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201 Overlay Between Th1 and Th2 pathways in Patients with Common Variable Immunodeficiency and Allergic disease



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RATIONALE: Common Variable Immunodeficiency (CVID) is defined by low serum immunoglobulins, history of recurrent sinopulmonary infections, and blunted response to immunization. It can be associated with immune dysregulation. Though not well documented, it has been clinically suspected that CVID may be associated with allergic disease. We set out to determine a possible connection.

METHODS: This retrospective study was conducted at the George Washington University. Study patients were identified with ICD-10 diagnoses of primary immunodeficiencies in an electronic medical record (EMR). Of 541 patients with one or more such diagnoses, 88 patients had a confirmed diagnosis of CVID.

RESULTS: Of the 88 patients, 43 (48.9%) patients were diagnosed with allergic rhinitis by an Allergist with 7 (78%) out of 9 patients reporting improvement in symptoms with allergen immunotherapy. 22 of the 88 patients underwent skin testing of which 20 (91%) were found to be positive. Of the 88 patients, 46 (52.3%) patients were receiving IVIG replacement therapy. 21 (45.7%) of these 46 patients were asked if IVIG helped their allergic symptoms of which 18 (85.7%) of the 21 patients reported improvement. Interestingly, the mean Immunoglobulin E (IgE) was found to be 67.5 and mean eosinophils were 200.

CONCLUSIONS: The high incidence of allergic disease, positive skin testing, and elevated IgE and eosinophils in these patients suggests a potential interaction between Th1 and Th2 immunity that might explain why patients with CVID have allergic disease. An improvement in allergic symptoms in CVID patients on IVIG further points to a possible connection between allergic disease and CVID.

Transcriptional Features of TH1, TH2, and TH17 priming migratory dendritic cells – a common role for CXCR5 and Chi3l1



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RATIONALE: In a mouse infection model with the nematode *Heligmosomoides polygurus (Hp)*, $T_{\rm H}2$ responses require CXCR5⁺ DC. The significance of CXCR5⁺ DCs in $T_{\rm H}1$ or $T_{\rm H}17$ infections is unknown. We probed the transcriptomes of migratory DCs in response to Hp ($T_{\rm H}2$), *Citrobacter rodentii (Cr)* ($T_{\rm H}17$), and *Leishmania major (Lm)* infection (BALB/c mice: $T_{\rm H}2$, C57BL/6 mice: $T_{\rm H}1$). We further parsed the transcriptomics of draining lymph node DCs to identify gene signatures associated with CXCR5⁺ DC.

METHODS: Wildtype mice were infected with Hp larvae or Cr by gavage. Irradiated mice reconstituted with a 1:1 ratio of wildtype (CD45.1) and CXCR5 deficient (CD45.2) bone marrow were infected with either Hp larvae or intradermal Lm. Migratory dendritic cells were sorted from mesenteric lymph nodes (msLN) of Hp or Cr infected mice and popliteal lymph nodes of Lm infected mice into CD103⁺ (cDC1) and CD11b⁺ (cDC2) subsets, then underwent RNA seq. In chimeric mice DC were also sorted by the congenic marker CD45.

RESULTS: Thousands of differentially expressed genes (DEG) were found in cDC1 and cDC2 from *Hp*, *Cr* and *Lm* infected mice. *Cxcr5* and *Chi311* were expressed by cDC2 in *Hp*, *Cr* and *Lm*. In contrast, few DEG were identified between CXCR5⁺ and CXCR5⁻ cDC2 during *Hp* or *Lm*

infection. The most differentially expressed gene, *Chi311*, was restricted to CXCR5⁺ cDC2.

CONCLUSIONS: cDC1 and cDC2 DEG differ in T_H1 (B6 Lm), T_H2 (Hp and BALB/c Lm) and T_H17 (Cr) infection, but in all settings Cxcr5 and Chi311 were expressed by cDC2. CXCR5 deficient cDC2 fail to express Chi311.

203 The Role of Antisense RNA in Gene Expression After Treatment with Autophagy Modulators



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RATIONALE: This study explores how molecular determinants of gene regulation contribute to the inflammatory response of MSCs in the presence of autophagy modulators. It is our hypothesis that antiRNA contributes to gene regulation in cells that are exposed to inflammation stimulation in the presence of autophagy modulators.

METHODS: We utilized a subset of MSCs termed "marrow-isolated adult multilineage inducible" (MIAMI) cells. These cells were initially treated with IFNg to stimulate the inflammatory response. The autophagy modulators tamoxifen (TX) and chloroquine (CQ) were concurrently used to activate and inhibit autophagy in MIAMI cells, respectively. By comparing mRNA between treatment groups, changes in gene expression were assessed. RNA sequencing was matched to online databases to uncover molecular determinants of gene expression regulation.

RESULTS: AntiRNA should typically decrease mRNA expression. For example, IL-6 mRNA expression was decreased after stimulation with IFNg and TX. However, the antiRNA for the inflammatory gene PYCARD did not affect gene expression regardless of treatment. We found that many of these direct relationships remained.

CONCLUSIONS: Further gene expression studies which will include other RNA species will be needed to discover all determinants of mRNA expression in the presence of TX or CQ.

204 COVID-19 and Common Variable Immunodeficiency



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RATIONALE: Common Variable Immunodeficiency (CVI) is rare primary immunodeficiency. The COVID-19 pandemics rised the risc os infection in these patients.

METHODS: We describe a 27 year old male patient with CVI, in regular replacement of human immunoglobulin (600mg/kg), with parotiditis and night sweating. The diagnosis os COVID was suspected. Two days later, he presented diarrhea. The diagnosis of COVID-19 was made by blood test -serology and a RT-qPCR for SARS-CoV-2. He received azithromycin, zinc, ivermectin and vitamin D, and he received human gammaglobulin 1 week in advance.

RESULTS: IgM anti-SARS CoV-2 serology of 4.73 AU / ml (Reference <1) and IgG negative. In addition, a C-reactive protein test was requested, which showed a high result 8.712 mg/dL. Chest CT scan was ordered and showed no changes related to early stages of viral infections. IL-6, fibrinogen and D-dimer were normal. At the time of infection IgG=1150 (700-1600mg/dL), IgA=28 (70-400mg/dL), IgM=19 (40-230mg/dL).

CONCLUSIONS: The literature is scarce with regard to the relationship between primary immunodeficiencies and SARS CoV-2 infection, however, there is a consensus that patients with primary immunodeficiencies mostly present more severe conditions when infected with this virus. Fortunately, this patient recovered well, and progressed to cure of the viral syndrome. CT chest scan was unremakable. To our knowledge, this is the first report of parotidis in a patient with CVI and COVID-19.