P47 Down regulation of PMA-induced gelatinase-B production by metoprolol in human leukemic U937 monocytes in vitro

Fatemeh Hajighasemi*[1], Baran Hajat Beigi[1]
Department of Immunology, Faculty of Medicine, Shahed University, Tehran, Iran

Background: Metoprolol, as a β-Blocker with anti-inflammatory properties, has been extensively used for treatment of some cardiovascular diseases such as angina, hypertension and myocardial infraction. Matrix metalloproteinases (MMPs), a large group of enzymes damage the extracellular matrix, are involved in many inflammatory diseases. Gelatinase- B (MMP-9) plays a critical role in inflammation. In this study effect of metoprolol on Gelatinase- B production in leukemic U937 cells has been evaluated in vitro. Materials and Methods: Human U937 leukemic cells were cultured in complete RPMI-1640 medium supplemented with 10 % FBS. Next the cells at exponential growth phase were stimulated with optimal dose of PMA and treated with different concentrations of metoprolol (1-1000 µg/ml) for 24 hours. Afterward level of gelatinase-B in culture supernatant were determined by enzyme-linked immunosorbent assay (ELISA). Results: Metoprolol significantly decreased the PMA- stimulated gelatinase- B production in U937 cells dose-dependently compared with untreated control cells. Conclusion: According to our data metoprolol could be a promising gelatinase- B down regulator. So anti-inflammatory effect of metoprolol, reported by other investigators, might be partly due to its suppressive effects on gelatinase- B excretion. Consequently metoprolol may be beneficial as an innovative therapeutic applicant for inflammatory diseases in which gelatinase- B is over-expressed. Key words: Metoprolol, U937, Gelatinase- B

P48 Helminth-driven fetomaternal crosstalk primes regulatory networks to modify inflammatory T cell responses.

Matthew Lacorcia[1], Sonakshi Bhattacharjee[1], Kristina Laubhahn[1], Andreas Muschaweckh[2], and Clarissa Prazeres da Costa[1]
[1]Institute for Medical Microbiology, Immunology and Hygiene, Technical University of Munich, Munich, Germany.
[2]Department of Neurology, University Hospital rechts der Isar, Technical University of Munich, Munich, Germany.

Question: Prenatal exposure to infections can modify immune development. Environmental disturbances during early life alter the incidence of inflammatory disorders and immune response priming. Infection with helminth Schistosoma mansoni alters immune responsiveness, and associated with variations in co-infection, allergy, and vaccine efficacy in endemic populations. Exposure to maternal schistosomiasis during early life, even without transmission of infection, can result in transgenerational effects on immune responses to bystander antigenic challenges, as we have previously shown with allergic asthma in a mouse model. This study explores the immunological priming effects of maternal helminth infection during pregnancy, as relate to allergic responsiveness and vaccination mediating by T cell activation. Methods: We employ a long-term chronic murine model of maternal schistosomiasis to evaluate effects on modified inflammatory T cell biology. Steady state analysis of immune priming within these offspring was coupled to functional assays including in vivo allergic and immunization models, anti-viral vaccination and challenge, as well as in vitro assays. Results: Maternal schistosomiasis altered CD4+ responses during allergic sensitization and inflammation in lungs, with skewed IL-4/B-cell-dominant response to antigenic challenge in priming lymph nodes. CD8+ T cell responses was also altered during immunization, dependent upon vaccine formulation, and modified efficacy of vaccination against viral infection in a murine Hepatitis B virus model. Modified CD8+ responses were associated with an altered dendritic cell phenotype sustained into adulthood, providing evidence for complex priming effects imparted by infection via fetomaternal crosstalk. Conclusions: We observed that transgenerational imprinting can modify T cell responses, altering sensitivity to unrelated allergens as well as limiting protective antiviral vaccine efficacy. Mechanistically, we identify a regulatory network consisting of a deviated IL-4/B-cell axis and a modified DC phenotype sustained into adulthood, with evidence of innate training pointing to complex immunological interactions imprinted during early life exposure.

P49 Laboratory mice with a wild microbiota generate strong allergic immune responses

Junjie Ma[1], Cajsa Classon[1], Julian M. Stark[1], Muzhen Li[1], Huey-Jy Huang[2], Susanne Vrtala[2], Stephan P. Rosshart[3,#], Susanne Nylén[1,#], Jonathan M. Coquet[1,#]
[1]Department of Microbiology, Tumor and Cell Biology (MTC), Karolinska Institutet, Solnavägen 9, Stockholm 17165, Sweden,
[2]Division of Immunopathology, Department of Pathophysiology and Allergy Research, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria
[3]Medical Center - University of Freiburg, Department of Medicine II, Gastroenterology, Hepatology, Endocrinology, and Infectious Diseases, Freiburg, Germany.

Allergic disorders are caused by a combination of hereditary and environmental factors. The hygiene hypothesis postulates that early life microbial exposures impede the development of subsequent allergic disease. However, unambiguous evidence that microbes reduce the development of allergic disorders is still lacking. Recently developed 'wildling' mice contain a rich and diverse commensal as well as a pathogenic repertoire of microbes typically encountered in the wild. Here, we probed the hygiene hypothesis by comparing the development of allergic inflammation in wildlings to that of genetically identical mice lacking diverse microbial exposure. We find that wildlings develop stronger allergic inflammation in response to house dust mites with allergic T cell responses driven not only by cognate peptide antigens, but also by innate cytokines. In all, the results suggest that high microbial content and diversity potentiates, rather than restricts, allergic immune responses.

P50 Control of systemic eosinophilia by a protozoan commensal dictates asthma severity.

Kyle Burrows[1], Louis Ngai[1], Pailin Chiaranunt[1], Eric Cao[1], Catherine J. Streutker[2]and Arthur Mortha[1]
[1]Department of Immunology, University of Toronto, Toronto, ON, Canada.
[2]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada

The local composition of immune cells within any given organ determines its susceptibility to infections and autoimmunity. The intestinal microbiome, a collection of bacteria, viruses, fungi and commensal protozoa, shapes the phenotype, function and abundance of adaptive and innate immune cells inside and outside of the intestinal tract across multiple gut-tissue axes. During asthma, group 2 innate lymphoid cells (ILC2), T helper (h) cells, B cells and eosinophils show marked alterations in function and abundance, collectively promoting the pathology of this disease. Here, we report for the first time, that the murine protozoan commensal Tritrichomonas musculis (T.mu) imprints a lung-specific immune landscape after colonizing the intestinal tract. Following permanent engraftment as a new member of the gut microbiota, mice carrying T.mu did not develop spontaneous asthma, despite showing significantly elevated levels of lung eosinophils. This adaptation in the local lung immune landscape was driven by a tripartite interaction of gut-derived, migratory ILC2s, and lung-resident Th cells and B cells. Mechanistically, locally activated, gut-resident ILC2s, migrated to the lung to promote eosinophil accumulation through an ICOS/ICOSL-dependent pathway. Strikingly, ILC2s were not sufficient to facilitate local eosinophilia in the lung and required interactions between Th cells and B cells to facilitate the protozoan-driven immune adaptation. Lastly, the permanent remodeling of the lung immune landscape following protozoan colonization, exacerbated the house dust mite-induced allergic airway inflammation. Collectively, our data demonstrates, that a gut commensal protist, as a permanent member of the gut microbiome, changes the lung immune landscape across the gut-lung axis via engagement of a tripartite immune network of lymphocytes to exacerbate allergic airway inflammation.

P51 Infection array – using the xMAP® technology for developing an immunological tool to screen antibody signatures of major bacterial pathogens

Nicole Normann[1,a], Matthias Gründling[2], Tanja C. Meyer[3,b], Stephan Michalik[3], Uwe Völker[3], Barbara M. Bröker[1], Silva Holtfreter[1], Dina Raafat[1,4]
[1] Department of Immunology, Institute of Immunology and Transfusion Medicine, University Medicine Greifswald, 17475 Greifswald, Germany
[2] Department of Anaesthesiology and Intensive Care Medicine, University Medicine Greifswald, 17475 Greifswald, Germany
[3] Department of Functional Genomics, Interfaculty Institute for Genetics and Functional Genomics, University Medicine and University Greifswald, 17475 Greifswald, Germany
[4] Department of Microbiology and Immunology, Faculty of Pharmacy, Alexandria University, 21521 Alexandria, Egypt
[a] current affiliation: Department of Obstetrics and Gynecology, University Medicine Greifswald, 17475 Greifswald, Germany
[b] current affiliation: Robert Koch Institute, 13353 Berlin, Germany

With an ever-increasing global threat of antibiotic resistance, an accurate pathogen identification is of paramount importance for the development of effective therapeutic interventions. However, pathogen detection by conventional microbiology and sequence-based tests still show major shortcomings regarding sensitivity, specificity and clinical relevance. Hence, we propose to complement these established diagnostic tools with a culture-independent serology-based approach ("infection array") for pathogen diagnostics in patients with suspected sepsis. Patients tend to develop an antibody response during infection that is highly spe-