LB1475
The immune-phenotype of small plaque psoriasis

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Small plaque psoriasis (SPP) presents as a unique morphology that resembles 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 TNF-α inhibitor (TNI) therapy, immune checkpoint inhibitor (ICI) therapy, and patients with concurrent SLE or ANA positivity and psoriasis. The pathogenesis of TNF-induced lesions is dominated by the type-1 interferon (IFN) pathway; increased expression of LL37 and IL36 by keratinocytes, activated plasmacytoid dendritic cells and release of type-1 IFN. These lessons expose 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 SPP-induced psoriasis, SLE and psoriasis, positive ANA and psoriasis, ICI-induced psoriasis (n=12) and chronic plaque psoriasis as control (n=3).

Immunohistochemistry was performed using antibodies against MxA, IL17, IL36 and CD8 T cells. Immunohistochemical evaluation revealed an increased expression of MxA (p<0.05), IL36(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 and to extend the phenotype observed in TNF-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 myeloablative treatment provide proof for T cell tissue-residency in human skin

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 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, EGFR cascades, farnesylating 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, GSE66531, GSE41745, GSE66530, GSE41746) of human epidermis, skin and peripheral blood, while a subset of dermal tissue biopsy pairs (n=39) and have identified only the IQGAP3 of the IQGAP family to be overexpressed significantly. As we suggested psoriatic keratinocytes to be the main source of IQGAP3 in skin, next we have analyzed the expression data from keratinocyte cell line and skin samples of healthy volunteers and patients with psoriasis. IQGAP3 expression was elevated in patients, inhibited by Ca2+-induced differentiation and wasn’t significantly altered by cytokine stimulation. We have confirmed the obtained results in vitro by the qPCR analysis of the HaCaT keratinocytes stimulated with proinflammatory cytokines as well as mitogens. The results obtained suggest that IQGAP3 could play an important role in the hyperproliferation of keratinocytes in psoriasis.

We will perform the further experimental verification of this hypothesis. The research is supported by funding AAAA-A16-11611611075-9

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 patientswith 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: 1.6 - 15.21, P=0.004) and 11.55 (95% CI: 1.74 - 76.62, P<0.001) in individuals in one with and 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 increase 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 throughout 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 disperse to lymph nodes and other internal organs. Early diagnosis is difficult as the histology overhangs 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 the disease 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 have cutaneous tumours and it is not clear whether advanced cutaneous MF develops 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 profile. 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 inflammatory responses as well as immunosuppression. Importantly, PAF-R agonists have been shown to modulate tumorigenesis and/or 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 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) model, in part via exhibiting anti-inflammatory effects. These findings indicate the diverse effects of systemic versus topical PAF-R agonist in modulating cutaneous inflammation and carcino-gensis. The current pilot studies were sought 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 significantly augmented C57BL/6 mouse tumor incidence/multiplicity 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 CD3+ T cells. These findings highlight the importance of systemic PAF-R agonist in modulating cutaneous carcinogenesis in response to diverse stimuli.