DENDRITIC CELLS
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M.45. TL1A Expression is Induced During Dendritic Cell Differentiation

Rivkah Gonsky, Richard Deem, Stephen Targan
Cedars Sinai Medical Center, Los Angeles, CA

IFN-γ plays a central role in generation and perpetuation of mucosal inflammation in IBD. TL1A synergizes with IL-12 and IL-18 to augment IFN-γ production. Enhanced TL1A expression is detected in IBD with a strong *TL1A* SNP association reported in Crohn's disease. TL1A expression is induced in peripheral monocytes and *in vitro* derived dendritic cells (DC) however, the molecular mechanisms remain poorly defined. The human monocytic cell line, KG-1, provides a model for DC differentiation. KG-1 develop DC-like cytoplasmic projections following PMA/ionomycin activation. A parallel induction of membrane TL1A and mRNA is observed. *TL1A* mRNA expression is detectable within 2 h and peaks at 8 h following stimulation. A similar kinetics of *TL1A* mRNA is seen following PMA/ionomycin stimulation of peripheral monocytes. DC maturation of KG-1 functionally enhances cytokine-induced IFN-γ production in $CD4^+$ T cells. LPS treatment of KG-1 results in further DC maturation and additional enhancement of TL1A expression. Transient transfection of *TL1A* promoter-constructs up to 1.5 kb in length reveals up to 90 fold enhanced expression compared to the promoterless vector. DC differentiation is accompanied by upregulation of nucleo-protein binding to a putative *TL1A* NFκB site as detected by EMSA analysis. Binding is competed by excess unlabeled wt *TL1A* NFκB, but not mutant, oligonucleotide and is likewise attenuated following proteasomal inhibition by MG132. Our data suggests that in the human monocytic KG-1 cell line, differentiation of immature cells towards a mature DC phenotype is associated with functional upregulation of surface TL1A expression and binding of NFκB to the *TL1A* promoter. These studies provide a molecular basis for future studies which may help elucidate the mechanism modulating TL1A expression during DC maturation.

M.46. Human Metapenumovirus Glycoprotein G Inhibits Immune Responses in Monocyte Derived Dendritic Cells in TLR 4 Dependent Mechanism

Deepthi Kolli, Xiaoyong Bao, Tianshuang Liu, Roberto Garofalo, Antonella Casola
University of Texas Medical Branch, Galveston, TX

Human metapneumovirus (hMPV), is a major cause of upper and lower respiratory infections in children and adults. Recent work from our group demonstrated that G protein of hMPV is an important virulence factor, responsible for inhibiting innate immune responses to hMPV infection in airway epithelial cells using recombinant hMPV lacking G protein expression (rhMPV-ΔG). Myeloid dendritic cells (DCs) are potent antigen presenting cells and play a major role in initiating and modulating the innate and adaptive immune responses. In this study we found that rhMPV-ΔG infected monocyte derived DCs (MoDC) produced higher levels of cytokines such as IL-6, IL-8, IL-10, TNF-α and chemokines such as MIP-1α, MIP-1β, and RANTES compared to cells infected with the wild type virus (rhMPV-WT), suggesting that G plays an inhibitory role in viral-induced inflammatory responses in MoDCs. We also found that inhibition of TLR 4 expression in MoDCs by siRNA significantly blocked hMPV-induced chemokine and type I interferon gene transcription, compared to cells transfected with control siRNA. To investigate whether the inhibitory role of G was TLR 4-dependent, we treated MoDCs with the TLR 4 agonist LPS following infection with recombinant viruses, WT or ΔG. We observed that LPS-induced cytokine and chemokine production was significantly inhibited by infection with rhMPV-WT, while little or no inhibition was observed when cells were infected with rhMPV-ΔG. Our results suggest that G protein inhibits the production of pro-inflammatory cytokines and chemokines in MoDCs by affecting TLR 4-mediated signaling pathway.

M.47. Toll-like Receptors Signals "Educate" Dendritic Cells to Imprint Gut-homing T Cells

Wang Sen[1], Villablanca Eduardo[1], Daniel Gomes[3], Deanna Nguyen[1], Scott Snapper[1], Hans-Christian Reinecker[1], Ramnik Xavier[1], Yair Benita[1], Cathryn Nagler[1], Nir Hacohen[1], Jonathan Kagan[2], Bartira Rossi-Bergmann[3], J. Rodrigo Mora[1]
[1]*Massachusetts General Hospital, Harvard Medical School, Boston, MA;* [2]*Children's Hospital, Harvard Medical School, Boston, MA;* [3]*Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil*

Migration ("homing") of lymphocytes to the intestinal mucosa is essential for both normal and pathological immune responses. We and others have shown that dendritic cells from gut-associated lymphoid tissues (GALT-DC) induce gut-homing receptors (CCR9 and alpha4/beta7) on lymphocytes upon activation. This tissue-specific property of GALT-DC depends on their selective capacity to produce retinoic acid (RA), a vitamin A metabolite. However, a key unresolved question is how GALT-DC are programmed to synthesize and secrete RA and hence, imprint gut-homing lymphocytes. Since the intestinal mucosa is constantly exposed to Toll-like receptor (TLR) agonists derived from commensal bacteria, we hypothesized that TLR signals are important for conferring GALT-DC with gut-homing imprinting capacity. Here we show that GALT-DC isolated from MyD88-deficient mice (which are deficient in most TLR signals) expressed lower levels of retinal dehydrogenase (raldh, critical enzymes for RA synthesis) mRNA and exhibited a decreased capacity to induce gut-homing receptors on activated T cells as compared to wild type GALT-DC. Importantly, pre-treatment of spleen-DC with TLR-agonists was sufficient to induce raldh 1 and 2 mRNA expression and to confer these extra-intestinal DC with gut-homing imprinting potential. Thus TLR signals appear to be necessary and sufficient to "educate" DC with gut-homing imprinting capacity.

M.48. Oral Immunization with OVA Plus CT Induces Hyper IgA Ab Responses, Inflammatory Cytokines and Foxp3 Expressing CD4+ T cells in the Intestinal Lamina Propria of PIR-B Deficient Mice

Ryoki Kobayashi[1], Hiromi Kubagawa[2], Toshiyuki Takai[3], Shinichi Sekine[1], Keiko Fujihashi[1], Rebekah Gilbert[1], Yoshiko Fukuyama[1], Tetsuro Kono[1], Jerry McGhee[1], Kohtaro Fujihashi[1]
[1]Immunobiology Vaccine Center, Birmingham, AL; [2]University of Alabama at Birmingham, Birmingham, AL; [3]Tohoku University, Sendai, Japan

Paired immunoglobulin-like receptors (PIR) of activating (PIR-A) and inhibitory (PIR-B) isoforms are expressed by many hematopoietic cells. In this study, we examined influence of PIR-B deficiency in mucosal immunity. PIR-B knockout (KO) and C57BL/6 mice were orally immunized with ovalbumin (OVA) plus cholera toxin (CT) three times at weekly intervals. Increased levels of Ag-specific secretory IgA and plasma IgE antibody (Ab) responses were seen in PIR-B KO mice when compared with controls. Further, increased levels of IL-5, IL-17, TNF-α and Foxp3 expressing $CD4^+$ T cells were seen in the intestinal lamina propria (iLP) of PIR-B KO mice. Since mucosal DCs play key roles in the induction and regulation of mucosal immunity, inflammation and tolerance, we characterized DC phenotype and function. A higher number of mature-type $CD11b^+$ DCs was seen in iLP of PIR-B KO mice than that of controls. In addition, DCs from PIR-B KO mice given oral OVA plus CT preferentially induce Foxp3 but not IL-17 and TNF-α expressing OVA-specific $CD4^+$ T cells. Taken together, $CD11b^+$ DCs in PIR-B KO mice play an essential role in the induction of Treg cells in order to control the inflammatory responses. Supported by NIH grants AG025873, DE12242 and AI42127.

M.49. Optimization of Clinical Grade Human Tolerogenic Dendritic Cells Culture Conditions for the Treatment of Crohn's Disease Patients

Julian Panes[1], Carolina España[2], Elena Ricart[1], Daniel Benitez Ribas[2]
[1]IDIBAPS. Hospital Clinic, Barcelona, Spain; [2]CIBEREHD, Barcelona, Spain

Intorduction: Crohn's disease (CD) is characterized by inappropriate responses to self-constituents or innocuous antigens leading to chronic inflammation. Dendritic cells (DCs) are crucially involved in generating tolerance against self/harmless antigens. This tolerogenic ability indicates a potential and novel therapy for autoimmune diseases to silence unwanted immune reactions. The aim of this study was to compare and characterize the tolerogenic properties of human DCs, generated in clinical grade culture conditions. Methods: DCs were generated in vitro from isolated monocytes from healthy donors. Tolerogenic agents: Dexamethasone (Dex), Vitamin D3 (VitD3) or rhIL-10 were added to the DCs. DCs were further activated by adding LPS or a cocktail of cytokines. Phenotype, cytokines secretion and their immunogenicity (T cell alloresponse) were evaluated to sort out the best culture condition. Results: The three tolerogenic agents tested were equally potent to inhibit the expression of costimulatory molecules on DCs and the alloresponse induction. However, the IL-10 secretion was increased when Dex or VitD3 were present. Conclusion: Dex or VitD3 potently induced tolerogenic DCs following clinical grade culture condition, in terms of phenotype, effect on T cell alloresponse and IL-10 secretion. We are currently exploring both tolerogenic agents before starting a clinical trial in CD patients.

M.50. Immune-modulating Effects of Lactic Acid Bacteria on Dendritic Cells: Direct Contact Versus Transwell Coculture System

Petra Klein, Ibrahim Elmadfa
University of Vienna, Vienna, Austria

Background: Lactic acid bacteria are permanent components of the microflora in the human gut, but separated from antigen-presenting cells, e.g. dendritic cells (DC) by the intestinal epithelial barrier. The objective of this study was to investigate the effects of lactobacilli on DC maturation in two different *in vitro* models. Methods: Human monocyte-derived DC were incubated with Lactobacillus delbrueckii and Lactobacillus rhamnosus for 24 h with direct contact and separated by a differentiated Caco-2 cell barrier in a transwell coculture system. The expression of specific surface markers (CD86/80/54/209/HLA-DR) was detected by flow cytometry. Cytokine levels (IL-1beta/-10/-12/TNF-alpha/Interferon-gamma) from cell-culture supernatants were analyzed by Cytometric Bead Array. Results: Direct contact of immature DC with both Lactobacilli caused an increased expression of the surface markers CD86, CD80, CD54 and HLA-DR and a down-regulation of CD209. Further, both strains induced an increase of the cytokines IL-1beta, IL-10, TNF-alpha, IL-12 and Interferon-gamma. Stimulation of DC through a differentiated Caco-2 monolayer in the transwell coculture system did not have an effect on the surface marker expression and the cytokine secretion of the cells. Conclusion: These results demonstrate that both tested Lactobacillus strains have a stimulating effect on DC maturation and cytokine production after direct contact only.

M.51. Cytofluorometric Characterization of Dendritic Cells from Human Mesenteric Lymph Nodes

Arwed Hostmann[1], Marianne Beutner[1], Kerstin Kapp[1], Jörg-Peter Rit[1], Anton Kroesen[3], Christoph Loddenkemper[1], Ralf Ignatius[1], Rainer Duchmann[2], Martin Zeitz[1], Reiner Ullrich[1]
[1]Charite, Berlin, Germany; [2]Hospital zum Heiligen Geist, Frankfurt, Germany; [3]Krankenhaus Porz am Rhein, Köln, Germany

Based on findings from murine models, dendritic cells (DC) in mesenteric lymph nodes (MLN) play an essential role in mucosal immunity but human studies are rare. To compare human DC subpopulations from MLN and peripheral blood (PB), mononuclear cells were isolated by ficoll density gradient centrifugation following collagenase D digestion from MLN of patients undergoing colon resection (6 f, 6 m; age 21-82 years), PB from intestinal bowel disease (IBD) patients (1 f, 1 m, 27-47 years) and PB from healthy volunteers (4 f, 2 m; age 24-56 years). Myeloid DC (mDC,

CD14-CD19-CD11c+BDCA-1+) and plasmacytoid DC (pDC, CD14-CD19-CD11c-BDCA-2+) were analyzed by flow cytometry. Except CD86, CD40, CD80, CD83, CD86, DC-SIGN and CD103 were expressed more frequently on MLN mDC compared to other DC populations. CCR6 and CX3CR1 were more frequent on MLN mDC than MLN pDC, whereas CCR7 was most frequent on PB pDC. Interestingly, within the markers found to be increased on MLN mDC, only CD40 was also increased on PB mDC from IBD patients vs. PB mDC from healthy volunteers. Thus, our findings indicate functional differences between mDC from MLN and PB rather than differences due to disease conditions present in patients undergoing colon surgery.

M.52. Parallels Between Respiratory and Gastrointestinal Viral Infection on Rodent Lamina Propria Dendritic Cells

Xiuxu Chen, Sarah Ehlenbach, Mitchell Grayson
Medical College of Wisconsin, Milwaukee, WI

Respiratory viral infections induce marked reduction in conventional dendritic cells (cDC) and a rapid increase in plasmacytoid dendritic cells (pDC). With respiratory viral infection both lung cDC and pDC express FceRIa, the high-affinity IgE receptor, and expression on cDC has been shown to be necessary to translate respiratory viral infections into atopic disease. It is not known if a gastrointestinal viral infection induces similar changes in lamina propria cDC and pDC. C57BL6 mice were infected with Mouse Norovirus-1 (MNV) or UV inactivated MNV and single cell suspensions from the lamina propria examined by flow cytometry. CD11c expressing cDC were primarily CD11b+CD8a-; with MNV infection their frequency was reduced acutely. In contrast, PDCA-1+ pDC frequency was markedly increased with MNV inoculation. Similar to the lung, cDC expressed FceRIa more highly following MNV infection; however, unlike the lung, pDC did not express FceRIa. Expression of the low affinity receptor for IgE, CD23, was also found to increase on cDC with MNV infection. Whether lamina propria cDC expression of FcεRI and CD23 links viral infection to atopic disease remains to be determined, but these data suggest a potentially novel mechanism for the development of gastrointestinal allergic diseases.

M.54. The Role of *Campylobacter Jejuni* Lipooligosaccharide (LOS) and Flagella in Phagocytosis by Human Monocyte-derived Dendritic Cells

Holly Stephenson[1], Dominic Mills[2], Nick Dorrell[2], Keith Lindley[1], Mona Bajaj-Elliott[1]
[1]Institute of Child Health, London, United Kingdom; [2]London School of Hygiene and Tropical Medicine, London, United Kingdom

Invasion of the gastrointestinal epithelium by *Campylobacter jejuni* results in pathology of the dysenteric form of infection. *C. jejuni*-mediated effects on epithelial innate immunity are well documented, however little is known about the interaction between the bacteria and the underlying Dendritic Cells (DCs). DCs are critical in activating adaptive immunity, which in turn amplifies innate response(s) that may result in bacterial clearance or pathogenic inflammation. The availability of isogenic LOS and flagella mutants of wild-type 11168 strain allowed us to investigate the role of these key structural components in phagocytosis by DCs. Immature DCs were generated by extracting monocytes from healthy volunteers and stimulating the cells with IL-4 and GM-CSF for 6 days. Time-dependent association of FITC-labelled WT and mutant *C. jejuni* with DCs was monitored by flow cytometry. Gentamicin protection assay allowed quantification of viable, internalized bacteria. Differential upregulation of maturation markers was observed between WT and mutant strains. Preliminary studies implicate that both the LOS and flagella of *C. jejuni* may contribute to early DC-pathogen interactions. Downstream signaling events activated upon engagement of *C. jejuni LOS* and flagella mutants are currently under investigation.

M.55. The A2B Adenosine Receptor Stimulates Dendritic Cell IL-6 and Promotes De Novo Generation of Th17 Cells

Jeffrey Wilson, Steven Black, Joel Linden, Peter Ernst
University of Virginia, Charlottesville, VA

Differentiation of naïve CD4+ T lymphocytes into appropriate effector subsets is an important event in generating protective immune responses. Host factors that control the development of IL-17 secreting CD4+ T cells (Th17 cells), which are constitutively present in intestinal lamina propria, remain poorly defined. Here we report that adenosine promotes Th17 responses by acting on dendritic cell (DC) adenosine A_{2B} receptor (A_{2B}AR). Naïve CD4+ T cells co-cultured with DC in the presence of the non-selective adenosine analogue NECA results in the differentiation of IL-17 secreting cells and elevation of mRNA encoding signature Th17 molecules such as IL-22 and ROR-γT. Specific experiments suggest that: 1) the effect is mediated via the DC; 2) the A_{2B}AR is largely responsible 3) intestinal DC preparations also express A_{2B}AR and; 4) the effect is associated with specific mediators. For example, the induction of Th17 cells is dependent on the presence of IL-6 and TGF-β-conditions which are selected by NECA-treated DC. Furthermore, in co-culture experiments the induction of adaptive FoxP3+ Treg by TGF-β1 is blocked by NECA and Th17 cells emerge. Although previously implicated in Treg development and function, these data suggest that under some circumstances adenosine acts via DC A_{2B}AR to favor the Th17 lineage.

M.56. Modulation of Human Monocyte and Lamina Propria Derived Dendritic Cell IL-12/IL-23 Axis in Response to *Campylobacter Jejuni*: Impact on T Cell Mediated Immunity

Lindsey Edwards[1], Kiran Nistala[1], Dominic Mills[2], Nick Dorrell[2], Keith Lindley[1], Lucy Wedderburn[1], Mona Bajaj-Elliott[1]
[1]Institute of Child Health, London, United Kingdom; [2]London School of Hygiene and Tropical Medicine, London, United Kingdom

Introduction: In recent years it has become increasingly apparent that microbes can differentially regulate the expression

of DC-derived IL-12 and its related family members (IL-23, IL-27 and IL-35); an immune axis that has a major impact on downstream T cell responses. The molecular nature of these interactions and subsequent T-cell responses to Campylobacter infection has not been studied to date. Methods: The effect of *C. jejuni* infection on IL-12/IL-23 immune axis in human monocyte-derived DCs (mDCs) and in lamina propria mononuclear cells (LPMCs) was investigated. The levels of DC cytokine expression were investigated via RT-PCR and ELISA. The effect of the DC derived cytokine mileu on TH17/IFNγ expansion was also investigated by Flow cytometry and ELISA. Results and Discussion: mDCs produced IL-12/IL-23 in response to Campylobacter infection, as did LPMCs although to a lesser magnitude. These results suggest that mucosal IL-12 and IL-23 production could be the result of sensing of *C. jejuni*, by resident DCs. Allogeneic T cells exposed to supernatants from *C. jejuni*-infected DCs showed expansion of both Th-1 and Th-17 single- and double-positive cells. In summary, the balance between the two arms may prove to be the defining point between successful bacterial clearance and protective immunity in a healthy host versus skewing towards a autoimmune response leading to disease.

M.57. Thymus and Activation Regulated Chemokine Deficient Animals are Protected in Murine Experimental Colitis

Antonia Faul, Alexander Heiseke, Anne Krug, Wolfgang Reindl
TU München, Munich, Germany

Background: Thymus and activation-regulated chemokine (TARC) is expressed by non-splenic conventional dendritic cells after stimulation by various TLR ligands and TNF-α. It attracts CCR4 positive cells to sites of inflammation. Results: To investigate the role of TARC in the context of experimental colitis we induced transfer-colitis by injecting CD4+CD62L+ T-cells into TARC-RAG double deficient animals and RAG deficient controls. TARC-RAG deficient animals lost significantly less body weight than RAG-deficient animals. Blinded analysis of colonic histology samples revealed enhanced mucosal regeneration in TARC-RAG deficient animals. Furthermore RT-PCR data indicate that in TARC-RAG deficient animals mRNA levels of IL-22 and NKp46 were strongly increased very early in the course of experimental colitis. In contrast, IFN-γ and Il-17 mRNA was upregulated in control animals. FACS analysis of isolated mesenteric lymph node, intraepithelial and lamina propria lymphocytes showed no difference in the recruitment of Foxp3+ regulatory T-cells. Summary: We hereby demonstrate that TARC deficient animals are less susceptible to T-cell transfer induced colitis than wild type mice. We argue that this is due to the secretion of protective cytokines by NKp46 positive cells that are normally suppressed or differentially regulated by TARC secreting dendritic cells.

M.58. CD11b+αL+ Dendritic Cells Play Crucial Roles in the Induction of Antigen-specific Mucosal IgA Antibody Responses against Recombinant Salmonella

Tomomi Hashizume, Tomoko Kurita-Ochiai, Masafumi Yamamoto
Nihon University School of Dentistry at Matsudo, Chiba, Japan

Previous study has revealed that PP are an essential site for the induction of mucosal IgA, but not systemic IgG, immunity against orally administered recombinant *Salmonella* expressing fragment C of tetanus toxin (r*Salmonella*-Tox C). This study further elucidated the role of PP in the induction of intestinal IgA responses. The results showed that the numbers of CD11c+CCR7+ DCs in MLN, but not spleen, of PP-null mice orally given r*Salmonella*-Tox C were lower than those of normal mice. On the other hand, oral immunization of normal mice with r*Salmonella*-Tox C resulted in the increased numbers of CD11c+CD11b+αL+ DCs in MLN and PP, but unchanged in ILF. These findings imply that this DC subset in PP migrates to MLN for induction of IgA immunity against r*Salmonella*-Tox C. Interestingly, however, PP-null mice also showed the increased numbers of CD11c+CD11b+αL+ DCs in MLN when given r*Salmonella*-Tox C, although Ag-specific mucosal IgA responses were not induced. Furthermore, the number of this DC subset was markedly increased in ILF, suggesting that CD11c+CD11b+αL+ DCs in ILF traffic to MLN. Taken together, these results suggest that CD11c+CD11b+αL+ DCs in PP, but not ILF, migrate to MLN in a CCR7-dependent manner for the induction of Ag-specific intestinal IgA immunity.

M.59. PPAR-gamma Activation Induces a Mucosal Phenotype in Dendritic Cells

Halide Tuna, Vishal Sindhava, Margarita Avdiushko, Charlotte Kaetzel, Subbarao Bondada, Donald Cohen
University of Kentucky, Lexington, KY

Tight regulation of the mucosal immune system is necessary to prevent damaging responses toward food antigens and commensal bacteria. In the intestine, mucosal dendritic cells (DCs) have a central role in antigen-specific stimulation of T cells and B cells. We investigated the role of peroxisome proliferator-activated receptor gamma (PPARg), a nuclear receptor family member, in regulation of DC phenotype and function. Activation of PPARg in bone marrow-derived DCs (BMDCs) induced IL-10 secretion and reduced expression of CD80 and CD86. PPARg activation also induced arginase I and reduced Nos2 gene expression. PPARg activation in BMDCs decreased IL-6 and TNF-alpha production in response to the commensal bacterium, Bacteroides thetaiotaomicron. LPS-matured, but not immature BMDCs were able to induce naïve T cell proliferation in a mixed lymphocyte reaction and activation of PPARg inhibited this BMDC function. Immature PPARg-activated BMDCs decreased naïve B-cell proliferation. In contrast, mature PPARg-activated BMDCs promoted LPS-stimulated B cell proliferation and IgA production. Finally, PPARg activation of mature BMDCs significantly enhanced both B cell proliferation and

IgA secretion. These data indicate that activation of PPARg in DCs induces a mucosal phenotype which inhibits inflammatory immune reactions and promotes mucosal IgA production. (H.T and V.S contributed equally to these studies.)

M.60. The Effect of Virulent Human Rotavirus Challenge on TLR3 and 4 Expression and Plasmacytoid Dendritic Cell Distribution in Gnotobiotic Pigs Vaccinated with Rotavirus-like-particles (VLPs)

Anastasia Vlasova, Marli Azevedo, Hugo Resque, Adam Hartzler, Linda Saif
Ohio State University, Wooster, OH

To investigate innate vaccine- and virulent human rotavirus (VirHRV)- induced immunity, we evaluated frequencies and distribution of plasmacytoid dendritic cells (pDC) and TLR (2,3,4,9) expressing mononuclear cells (MNCs) in ileum, spleen and blood of gnotobiotic pigs vaccinated with rotavirus-like particle (VLP) vaccines and challenged with VirHRV. Frequencies of pDCs (CD4+/SWC3a+) and MNCs expressing TLRs were measured before (PID28/PCD0) and after (PID35/PCD7) VirHRV challenge using antibodies to human TLRs and to porcine SWC3a, CD4, CD3 and CD8 markers in flow cytometry. As expected 2–3-dose VLP vaccines (lack dsRNA) did not affect TLR3/4 MNC or pDC frequencies at PID28, whereas at PCD7 to VirHRV, we observed substantially increased frequencies of TLR3+ MNCs in gut and pDCs in spleen but not in ileum or blood. TLR3 expression was not strongly associated with any markers tested suggesting that a mixed MNC population in ileum expresses TLR3. TLR4 expressing MNCs were mainly CD4+ (SWC3a-/CD3-/CD8-) and inexplicably decreased in all tissues tested [concomitant with systemic depletion of CD4+ cells] after HRV challenge. TLR2/9 expressing MNCs were not detected. Our findings demonstrate limitations of VLP-based vaccines in stimulation of innate immunity and highlight the effect of VirHRV versus nonreplicating VLPs on distinct MNC populations.

M.61. Uterine Epithelial Cells Regulate the Differentiation and Toll-like Receptor Mediated Activation of Human Dendritic Cells

Daniel Ochiel, Mimi Ghosh, John Fahey, Paul Guyre, Charles Wira
Dartmouth College, Lebanon, NH

Introduction: The balance between immunity and tolerance in the human female reproductive tract (FRT) is governed by the dynamic interactions of uterine epithelial cells (UEC) and immune cells including Dendritic cells (DCs). In this study, we have defined the role of uterine epithelial cells in the differentiation and activation of DCs. Methods: UEC were isolated and grown to confluence on cell inserts. Conditioned medium (CM) from epithelial cells was harvested after 24 hr of culture. DCs were differentiated from monocytes in the absence (Control DC) or presence (CM-DC) of CM. DCs were activated with TLR3 agonist, poly I:C or TLR4 agonist (LPS) for 48 hr prior to FACS analysis. Results: UEC CM significantly lowered surface expression of CD86 on DCs. Upon activation, surface expression of CD80, CD86 and CD83 were significantly lower on CM-DC relative to controls. Further, when RNA was analyzed by real time PCR, DCs differentiated with CM had significantly higher expression of Indoleamine 2,3-Dioxygenase (IDO). Conclusion: Our results provide evidence for the regulation of DCs by UEC. These findings suggest a novel mechanism for the regulation of adaptive immunity within the FRT. Supported by NIH grant AI51877, AI-071761 (CRW).

M.62. Differential Regulation of Adipokines by Nuclear Receptor Ligands in Bone Marrow-derived Dendritic Cells

Razvan Arsenescu, Violeta Arsenescu, Halide Tuna, Margarita Avdiushko, Willem de Villiers, Donald Cohen
University of Kentucky, Lexington, KY

Dendritic cells (DCs) are paramount for detection of microbial infection and response to foreign antigen (Ag). During Ag presentation, the maturation state of DCs determines the differentiation of T cells toward Th1, Th2, Th17 or Treg. Adipocytes can also sense microbial antigen via engagement of Toll-like receptors leading to release of immunomodulatory factors like adiponectin and angiotensinogen. We hypothesized that ligands for PPARγ and retinoic acid (RA) may affect adipokine synthesis by DCs and alter their functional phenotype. Bone marrow derived murine yeloid DCs were cultured in the presence of PPARγ and RXRα nuclear receptors agonists rosiglitizone (Rosi) and 9-cis-retinoic acid (9cRA). Both ligands upregulated adiponectin and adiponectin receptors (AR1/2) while angiotensinogen, angiotensin converting enzyme and angiotensin receptor 1 (AT1) were downregulated. Interestingly LPS or anti-CD40L had the opposite effect and PPARγ /RA treatment reverses the adipokine balance. PPARg activated AMPK downstream of adiponectin receptors. DC expression of Th1 and Th2 cytokines correlated with angiotensin and adiponectin respectively. We conclude that and RXRα agonists induce the anti-inflammatory cytokines adiponectin and IL-10 during classical activation of DCs. High AR2 and low AT1 expression define a sub-population of IL10-producing DCs. Supported by Broad Foundation, CCFA, NIH.

M.62.5. Regulation of Humoral and Cellular Gut Immunity by Lamina Propria Dendritic Cells Expressing Toll-like Receptor 5

Satoshi Uematsum Shizuo Akira
Osaka University, Osaka, Japan

While intestine maintains homeostasis by immunological tolerance, it properly induces immune responses by recognizing the invasive pathogens. However, it remains unknown what kinds of cells in the intestine initiate immune responses and how they activate host immunity. Recently, we showed that CD11c+ lamina propria cells (LPCs) in intestine express high amounts of Toll-like receptor (TLR) 5 and induce inflammatory responses when stimulated with the TLR5 ligand bacterial

flagellin. CD11c+ LPCs consist of four subsets distinguished by differential expression patterns of CD11c and CD11b. Here, we identify a subset of CD11chighCD11bhigh LPDCs as TLR5-expressing cells. When stimulated by the TLR5 ligand flagellin, TLR5+ LPDCs induced differentiation of naïve B cells into immunoglobulin A (IgA)-producing plasma cells; this plasma cell generation took place in a gut-associated lymphoid tissue (GALT)-independent fashion. In addition, in a manner dependent on TLR5 stimulation, these LPDCs promoted differentiation of antigen-specific TH-17 and TH1 cells. Unlike spleen DCs, LPDCs specifically produced retinoic acid, which, in a dose-dependent manner, supported the generation and retention of IgA-producing cells in the LP and positively regulated TH-17 cell differentiation. These findings reveal unique properties of LPDCs and the importance of TLR5 for adaptive immunity in the intestine.