairs) and have identified only the IQGAP3 of the IQGAP family to be overexpressed significantly. As we suggested psoriatic keratinocytes to be the source of SPP, our further experimental verification of this hypothesis. The research is supported by funding AAAA-A16-11611161075-9.

**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. The estimated OR for melanoma was 5.05 (95% CI: 1.68 - 15.21, P = 0.004) and 11.55 (95% CI: 1.74 - 76.62, P = 0.011) in individuals in one with one or two or more MC1R sequence variants, respectively. The risk of melanoma was not modified significantly by skin phototype and hair color. Conclusions: Bearing a carrier of one MC1R variant is associated with an increase melanoma risk, if the individual has two or more, the risk is even higher. This predispension 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 dissease to lymph nodes and other internal organs. Early diagnosis is difficult as the histology overlapps 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 tumor 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 tumor evolution and resistance to therapy. We plan to address this objective using Whole Exome Sequencing (WES) of MF tissue prepared by laser microdissection. Patients with MF usually 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 subclonal population. This result provides us the first evidence intratumor heterogeneity at genotypic 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 as well as immunosuppression. Importantly, 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 implanted 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 protocols. We have demonstrated that PAF-R agonists induce cutaneous inflammation and cutaneous carcinogenesis. The current pilot studies were sought to determine the systemic effects of a PAF-R agonist on implanted murine melanoma tumors in a PAF-R-dependent manner. However, its topical applications suppressed tumor incidence/multiplicity and growth of non-melanoma skin cancer (NMSC) compared to 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 significantly augmented cutaneous melanoma as well as NMSC. These effects were mediated via mechanism in part associated with increased chronic inflammation and decreased numbers of intra-tumoral CD3+ T-cells. These findings highlight the importance of systemic PAF-R agonist in modulating cutaneous carcinogenesis in response to diverse stimuli.