

European Mucosal Immunology Group (EMIG) meeting 2012

Conference report

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This year's EMIG meeting (organized by Edward Lavelle) was held at the Burlington hotel in Dublin, Ireland from the 10th-13th October 2012. The conference started off with a keynote lecture by **Jan Holmgren** (Univ. of Goteborg, Sweden) who addressed the challenges in the development of mucosal vaccines. He highlighted the lack of good animal models and basic problems like tolerance induction and the lack of correlates of successful protection that need to be overcome. He mentioned the practical challenges of mucosal vaccines, e.g. how to measure the immune response and the importance of safe mucosal adjuvants. He pointed out that protection of mucosal vaccines also needs to be seen with regard to "herd protection" which can greatly increase a vaccine's overall protection within a population. Another aspect of the talk was the different levels of protection induced by mucosal vaccines in developed and developing countries. In the later, vaccines are often less effective. This problem might be due to a competing gut flora, topical enteropathies, nutritional factors, helminth infections or immunological ignorance/ exhaustion (a state in which the immune system is overwhelmed with antigens and does not adequately respond). Next, **Luke O'Neill** (Trinity College Dublin) gave a talk on innate sensing at mucosal surfaces. The first part of the talk addressed the different effects that TLRs have on gut epithelium in comparison to the TLRs in intestinal macrophages. While TLR2 and TLR4 seem to be beneficial in the epithelium for wound healing, they seem to be connected to inflammatory responses in macrophages. Mice lacking the TLR4-adaptor protein Mal are susceptible to more severe DSS-colitis than wild type mice and have decreased control over a Salmonella infection since macrophages do not respond properly. Mal-deficient mice also develop intestinal barrier problems due to defective tight junctions. Luke O'Neil continued his talk by introducing the molecule succinate as a key signal in inflammation. Succinate plays a role in aerobic glycolysis which can be detected in tumor cells and other highly proliferating tissues and also has importance in Th17 cells, activated dendritic cells and macrophages. Succinate increases after LPS stimulation and signals further via PHD, HIF1 and IL1-beta.

Heike Dornhoff (Univ. of Nuremberg) highlighted the role of IL-28A in the gut. Intestinal CD11c+ macrophages and dendritic cells produce IL28A which was shown to enhance proliferation of the gut

epithelium. Mice lacking the IL28 receptor alpha are highly susceptible to colitis. IL28A seems to be important in keeping the intestinal barrier intact and facilitates wound repair of the epithelium.

Michael Schumann (Charité Berlin) gave a talk on IL-22 in the gut. Its receptor, IL22R, is expressed in epithelial cells and myofibroblasts, mainly in the small intestine. In Crohn's disease and colitis the receptor is up-regulated. IL22 seems to have functions in intestinal wound healing and barrier defects. **Alan Mowat** (Univ. of Glasgow) gave an interesting talk on murine gut macrophages. These cells usually do not produce many proinflammatory cytokines. By analyzing expression of the marker CX3CR1 and CD11b different cell subsets can be differentiated and gut macrophages are positive for both markers. The expression level of CX3CR1 defines the colonic macrophage function: CX3CR1⁺⁺ cells express TNF constitutively and IL10, while CX3CR1⁺ cells only express TNF after LPS treatment and much less IL10. During DSS colitis, the CX3CR1⁺⁺ cell subset is reduced while CX3CR1⁺ cells dominate. These cells appear heterogeneous and can be further divided into a small population of Ly6C⁺ MHCII⁻ cells and a larger population of Ly6C⁻ MHCII⁺⁺ cells. Some of the latter are in fact CD11c⁺ dendritic cells. Resting gut macrophages produce mainly IL10, are activated, scavenge invading bacteria and produce trophic factors for the epithelium.

Cornelia Lindner (Hannover Medical School) presented her data on the IgA repertoire in the intestine. She explained that the IgA repertoire expands when the number of bacterial species increases and how a large repertoire depends on a complex microflora. She further demonstrated that expanded and infrequent clones combine to form highly diverse polyclonal IgA repertoires which hardly overlap between individual mice. **Olivier Lantz** (Institute Curie, Paris) gave a talk on mucosal associated invariant T (MAIT) cell. These cells are an evolutionary conserved subset and display a semi-invariant T cell receptor and MR1, a molecule related to the major histocompatibility complex. MAIT cells are CD161⁺⁺, NKG2D⁺, CD45RO⁺ IL2R⁺, IL18R⁺, IL23R⁺. MAIT cells are present in blood, liver and the gut and respond to bacterial infections which makes them an important subset in immunity. **Philippe Jay** (Inserm, France) presented data on Tuft cells, a small population present in the gut epithelium. They make up only 0.4% of epithelial cells in the mouse intestine. The function of Tuft cells is still unknown but they were shown to have apical microvilli and a multivascular cytoplasm. They also express COX-1, villin, and Dclk1 (a protein associated with microtubules). **Andrea Cerutti** (Catalan Institute for Research and Advanced Studies) gave a keynote talk on the immunological function of intestinal mucus. The mucus layer has a firmly attached lower part of about 30 μ M thickness and a more loosely attached upper part of 450 μ M. The mucus over Peyer's patches is less organized than in the rest of the intestine, probably to allow contact of bacteria with M cells and dendritic cells. A prominent protein in mucus is MUC2 which interacts with dendritic cells via carbohydrate receptors. In mice deficient for MUC2, CD103⁺ dendritic cells

produce increased levels of IL12 and IFN γ but low levels of IL10 and Foxp3. This state could be reverted when MUC2 $-/-$ mice received MUC2 protein orally. When dendritic cells interact with MUC2, a reduction in NF κ B activation of the IL12 gene promoter could be detected. Cerutti concluded that MUC2 might be important for enhancing tolerance.

Other highlights of EMIG included a talk from **Per Brandtzaeg** (Univ. of Oslo) who gave an overview of the current understanding of mucosal plasma cells and IgA, and **Frits Koning** (Leiden Univ. Medical Centre) who shed some light on the complexity of Celiac disease. The meeting was closed by **Maria Rescigno** (European Institute of Oncology, Milan) who presented her latest data on gut dendritic cells. Of the different subsets, the CX3CR1 $+$ dendritic cells take up antigen and hand it over to the CD103 $+$ dendritic cells via gap junctions. This process requires the gap junction protein connexin 43. EMIG 2012 was a very well organized and pleasant meeting which sparked interesting discussions amongst all delegates. An important highlight worth mentioning was the social event at the Old Jameson Distillery which included the conference dinner, whiskey tasting and entertainment in this fabulous venue.