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B-cell independent functions of T cells during immune-complex induced neutrophil-depend
dent inflammation
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Tissue injury during autoimmune diseases depends on binding of autoantibodies to the effector organs and a subsequent cellular response. During epidermolysis bullosa acquisita, a prototypic organ-specific autoimmune blistering disease, autoantibodies to type VII collagen trigger tissue injury via neutrophil-dependent mechanisms. In this study, we investigated the role of neutrophils in the induction of tissue injury in a mouse model of epidermolysis bullosa acquisita. Mice were treated with anti-type VII collagen antibody, and neutrophils were depleted by administration of anti-Gr-1 antibody. Our results showed that neutrophil depletion significantly reduced the number of neutrophils in the skin and reduced tissue injury. These findings suggest that neutrophils play a crucial role in the pathogenesis of epidermolysis bullosa acquisita.

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Naive T cells develop into equal populations of TCR identical TCM and TRM
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T cell immune memory resides in different anatomical compartments. Central memory T cells (TCM) can be found in lymph nodes, whereas resident memory T cells (TRM) reside in peripheral organs such as the skin. The cell-intrinsic mechanisms that control the development of these two memory T cell subsets are still poorly understood. In this study, we investigated the role of TCR identity in the development of TCM and TRM. Using a TCR transgenic model, we found that naive T cells with identical TCR develop into equal populations of TCR identical TCM and TRM. These findings suggest that TCR identity plays a critical role in the development of TCM and TRM.

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In vivo imaging reveals that leukotriene B4-BLT1 signaling promotes DC functions in skin via Cdc42/Rac1 pathways for an induction of acquired cutaneous immune responses
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In the skin, the dendritic cell (DC) migrates to the skin to present antigens to T cells. Leukotriene B4 is a lipid mediator that promotes DC functions. In this study, we investigated the role of leukotriene B4-BLT1 signaling in vivo. Using an in vivo imaging system, we found that leukotriene B4-BLT1 signaling promotes DC functions in skin via Cdc42/Rac1 pathways. These findings suggest that leukotriene B4-BLT1 signaling plays a critical role in the induction of acquired cutaneous immune responses.

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Generation of an IL-2-functionalized nanoparticle-based drug delivery system for specific CD25+ T cell targeting
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We have developed a novel drug delivery system that specifically targets CD25+ T cells. Using a nanoparticle-based approach, we functionalized nanoparticles with IL-2 and targeted them to CD25+ T cells. In vivo imaging revealed that the nanoparticles were selectively taken up by CD25+ T cells in skin lesions. These findings suggest that the nanoparticles can be used as a novel drug delivery system for specific T cell targeting.

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CD163+CD206+Arginase 1+ M2 macrophages in mycosis fungoides acquired immunostimula
tory function by interferon alpha2a
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Mycosis fungoides (MF) is a chronic inflammatory skin disorder. In MF, CD163+CD206+Arginase 1+ M2 macrophages are increased in skin lesions. In this study, we investigated the role of CD163+CD206+Arginase 1+ M2 macrophages in MF. Using in vitro and in vivo models, we found that CD163+CD206+Arginase 1+ M2 macrophages acquire immunostimulatory function by interferon alpha2a. These findings suggest that CD163+CD206+Arginase 1+ M2 macrophages play a critical role in the pathogenesis of MF.

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Topical Delivery of a Potent and Selective RORg Inhibitor Abrogates Th17 Cytokines from Human Skin Resident Immune Cells
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Psoriasis is an chronic inflammatory skin disorder involving marked inflammatory changes, including the expression of Th17 cytokines (IL-17A, IL-17F and IL-22). Recently, the central role of IL-17 to psoriasis was validated with biologics, where the systemic neutralization of IL-17 family cytokines resulted in a significant improvement in clinical measures. The transcription factor RORγt has been described as the master regulator for IL-17 production and is therefore considered a prime target for therapeutic treatment. Herein we describe a novel, potent and highly selective inverse agonist for RORγt in human skin resident immune cells. In a skin explant model, we found that a novel, potent and highly selective inverse agonist for RORγt inhibited IL-17 production in human skin resident immune cells. These findings suggest that RORγt is a novel therapeutic target for the treatment of psoriasis.

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A newly developed kappa-opioid receptor agonist ameliorates ongoing inflammation
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Opioids are known as powerful drugs for pain treatment and can induce analgesia by binding to peripheral opioid receptors (OR). Here, we investigated the role of a newly developed kappa-opioid receptor agonist (KORA) on the progression of inflammation. Therefore, human and mouse immune cells were treated with KORA in the presence of IFNγ and the cytokine expression, cell activation and proliferation was analyzed revealing a potent anti-inflammatory effect of KORA. To investigate the anti-inflammatory properties in vivo mice were treated with the toll-like receptor 7 (TLR7) agonist R848 in the presence of IFNγ and MCP-1 expression. Compared to PBS-injected controls, recipients of KORA showed a down-regulated expression of IL-23 and increased levels of TH1 and TH17 cells in lesion skin. Since TH17 ligation is implicated in the development of itch and signaling via OR modulates itching we quantified the scratching frequency in TH1 and TH17 mediated inflammation. Of note, this effect was mediated by binding of KORA to KOR since blocking KOR by co-injecting the antagonist nor-BNI abrogated the GM-CSF expression effects. To investigate whether KORA ameliorated ongoing inflammation in other organs than the skin coitus was induced by adding destanum sodium sulfate (DSS) to the drinking water. KORA prevented mice from weight loss and reduced epithelial damage, ulceration and significantly increased cell survival of keratinocytes. To investigate whether KORA ameliorated ongoing inflammation in the skin as well as the gut and down-regulated theTH1/TH17 immune response, recipients of KORA showed reduced numbers of neutrophils and a reduced myeloperoxidase activity in the gut. KORA prevented mice from weight loss and reduced epithelial damage, ulceration and significantly increased cell survival of keratinocytes. To investigate whether KORA ameliorated ongoing inflammation in the skin as well as the gut and down-regulated theTH1/TH17 immune response, recipients of KORA showed reduced numbers of neutrophils and a down-regulated myeloperoxidase activity in the lamina propria and mesenteric lymph nodes. Together, our data demonstrate that KORA, by binding to KOR, ameliorated ongoing inflammation in the skin as well as the gut and down-regulated the TH1/TH17 immune response, supporting the use of KORA as a promising novel compound for the treatment of inflammatory/itchy disorders.

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Antagonistic regulation of IL-17 and GM-CSF in human T helper cells - implications for skin and central nervous system inflammatory diseases
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Although TH2 and TH17 cells have been acknowledged as crucial mediators of autoimmune disease, the role of TH2 and TH17 cells in human autoimmunity remains controversial. Here, we analyzed the regulation of GM-CSF expression by human T helper cell subsets. Suprisingly, the induction of GM-CSF expression by human T helper cells is constrained by the IL-23/ RORϐ/gTH17 cell axis and is only induced when TH17 cells are induced by means of cytokines. The effect is independent of cytokines signaling induced by T helper cells, while STAT3's signaling blocked by the antagonist TAC-1. The opposite effect was observed in IL-8 expression. Ex vivo, GM-CSF+ T helper cells that co-express IFNγ and T-bet could be distinguished by differential chemokine receptor expression from a previously uncharacterized subset of GM-CSF only producing T helper cells that did not express TH1, TH2 and TH17 signature cytokines or master transcription factors. Our findings demonstrate distinct and counter-regulatory pathways for the generation of IL-17 and GM-CSF producing cells and also suggest a protective role for GM-CSF+ T cells in the in vivo setting, but a pathogenic role in multiple sclerosis. This not only provides a scientific rationale for depleting T cell derived GM-CSF in multiple sclerosis patients but also multiple new molecular checkpoints for therapeutic GM-CSF suppression, which unlike in mice do not associate with the TH17 axis instead.

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Cigarette smoking and oxidative/antioxidative status in active systemic lupus erythematosus
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An overproduction of oxygen radicals (cell metabolism, UV light, cigarette smoke, environmental pollutants, gamma radiation) or insufficient antioxidative capacity leads to a dangerous imbalance in the organism. The authors aimed to investigate the effect of chemical reactive substances from tobacco/ tobacco smoke on oxidative/antioxidative status in active systemic lupus erythematosus patients (SLE). The study included 42 healthy volunteers without known pathologic age (16, 14.2 ± 1.6) and 42 patients with active SLE without treatment (age 37, 8.4 ± 2). All the patients gave their consent for monitoring in the study. The two groups were divided in smokers (11 women, 10 men) – over 20 cigarettes/day for more than two years – and non-smokers (11 women, 10 men). The patients were grouped for demographical, nutritional characteristics. Total antioxidative status (TAS) and oxidative status (TOS) were determined by photometric tests. In control group, TOS presented no statistically significant variation between smokers and non-smokers (273, ± 37, 4umol/l, p<0.05 versus 273, ± 37, 4umol/l, p>0.05). In control samples, TOS had medium values in nonsmokers and low values in smokers (302, ± 62, 5umol/l, p<0.05 versus 264, ± 44, 1umol/l, p=0.05). In active SLE, TAS was low, with statistically significant differences between nonsmokers and smokers (201, ± 42, 1umol/l vs 174, ± 8, 7umol/l, p<0.05). A statistically significant negative correlation was determined between TAS and TOS in control group (r=-0.343, p<0.05) in smokers with active SLE (r=-0.827, p<0.05) and nonsmokers with active SLE (r=-0.521, p<0.05). These results showed that smoking influence LES development by reducing TAS. Antioxidant therapy in SLE patients could improve their prognosis.

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Development of short-term ex vivo culture of psoriatic skin as a translational model
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Psoriasis is a chronic inflammatory skin condition driven by cross-talk between skin-infiltrating T cells and keratinocytes via secretion of soluble mediators, including interleukin (IL)-12, IL-17A, IL-17F, IL-23 and interferon (IFN)-γ. To investigate inflammatory responses in psoriatic skin, we explored the feasibility of ex vivo culture of psoriatic skin. Keratinois biofilms from psoriatic plaques were obtained from patients with active disease not using any anti-inflammatory therapy. Skin punches from keratinois biofilms were immediately snap frozen (representing the in vivo situation) or cultured in media containing agents suitable for stimulating keratinocyte and T cell activation in a manner that mimics the inflammatory environment in vivo. Importantly, maintenance of TH17 cell activity was achieved by supplementation with IL-2, IL-23 and anti-CD123/CD28 antibodies. After ex vivo culture, histological and immunohistochemistry analysis confirmed the presence of epidermal hyperplasia with increased proliferation (Ki-67+ cells), expression of KRT16 and active skin inflammation with infiltration of CD4+ and CD8+ T cells in the dermis and epidermis respectively, recapitulating the hallmark of psoriatic skin. The activity of skin resident T cells was evaluated by measuring the level of T cell-related cytokines released T cells in the in vitro setting and for evaluating new treatments for psoriasis.
Epidermal Tissue-Resident Memory T cells Cell a Localised Memory in Clinically Healed Psoriasis

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Psoriasis is a common and chronic inflammatory skin disease characterized by massive infiltration of leukocytes into the skin. Th17 associated cytokines, IL-17 and IL-22, play a critical role in the pathogenesis of psoriasis and effective therapies targeting IL-17 are emerging. Effective treatments need to be established, but they often involve a variety of unrelated side effects. Their role in chronic inflammatory diseases remains to be elucidated. We propose that specific disease-mediating forms develop during active disease. Tissue-resident memory T cells (Trm) have recently been identified in peripheral tissues after viral infection and provide a first line of defence. Their role in chronic inflammatory diseases remains to be elucidated. We propose that Trm could drive a local pathogenic tissue inflammation. Here we investigated Trm in resolved psoriasis lesions. Three common and effective therapies, randomized-LVIB treatment and long-term systemic inhibition of TNF or IL-12/23 signalling were studied. Our result showed that epidermal T cells were highly activated in psoriasis and that a significant population of epidermal CD8 T cells expressed the Trm marker CD49a. In resolved psoriasis, epidermal CD49a+ CD8 T cells were retained and a distinct Trm population co-expressing CD8, CD101, CD6 and IL38 was enriched in re-lesioned patches. IL-22, a Th17 cytokine, also showed a dose-dependent reduction in cell surface CD3 expression in anti-CD3-stimulated but not TNF-α and CD8+ T cell proliferation (p=0.0239 and p=0.0002, respectively) and release of interferon-γ, CD45RO+ memory T cells (median reductions of 49.0% and 73.6% by 10 μg cell activation. Flow cytometry using a phospho-specific assay indicated that inhibition of PI3Kδ in unstimulated T cells. The results indicate that targeting PI3Kδ in psoriatic individuals may offer a potential therapeutic benefit in the future treatment of psoriasis.

Gene expression profiling in Chronic Spontaneous Urticaria

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The pathogenic and inflammatory potential of Trm must be taken into account in new vaccination strategies targeting formation of Trm population in peripheral tissues.

Inhibition of phosphatidylinositol-3-kinase delta reduces psoriatic T cell activity

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Psoriasis is a chronic inflammatory skin disorder, affecting 2–3% of the population, which is characterised by epidermal hyperproliferation, vasodilation and an immune cell infiltrate. The phosphatidylinositol-3-kinase (PI3K) pathway influences T cell differentiation and may influence the balance between T helper 1 and 2 (Th1/Th2) responses. The PI3Kδ pathway is abundantly expressed in psoriatic skin lesions and is activated upon TCR engagement. The following co-localisation of phospho-P38δ with dermal CD3+ cells in skin in situ, T cells were isolated from lesional skin (n=8) and blood (n=8) of psoriatic individuals and incubated with incremental doses (0.1–10 μM) of a selective PI3Kδ inhibitor (UBC6587) or vehicle control prior to anti-CD3/CD28-mediated T cell activation. Flow cytometry using a phospho-specific assay indicated that inhibition of PI3Kδ significantly reduced phospho-P38δ levels in peripheral blood CD3+ T cells and in psoriatic dermal CD4+ memory T cells (median reductions of 49.0% and 73.6% by 10 μg UBC6587, p=0.017 and p<0.0001, respectively). Similarly, PI3Kδ inhibition significantly prevented TCR-mediated CD4+ and CD8+ T cell proliferation (p=0.0239 and p<0.0002, respectively) and release of interferon-γ, TNF-α and IL-17 to levels comparable to unstimulated control. Furthermore, inhibition of PI3Kδ caused a dose-dependent reduction in cell surface CD3 expression in anti-CD3/CD28-stimulated but not in anti-CD3/CD28-stimulated control. Thus, in vivo, psoriatic individuals may offer a potential therapeutic benefit in the future treatment of psoriasis.

Evaluation of anti-inflammatory activity of N-Oleylethanolamine (NOE) as a topical agent

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Our current understanding of the pathogenesis of atopic dermatitis (AD) is largely based on results from studies using the Atopy Patch Test (APT) as an in vivo model for AD. The immunological changes in lesional AD skin are largely comparable to changes in the APT. However, comprehensive molecular profiling of the APT has not been performed. We sought to validate the APT as model for the induction of AD by comparing APT skin biopsies to lesional skin samples from individual AD patients. We performed a microarray analysis, comparing APT and lesional AD skin gene expression. High levels of similarity in gene expression profiles between APT (24 and 48 hours) and lesional AD skin samples were found. Genes up-regulated in APT (0–24 h) showed a dynamic regulation with many genes showing a peak expression at 12-24 h. Several genes were up-regulated in APT compared to lesional AD skin samples. NOE significantly accelerated the epidermal permeability barrier recovery after acute disruption. As a result, treatment of NOE induces accumulation of ceramide in cells. Previously, it was reported that treatment of NOE on cultured normal human epidermal keratinocyte (NHEK) resulted in the induction of expression of the gene encoding NOE and cannabinoid receptor 1 (CB1R), which is a key enzyme for in situ ceramide formation and transthyretin, which suggest a potential application of NOE for normalizing the hyper proliferation in inflammatory skin diseases. We have also reported that the topical application of cannabinoid receptor 1 (CB1R) agonist alleviated the inflammatory symptoms in atopic dermatitis animal model. Based on the structural similarity between NOE and previously reported CB1 agonist, it is hypothesized that topical application of NOE can be a therapeutic candidate for atopic dermatitis, at least in part, through the activation of CB1R. As results, topical application of NOE significantly accelerated the epidermal permeability barrier recovery after acute disruption. Anti-inflammatory activity of NOE was also observed in both TPA-induced acute dermatitis model and oxazolone-induced atopic dermatitis animal model, which was also confirmed by histological assessment. These results suggest that, NOE can be used as an anti-inflammatory agents for skin diseases including atopic dermatitis.

Human endothelial cells promote T cell proliferation and enhance regulatory T cell suppressive function

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Endothelial cells (ECs), which line blood vessels, play key roles in regulating leukocytes, presenting antigens and proliferating costimulatory pathways that induce T cell activation. Our current understanding of ECs suggests that endothelial cells that mediate peripheral tolerance, a mechanism necessary to prevent autoimmunity and chronic inflammation. This study investigated ECs’ effects on Treg and T effector (Teff) activation and function as a potential target for intervention in inflammatory skin disease. To study EC-T cell interactions, human umbilical cord vein (UCV) ECs were co-cultured with human ECs for 72 or 120 hours with phytosanagglutinin (PHA) or stimulatory aCD3/aCD28 antibodies. Cell proliferation and phenotype were analysed using flow cytometry. CD4 T cells in these EC-T cell co-cultures showed strong NOE expression at 72 hours compared to unstimulated ECs (p=0.0011, n=10); 60–80% of T effs in these co-cultures became FOXP3+, compared to T effs from T cell alone cultures which showed no FOXP3 expression (p<0.05; n=4). In the absence of T cell mitogens, CD4 T cells showed significant proliferation by 120 hours in co-cultures of ECs and TNF-α-prestimulated ECs compared to T cell alone cultures (p<0.01; n=10). To study the contact dependent nature of this modulation, Tregs were cultured in a Transwell assay above IFN-γ-stimulated ECs. Interestingly, these Tregs showed further increased suppressive function compared to direct contact mediated suppression (p=0.04; n=4), indicating both contact dependent and independent mechanisms of activation. The results indicate that ECs regulate human T eff and Treg function and suggest that the endothelium may provide a novel target for therapeutic intervention in inflammatory skin disease.

Human leukocyte antigen (HLA) allele frequencies of suburban, urban and rural people

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HLA allele frequencies were investigated in a population of 216 people from suburban, urban and rural areas. The frequencies of the most common HLA alleles, HLA-A2, HLA-B7, HLA-Cw3 and HLA-DRB1*0401, showed no significant difference between the three groups. However, the frequencies of the remaining alleles were significantly different between the three groups. The greatest difference was seen for HLA-B*4001, which was significantly more frequent in the suburban group compared to the urban and rural groups. The results suggest that the HLA allele frequencies in suburban, urban and rural areas differ and that the frequency differences may be related to environmental factors.
420 Withdrawn

421 Receptor activator of nuclear factor kappa-B ligand (RANKL)/ RANK signaling promotes cancer-related inflammation through M2 macrophages
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RANKL signaling promotes the survival of conventional dendritic cells (cDCs) and ensures T cell priming and activation, thereby enhancing the acquired immune response. On the other hand, in skin, RANKL-treated DCs maintain the number of Foxp3-positive Tregs to suppress the immune response against self-antigens, food and commercial flora. In addition, as we previously reported, human monocytes-derived M2 macrophages (MoM2) express RANK on its surface in an IL-4 dependent manner, and when stimulated by soluble sRANKL. These cells produce TNF and regulatory T cell-related cytokines, including CCL17. In this study, to further elucidate the molecular mechanisms of the effects of sRANKL on M2 macrophages, we examined its effects on mRNA expression in MoM2 macrophages by stimulating sRANKL. Using a microarray and gene ontology, we identified 373 upregulated (including CCLX1, CCLX2, CCL5, IL-1β, IL-6 and IL-8) and 458 down-regulated (including CCL27) genes. The DNA microarray results were verified using real-time PCR. These proinflammatory chemokines and cytokines described above are reported to contribute to cancer-related inflammation to promote the tumor progression. Thus, our present data suggested the therapeutic possibilities of a fully human monoclonal antibody to RANKL, denosumab, in cancer-related inflammation through M2 macrophages.

422 Reduced frequency of IL-17+CD8+ T cells in psoriatic lesions after calcipotriol treatment
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The vitamin D analogue calcipotriol is an immune-modulatory drug used to treat psoriasis; however, its effect on the immune system in psoriasis lesions is not fully understood. This study investigates the effect of calcipotriol on the distribution of CD4+ and CD8+ T cells and innate lymphoid cells (ILCs) and their production of IL-17A, IFN-γ and IL-22 in psoriasis lesions in patients with chronic plaque psoriasis. Eighteen patients with psoriasis were included and two similar psoriasis lesions were chosen for each patient. One lesion was treated with calcipotriol (50 μg/ml) and the other with vehicle for 14 days. The clinical effect was measured by degree of erythema, scaling and induration in each lesion (SUM score). Skin biopsies were collected for histological and immunohistochemical analyses. Skin-derived cells were isolated and analysed by flow cytometry. After 14 days of treatment with calcipotriol a significant clinical and histological effect was seen; however, we found no differences in the distribution of CD4+ and CD8+ T cells or ILC between calcipotriol- and vehicle-treated skin (N=12). The main finding was a significant decrease in IL-17+CD8+ T cells in skin-derived cells from calcipotriol-treated skin (CD4+ 6.3 ± 2.7%; CD8+ 2.8 ± 1.4% in controls vs. 0.6 ± 0.3% and 0.5 ± 0.2% in calcipotriol-treated skin, p<0.03) and a further reduced expression of IL-17A in vehicle-treated skin (vehicle 15.4 ± 11.3% vs. calcipotriol 6.6 ± 11.3%). Our findings show that the vitamin D analogue calcipotriol reduces the frequency of IL-17+CD8+ T cells in psoriasis lesions concomitant with early clinical improvement.

423 Receptor activator of nuclear factor kappa-B ligand (RANKL)/ RANK signaling promotes cancer-related inflammation through M2 macrophages

424 Regulatory B cells in Human Chronic Graft-versus-host Disease
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Chronic graft-versus-host disease (cGVHD) is an incurable and highly disabling complication of allogeneic hematopoietic stem cell transplantation (HSCT). This study was aimed at investigating any regulatory B cells (Bregs) defect associated with the development of cGVHD. The inclusion criteria were: i) prior allogeneic HSCT; ii) written informed consent given by the patient for study enrolment. The study was approved by the local ethics committee. Bregs were defined as CD19+ B cells after 66 hours in vitro stimulation of total peripheral blood mononuclear cells with anti-CD40 and IL-4. To date, the significance of the acquired immune response in patients with cGVHD remains unknown. In this study, we identified 337 upregulated (including CXCL1, CXCL2, CCL5, IL-1b, IL-6 and IL-8) and 458 down-regulated (including CCL27) genes. The DNA microarray results were verified using real-time PCR. These proinflammatory chemokines and cytokines described above are reported to contribute to cancer-related inflammation to promote the tumor progression. Thus, our present data suggested the therapeutic possibilities of a fully human monoclonal antibody to RANKL, denosumab, in cancer-related inflammation through M2 macrophages.

425 Th1 cell-mediated control of differentiation during malignant transformation of cancer cells
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Oncogetic expression of T antigen (Tag) under the control of the rat-insulin-promotor (RIP) leads to the development of malignant beta-cell carcinomas in RIP1-Tag2 mice. Due to the unrestricted proliferation of beta-cancer cells, the mice are no longer capable to control their blood glucose levels and die at the age of 13-15 weeks. As shown previously, interferon-gamma (IFN-gamma) and tumor necrosis factor (TNF)-producing, Tag-specific T helper 1 (Th1) cells prolonged the survival rate of mice by driving the beta-cancer cells into a pre-malignant senescent state in the absence of beta-cancer cell death. As a consequence, the Th1 cell-treated mice did not develop a diabetic phenotype but instead expressed the cytokines necessary to maintain glucose levels. To investigate what senescence induction is associated with a higher differentiation status, we analyzed the expression of 3 beta-cancer cell markers in RIP1-Tag2 mice at well-defined steps of carcinogenesis. For this, we stained isolated tumor cells from mice of different age with antibodies against synaptophysin, insulin and the glucose transporter 2 (Glut2). Furthermore, we measured the response of the isolated beta-cells to high glucose concentrations (30 mM) in a tyrosine phosphorylation assay. Our data show complete loss of Glut2 and a partial loss of insulin during carcinogenesis, whereas synaptophysin was still expressed by the beta-cancer cells. The loss of their differentiation marker Glut2 concurred with the inability of the beta-cancer cells to respond to glucose stress. Th1 cell-mediated immunotherapy prevented the phenotypical as well as the functional dedifferentiation of the beta-cancer cells during malignant transformation. Ongoing experiments using recombinant IFN-gamma and/or TNF in vitro, demonstrated a cytokine-dependent regulation of the beta-cell differentiation markers. In conclusion, Th1 cells may arrest malignant transformation by keeping the tumor cells in a differentiated state.
The characterization of CARD18, a novel negative regulator of inflammasome signaling in human epidermal keratinocytes

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ZC3H12A encodes a ribonuclease highly expressed in psoriasis

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MART-1 short peptides, derived from a melanoma antigen (MART-1), have been used to elicit autologous CD8(+)-T-cell cytotoxic responses in patients with melanoma. These responses can be monitored by analyzing MART-1 tetramer uptake by T cells, and are used clinically to assess the immunotherapeutic efficacy of MART-1 vaccination protocols. Recently, it has been shown that MART-1 peptides can induce activating FcγR expression on CD8(+) T cells. The aim of this study was to determine the effect of MART-1 short peptides on activating FcγR expression on MART-1-specific CD8(+) T cells of melanoma patients. MART-1 short peptides were synthesized and used to prime autologous CD8(+) T cells in vitro. FcγR expression on activated MART-1-specific CD8(+) T cells was evaluated by flow cytometry and MART-1 tetramer uptake was used as a marker of cell activation. MART-1 short peptides induced an upregulation of activating FcγR expression on MART-1-specific CD8(+) T cells. This upregulation correlated with an increase in MART-1 tetramer uptake by these cells. The expression of activating FcγR on MART-1-specific CD8(+) T cells was not observed in control T cells, which indicates that this upregulation is specific to MART-1-specific CD8(+) T cells. These results suggest that MART-1 short peptides can induce activating FcγR expression on MART-1-specific CD8(+) T cells, which may have implications for the use of MART-1 vaccination protocols in the clinic.