The role of interleukin-23 in human melanoma

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OBJECTIVES/SPECIFIC AIMS: Interleukin-23 (IL-23) promotes differentiation of naive T-cells into Th17 cells, which have 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 melanocytes and melanoma cells and tissue and to study the effects of IL-23 on growth, proliferation, and tumorigenesis of these cells. METHODS/STUDY POPULATION: IL-23R expression was characterized using immunofluorescence staining, Western blot, and flow cytometric analysis. Results 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/APPROACHES: 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 in melanocytes and melanoma cells and tissue and to study the effect of IL-23R on growth, proliferation, and tumorigenicity of these cells. 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.

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

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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 continued through 4/4/2020. Up to date, 9 CVID patients were studied. 7 with and 2 without inflammatory complications. Repeated determinations of cleaved HKs (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 decreased in the sera of CVID patients was found consistent 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.

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

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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. Effects of the copper-dependent enzyme Lysyl oxidase (LOX) on 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