IFNy production after 4 days of culture at 0.0625 mM and 0.25 mM of butyrate, respectively. Assays using purified LP CD4 T cells demonstrated that butyrate directly decreased LP CD4 T cell activation, proliferation and cytokine production in response to TCR/CD28 stimulation. Studies on specific T helper subsets revealed that butyrate inhibited proliferation of Th17 cells at lower concentrations (IC50:0.147 mM) compared with Th1 (IC50:0.229 mM) and Th22 (IC50:0.258 mM) and Th non-IL-22/IL-17/IFNy producing (IC50:2.14 mM) subsets. In addition, it appeared there was a paradoxical increase of HIV-1 infection levels at lower concentrations of butyrate (0.125 mM). DISCUSSION/SIGNIFICANCE OF IMPACT: The addition of butyrate to activated LP CD4 T cells decreases TCR-mediated activation in a dose-dependent manner, and butyrate acts directly on purified LP CD4 T cell populations independent of other cell populations. Butyrate differentially inhibited the proliferation of Th17, Th1, and Th22 subsets, with Th17 cells being the most sensitive to butyrate but increased the infection levels of all T helper subsets at low concentrations. Further studies are needed to determine the mechanism of butyrate's actions on LP Th cells and the sensitivity of Th17 cells to the inhibitory effects of butyrate. These results could help direct targeted manipulation of the colonic microbiome of HIV-1 infected individuals to help resolve inflammation and limit the impact of the infection in the gut mucosa and systemically.

2349

The role of interleukin-23 in human melanoma

Aditi Jani, Sandeep Chaudhary, Zorica Janjetovic, Mohammad A. Sherwani, Nabiha Yusuf, Andrzej Slominski, Mohammad Athar and Craig Elmets
University of Alabama at Birmingham

OBJECTIVES/SPECIFIC AIMS: Interleukin-23 (IL-23) promotes differentiation of naïve T-cells into Th17 cells, which drive the pathogenesis of autoinflammatory conditions such as psoriasis. IL-23-neutralizing antibody therapies are now in use for treatment of psoriasis, with promising results. Studies in mice have shown that IL-23 plays a role in inhibiting the growth, progression, and metastasis of melanomas. Thus, therapeutic neutralization of IL-23 in patients may inadvertently increase their susceptibility to development of melanoma. In this study, we aim to characterize expression of IL-23 receptors (IL-23R) in human melanocytes and melanoma cells and tissue and to study the effect of IL-23 on growth, proliferation, and tumorigenicity of these cells. METHODS/STUDY POPULATION: IL-23R expression was characterized using immunofluorescence staining, Western blot, and flow cytometric analysis. Response of melanoma and melanocytes to recombinant IL-23 treatment will be studied through similar methods in addition to assays of cell proliferation and tumorigenicity. RESULTS/ANTICIPATED RESULTS: Preliminary immunofluorescence staining and flow cytometry results indicate that both human melanoma and primary melanocytes express IL-23 receptors. Western blot analysis showed that melanoma cell line A375 expressed nearly twice the amount of IL-23R versus normal melanocytes ($p < 0.05$). Based on previous studies, we anticipate that addition of recombinant IL-23 to cultures of melanoma will reduce proliferative potential, and we expect similar addition to normal melanocytes will increase DNA repair mechanisms. DISCUSSION/SIGNIFICANCE OF IMPACT: In showing that human melanocytes and melanoma cells express IL-23 receptors, and potentially showing the inhibitory effect of IL-23 in the development of melanocytic neoplasms, our findings imply that using IL-23 neutralizing therapies may increase risk of developing melanoma, especially in patients who are already susceptible. As such, these therapies must be used with great care in these patients.

2153

The plasma contact system and its role in common variable immunodeficiency (CVID): An explorative study

Tukisa Smith[1], Manish Ponda[2], Jan Breslow[2] and Cunningham-Rundles Charlotte[2]
[1] Rockefeller University; [2] Division of Clinical Immunology, Icahn School of Medicine at Mount Sinai

OBJECTIVES/SPECIFIC AIMS: Assess the presence of contact activation at baseline in sera from common variable immunodeficiency (CVID) patients with and without inflammatory complications compared with healthy controls. METHODS/STUDY POPULATION: CVID patients were recruited in the outpatient setting and the measurement of cleaved plasma HK (cHK) levels was determined by Western blot analysis, under reducing conditions, with quantitation of total and cHK bands using an Odyssey imaging system (Licor). One-way ANOVA test for differences among the 3 studied groups will be applied. Biomarkers C3, C4, C1 inhibitor levels and hs-CRP were also measured. RESULTS/ANTICIPATED RESULTS: Participant enrollment continues and to date, 9 CVID patients were studied, 7 with and 2 without inflammatory complications. Repeated determinations of cleaved HK% (cHK%) revealed an average of 1.20% (range: 0.46%–2.66%) in CVID patients with inflammatory complications and those without complications averaged 1.07% (range: 0.79%–1.35%). Healthy controls had an average cHK of 1.15% (range: 0.60%–2.10%). DISCUSSION/SIGNIFICANCE OF IMPACT: Cleaved kininogen detected in the sera of CVID patients was found at similar levels compared with healthy controls (cHK < 5%). Findings suggest that systemic activation of the contact system might be absent in CVID, however, future considerations include developing detection methods for local tissue activation.

2356

The nasopharyngeal microbiome is perturbed and associated with increased clinical severity during acute respiratory viral infection

Darrell Dinwiddie, Ashlee K. Bradley, Jesse L. Denson, Joshua L. Kennedy, Walter N. Dehority, Kurt C. Schwalm and Stephen A. Young
Clinical and Translational Science Center, University of New Mexico

OBJECTIVES/SPECIFIC AIMS: We sought to investigate the role of the host microbiome during severe, acute respiratory infection (ARI) to understand the drivers of both acute clinical pathogenesis. METHODS/STUDY POPULATION: Nasopharyngeal swabs comprised of mixed cell populations at the active site of infection were collected from 192 hospitalized pediatric patients with ARI. We combined comprehensive respiratory virus detection and virus genome sequencing with 16S rRNA gene sequencing to evaluate the microbial content of the airway during ARI. This data was coupled with 11 clinical parameters, which were compiled to create a clinical severity score. The microbiome profiles were assessed to determine if clinical severity of infection, and/or specific virus was associated with increased clinical severity. RESULTS/ANTICIPATED RESULTS: We identified 8 major microbiome profiles classified by dominant bacterial genus, Moraxella, Corynebacterium, Staphylococcus, Haemophilus, Streptococcus, Alloiococcus, Schlegelella, and Diverse. Increased clinical severity was significantly associated with microbiome profiles dominated by Haemophilus, Streptococcus, and Schlegelella, whereas Corynebacterium and Alloiococcus were more prevalent in children with less severe disease. Independent of the microbial community, more than 60% of patients with the highest clinical severity were infected with either respiratory syncytial virus or rhinovirus. DISCUSSION/SIGNIFICANCE OF IMPACT: Our results indicate that individually and in combination, both virus and microbial composition may drive clinical severity during acute respiratory viral infections. It is still unclear how the complex interplay between virus, bacterial community, and the host response influence long-term respiratory impacts, such as the development of asthma. Nonetheless, during ARIs therapeutic interventions such as antibiotics and probiotics may be warranted in a subset of patients that are identified to have both a virus and microbiome profile that is associated with increased pathogenesis to limit both acute and long-term phenotypes.

2027

The role of lysyl oxidase in systemic sclerosis-associated lung fibrosis

Xinh-Xinh Nguyen, Tetsuya Nishimoto, Takahisa Takihara, Logan Mlakar, Ellen Riemer, Jonathan Heywood, Amy Bradshaw and Carol Feghali-Bostwick
Medical University of South Carolina

OBJECTIVES/SPECIFIC AIMS: Systemic sclerosis (SSc) is a connective tissue disease of unknown etiology characterized by progressive fibrosis of the skin and multiple visceral organs. Effective therapies for SSc are needed. Lysyl oxidase (LOX) is a copper-dependent amide oxidase that plays a critical role in the crosslinking of the extracellular matrix (ECM). In this study, we investigated the role of LOX in the pathophysiology of SSc. METHODS/STUDY POPULATION: LOX expression and protein levels were measured in lung tissues and primary fibroblasts from patients with SSc and healthy controls. The effects of recombinant LOX (rLOX) were measured in vitro in primary fibroblasts, ex vivo in human lung tissues and in vivo in mice given bleomycin in combination with rLOX. LOX levels and activity were evaluated in lung fibroblasts treated with an endostatin-derived peptide that ameliorates fibrosis

https://doi.org/10.1017/cts.2018.137 Published online by Cambridge University Press