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Immunology of Ageing

Abstract

The Immunology of Ageing, Monday, 24 February 2014, 09:00-17:00 at Cineworld: The O2, London, SE10 0DX, UK. This event was part of Euroscicon's 2014 Ageing Summit. The meeting Immunology of Ageing took place at Cineworld: The O2 in London. The Meeting Chairs were Dr. Neil A Mabbott, the Roslin Institute & Royal School of Veterinary Sciences, University of Edinburgh, Scotland, UK and Dr. Milica Vukmanovic-Stejic, Senior Research Fellow, UCL Medical School, London, UK. Different investigators , senior and junior scientists, research managers, research students as well as biotech and pharma industry, i.e. all working with and interested in the immunology field with focus on ageing, were attended the meeting. Senior researchers were invited to give their newest research data, some to be published in the nearest time. The meeting had an informal character, which encouraged and stimulated to discussion. After the lunch break it was an interesting, instructive and rewarding discussion section with all the speakers on stage, not for questions about specific talks, but for a general discussing or specific topics.

Keywords: innate and adoptive immune systems, ageing, immunosenescence, infections, vaccination, autoantibodies

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Abbreviations: FAE, follicle-associated epithelium; CEM, centre experimental medicine; AMD, age-related macular degeneration; CCS,calpain-calpastatin system; NK, natural killer cell; KIRs, killer cell receptors

Meeting Report

The first speaker, Dr. Deborah Dunn-Walters, Dept. of Immunobiology, King´s College London School of Medicine, UK, addressed her talk and discussion about their findings on B cell repertoire changes with age, and different types of B cells that respond to dissimilar types of antigen challenges. Older people are prone to infection, less able to respond well to vaccine and generally have more autoantibodies in their blood. Her research group have studied apparently young and older individuals 65-85 years, with focus on responses of pneumococcal and influenza H1N1 vaccine. They found different spectra-types before and after vaccination when comparing Day 0, Day 7, and Day 28 depending on if the subject was young or old. In summary, they found inappropriate expansions of cells in absence of challenge and decreased diversity, decreased timely proliferative response to challenge- particularly IgA1 expansion and IgM memory activation, alterations in the IgG1/3 IGHV repertoire to become more like that of IgG2/IgM memory, and more IgG2 if you were old. Also, larger CDRH3 size, even in naive/transitional/immature B cells, but not in preB cells, could be seen.[1,2]

One of the chairs continued, Dr. Neil A Mabbott, talking about the mucosal immune system. The gastrointestinal tract is continuously exposed to large amounts of commensal and pathogenic microorganism. It must give an effective immune response against food-borne pathogens and must also recognise the harmless antigens associated with food and develop immunological tolerance against them. He talked about the importance of the transcytosis of antigens across the follicle-associated epithelium (FAE) of Peyer's patches by M cells to get an efficient immune response. His research group has found that M cell density in the FAE of aged mice was dramatically reduced. Ageing also dramatically impaired CCL20 expression by the FAE. The consequences revealed an important aging-related defect in the mucosal immune system´s, and that M cells are important portals of entry for some gut pathogens e.g. prions.[3,4]

Dr. Heping Xu, Centre Experimental Medicine (CEM), Queen's University Belfast Institute of Clinical Science, Ireland, focused his talk on para-inflammation and Age-related Macular Degeneration (AMD). The definition of para-inflammation is an immune response to chronic noxious stimuli at a low magnitude that lies between the basal homeostatic state and overt inflammation. AMD is a multiple factorial disease where genetic and environmental risk factors together with old age are important. AMD affect people over 60 years of age, 15-30% is affected, which means 50 million worldwide, and in UK AMD accounts for up to 50% of all cases of blindness. In the aging retina, the inducers in para-inflammation are mostly oxidative lipids, proteins, and extracellular matrix. The responses are microglial activation, macrophage/microglial sub retinal accumulation and complement activation in order to maintain homeostasis. In aged people the para-inflammatory response is a general phenomenon and the hypothesis is that AMD is caused by the loss of retinal homeostasis during aging.[5]

Next speaker, Professor Jacek Witkowski, Dep. of Pathophysiology, Medical University of Gdansk, Poland, continued with talking about the calpain-calpastatin system (CCS). CCS regulates the activities of signal transduction molecules, receptors, transcription factors and elements of cell division machinery known to be modified by aging. He reported about a recently launched international (Polish-Italian) collaboration named CALPACENT®. The CALPACENT® project aim to assess if the varying activity of CCS of regulatory proteolysis in peripheral blood T lymphocytes may be associated with their ageing-related malfunctioning, thus predicting shorter or longer (ultimately centenarian) life.[6]

Mr. Huayqui Volt Valdivia, Biomedical Research Center, University of Granada, Spain, led us into the studies of the effect of melatonin on the age-dependent dysregulation of the NF-κB/mitochondrion/NLRP3 activation in sepsis. Since the age-related changes of the immune system involve a persistent inflammatory state, it contributes to enhancing the susceptibility of the elderly to several acute and chronic inflammatory diseases, including sepsis. Melatonin has the potential therapeutic value to enhance immune function in aged individuals and in patients in an immunocompromised state.[7] Mr Volt and his study group had explored whether the anti-inflammatory actions of melatonin can protects against NF-κB/NLRP3 activation

in aged mice. The results support NLRP3 inflammasome as a novel molecular signalling pathway during sepsis, identify it as a main target for the anti-inflammatory action of melatonin, and support further studies of potential drug treatment.

After the panel discussion Prof. Ioakim Spyridopoulos, Hon. Consultant Interventional Cardiology, Newcastle University and Freeman Hospital, UK, gave focus on the role of human cytomegalovirus (CMV), which is never cleared from individuals following primary infection. His talk looked into the potential link between an ageing immune system, CMV infection and progression of atherosclerosis. On the Newcastle 85+ study, were the individuals were divided into CMV positive and CMV negative individuals and compared to young individuals, his group has studied the telomere biology and inflammation. They have found that short telomere length predict coronary heart disease, especially cellular changes in the CD8 T cell compartment secondary to CMV.[8]

Dr. James Turner, Dept. of Health, University of Bath, UK, continued to talk about the role of CMV in the ageing process. As part of the discussion panel at the meeting, Dr. Turner raised the question "when does immunological ageing begin?". During his talk, Dr. Turner showed that the rudimentary signs of immunosenescence (i.e. the effect of ageing on human immunity) are apparent in a chronologically young population of healthy CMV+ university students (aged≈22 years), and compared his results with the OCTO/NONA study performed by A. Wikby et al. 2002[9] where the characteristics of the "immune risk profile" were defined. Dr. Turner also presented data showing that infection with CMV amplifies lymphocyte trafficking in response to psychological stress and strenuous exercise.[10] A possible consequence could be that repeated acute stressors in CMV positive people might aggravate inflammatory processes, such as T cell infiltration into atherosclerotic plaques. If proven to be correct, this could provide an explanation for adverse effects of CMV infection with cardiovascular disease.

The last speaker of the day, Dr. Irene Maeva Rea, Queens University Belfast and Belfast Health and Social Care Trust, Northern Ireland, took us into the field of Natural Killer Cells and Cytokine profile. Natural Killer Cell (NK), Killer Cell receptor complexes (KIRs) and associated cytokine profiles are highly effective collaborators in controlling, patrolling and protecting, as she said, our immune landscape. KIR receptors are type 1 transmembrane receptors of the Immunoglobulin Super Family expressed on NK cells, using HLA class I as a ligand on target cells and produce both inhibitory and activation signals. Her studies were based on the subjects from the BELFAST study – Belfast Elderly Longitudinal Free-living Ageing Study. Individuals included in BELFAST are over 80 years of age, apparently well, free-living in the community in the Belfast area, and mentally cognitively competent. Her group has found that there are relationships between NK cells and NK-related subsets, KIR A and KIR B haplogroups and cytokines. The amount of NK cells and proinflammatory cytokines, such as IL -6, increase with age. They have found that there is a global difference in frequency of KIR haplotypes and different haplotype are related to different cytokines.[11] In summary Dr. Rea stated "successful ageing" is to avoid cardiovascular disease, have a competent immunological system, genetic profile, together with a good nutritional profile.

Euroscicon's 2015 Ageing Summit will take place from the 10th-12th February 2015

www.regonline.co.uk/Ageing2015

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Conflicts of Interest

There is no conflict of interest.

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