Su.3. Immunoparalysis in Acute Pancreatitis
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Introduction: Alteration of the immune system is one of the major mechanisms responsible for early and late mortality in severe acute pancreatitis (SAP). In SAP immunologic impairment in the early phase may be linked to subsequent infectious complications. IL-10 has prominent anti-inflammatory properties. However, the high levels of IL-10 have the immunosuppression effect. Materials and methods: A total of 31 patients with acute pancreatitis (15 - mild, 16 - severe) were analyzed. Six patients with SAP have septic complications after 1st week from admission. Populations and subpopulations of lymphocytes were evaluated using the differentiation antigens. The serum levels of interleukin-10 were measured by ELISA. Results: The lymphocyte count was decreased below the normal range, and was significantly negatively correlated with severe score. CD4- and CD8-positive lymphocyte counts on admission and the lymphocyte count on day 14 after admission may be useful for predicting infection. During all period of observation the insignificant elevation of IL-10 levels were noted in patients with mild pancreatitis and uncomplicated course of SAP. Starting from the seventh day the obvious rise of IL-10 concentration was noted in patients who subsequently developed septic complications. Conclusion. A significant depletion of circulating lymphocytes was found in severe acute pancreatitis with infectious complications. This is correlated with uncontrolled synthesis of interleukin 10.

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Su.4. DNA Vaccine Reduces the Schistosoma mansoni-induced Tissue Damage
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Helminthiasis are known to elicit a broad range of immunomodulation characterized by dominant Th2 type immune responses. Indeed, studies conducted in humans living in helminth-endemic areas and with animal models showed that helminth infection makes the host more permissive to mycobacterial infections and less able to benefit from vaccination. One of the clinical manifestations of helminth infection is the presence of type 2-granuloma and the lung is the primary site of organ involvement in a range of granulomatous conditions. The immune response to Schistosoma mansoni eggs in mice results in the development of pulmonary granulomas leading extensive fibrosis. Our group previously demonstrated that a DNA vaccine encoding the mycobacterial 65-kDa heat shock protein (DNA-Hsp65) protected mice from challenge with Mycobacterium tuberculosis. As predicted, Th2 pattern could influence protection against tuberculosis, in this sense we demonstrated the influence of a DNA-Hsp65 treatment on type 2-granuloma establishment. The immunization after granuloma induction increased the levels of inflammatory-related cytokines, IFN-γ, IL-13 and IL-10. Also, the DNA immunization was able to reduce collagen accumulation and 16 days after granuloma induction, the collagen among perivascular and peribronchial areas was minimum and the granuloma structure showed a lesser arrangement. The DNA-hsp65 has been focused by our group as a vaccine antigen in several pathologies, including tuberculosis, leishmaniasis, diabetes, arthritis and cancer. For the first time, in we demonstrated the protective role of DNA-hsp65 in a helminthiasis model, suggesting the importance of immune response regulation by immunization with an unrelated antigen.

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Su.5. Evidence that the Majority of People are Naturally Immune to Esophagus, Stomach, Colorectal, and Pancreatic Cancers is Predicted by a Novel, Inherently Saturated, Ordered Mutation Model
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A novel saturated ordered mutation model is constructed and applied to the USA (SEER) incidence data for esophagus, stomach, colorectal, and pancreatic cancers. The percentages of the White Male risk population that are naturally immune to these cancers predicted by the modeling are 97.0% (esophagus), 90.8% (stomach), 70.5% (colorectal), and 93.6% (pancreatic), respectively, suggesting that at least one of the risk factors is ingested. These results are consistent with the latest ideas in immunosurveillance and immunoeediting. Similar results are obtained for the other nine risk populations. The minimum number of mutations (m) necessary to cause any one of these four cancers was found to be seven since the mean time between consecutive mutations T(m) is given by the amazingly simple formula T(m) = (64.8 years)/(m-6) m = 7, 8, 9,... Thus, the same diverse pathways are open to each of these cancers, suggesting that a common cell type and perhaps identical mutagens are involved in all four cancers. The model predicts a maximum mean time between cellular turnovers of 0.21 years for White Males and 0.14 years for White Females, results that agree with measured values in the literature; thus, the model passes an important credibility test. Since gastric cancers can develop without Helicobacter pylori bacterial infection, there must be other cofactors. Delineating the
Su.6. KIR3DS/L1 Alleles and Reduced Risk of HIV Infection in Exposed Persistently Seronegative Subjects

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Background: Individuals exposed repeatedly to HIV while remaining uninfected (EU) are reported to have increased NK cell activity versus low risk controls, suggesting innate immune mechanisms may contribute to protection from HIV infection. In HIV infected subjects, certain MHC class I ligand-NK receptor combinations are linked to slower HIV disease progression, notably HLA-Bw4-Ile80 alleles (which includes HLA B*57) co-expressed with KIR3DS1/L1 alleles, such as the activating receptor KIR3DS1 or KIR3DL1*h/y, a potentially potent inhibitory genotype lacking weakly expressed NK cell surface expressed alleles. We questioned whether these genotypes also play a role in protection from infection. Methods: Eighty HIV-exposed EU and 304 MHC class I-typed subjects from the Montreal Primary HIV Infection (PI) cohort were studied. KIR3DS/L1 genotyping was done by PCR sequence-specific priming and KIR3DL1 homozygotes (39 EU and 186 PI) were subtyped by sequencing. We evaluated the significance of differences in the genetic distribution of KIR3DS/L1-MHC class I genotypes in EU and PI subjects using Fisher’s exact-test. Results: EUs, but not PI, deviated from Hardy-Weinberg equilibrium for KIR3DS/L1 distribution due to an increased proportion of KIR3DS1 homozygotes (11/80 versus 16/304; p = 0.013). The proportion of individuals carrying both KIR3DS1 and HLA Bw4*Ile80 was similar in both groups. The combined B*57-3DL1*h/y genotype was more frequent in EUs (5/39) than PI (5/186) (p = 0.017; OR = 5.03). Conclusion: Expression of certain KIR3DS/L1-MHC class I ligand combinations that may confer a potential for potent NK activation is associated with reduced risk of HIV infection. The mechanism underlying this association warrants further exploration.

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Su.7. Identification of Human Antigen-specific Regulatory T Cells, Phenotyping and Functional Analysis

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CD4+CD25+CD127lowFoxp3+ regulatory T cells (Tregs) have a role in maintaining tolerance to self-antigens and coordinating immune responses to pathogens. More recently, there has been increased interest in antigen-specific Tregs as they have potential as a novel immunotherapeutic agent in the treatment of autoimmune disease and cancer and may also have therapeutic role in transplantation and vaccine regimes. Using recall responses and a new gating strategy for which includes Foxp3, CD124 and CD39, we aimed to identify, phenotype and study the function of Tregs responding to re-stimulation with epitopes from CMV pp65. In healthy CMV+ donors we found that 1.41±0.37% (mean±SEM) of peripheral CD4+ T cells were specific for pp65. Surprisingly, a majority of these cells (70.80±1.00%) were bona-fide Foxp3+ antigen-specific Tregs. This subpopulation was isolated by FACS and studied in suppression assays. Antigen-specific CD39+Foxp3+ Tregs were found to be better suppressors than CD39- Foxp3+Tregs. To determine the source of these Tregs, the TCRβ/C DR3 region of these subsets and other subsets of effector/memory cells is currently being amplified for clonotypic analyses. The results will determine whether antigen-specific Tregs are derived or not from effector/memory cells, which then undergo clonal expansion when encounter antigen.

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Su.8. Regulatory T Cell Abnormalities are Associated with Aberrant CD4+ T Cell Responses in Patients with Immune Inflammatory Syndrome (IRIS)

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Up to 30% of patients with HIV commencing antiretroviral therapy (ART) late in the disease, restore a pathogen-specific cellular immune response that is immuno-pathological and causes disease reffered as immune reconstitution inflammatory syndrome or IRIS. We report that in HIV-infected patients who developed IRIS to mycobacteria, a large expansion of CD4+ T-cells specific for M. avium complex (MAC) antigens producing high levels of IFN-γ and IL-2 (P<0.01) was observed. Surprisingly, we found an even larger proportion of expanded CD127loFoxp3+CD25+Tregs in these patients compared to healthy controls (17.8%±2.51% c/w 6.81%±0.35%, p<0.05) or to HIV+ patients before commencing (4.5%±2.12%, p<0.01) or 4 weeks after starting ART (4.3%±1.61%, p<0.01). However, these Tregs are defective in their ability to suppress effector T cell proliferation and production of inflammatory cytokines (IL-6, TNF-α). This may explain the aberrant immune responses observed in these patients. To further investigate the suppressive dysfunction, we assessed CD39 and CD73 expression and function. These two ecto-enzymes have been reported recently to play a major role in Tregs function. Interestingly we found that, although CD39 expression was elevated in IRIS patients compared to controls (12.48%±2.069% c/w 2.67%±0.38%, p<0.05), CD73 expression was very low or absent compared to controls (1.045%±0.18% c/w 5.028%±1.18%, p<0.01). The imbalance in expression of these 2 regulatory ecto-enzymes that normally work in tandem may help explain the observed defect in suppressive function of Tregs, allowing the excessive proliferation and

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