The Immunology of Ageing

Monday, 24 February 2014 09:00 - 17:00
Cineworld: The O2, London, SE10 0DX, UK

It is clear that the immune system undergoes age-associated alterations, producing a progressive deterioration in the ability to respond to infections and to develop immunity after vaccination. This event will discuss this Immunosenescence, both within the innate and adaptive immune systems. While discussing the mechanisms that contribute to immunosenescence, there will be plenty of networking opportunities and also debate relating to potential therapies that could be employed to help the population live longer, fuller and healthier lives. This event has CPD accreditation. This event is part of the 2014 Ageing Summit: **www.AgeingSummit2014.com**

Meeting Chairs:
Dr Neil A Mabbott, The Roslin Institute& Royal (Dick) School of Veterinary Sciences, University of Edinburgh, Scotland, UK
Dr Milica Vukmanovic-Stejic, Senior Research Fellow, UCL Medical School, London, UK

Who Should Attend
Biotech and Pharma Industry: CEOs, Chief Scientists, Group Heads, Senior and Junior Scientists, Research Managers
Academic and Research Institutes: Group and Lab Heads, Postdoctoral Scientists and Research Students

The deadline for abstract submissions for oral presentation has now passed. Abstracts for *poster presentation only* can be submitted up to two weeks before the event. **You can download the instructions for authors at www.euroscicon.com/AbstractsForOralAndPosterPresentation.pdf**

Talk times include 5 – 10 minutes for questions

9:30 – 10:15 **Registration**

10:15 - 10:30 **Introduction by the Chairs**:
Dr Neil A Mabbott, The Roslin Institute& Royal (Dick) School of Veterinary Sciences, University of Edinburgh, Scotland, UK
Dr Milica Vukmanovic-Stejic, Senior Research Fellow, UCL Medical School, London, UK

10:30 – 11:00 **Old B cells, what are the chances they will help us?**
Dr Deborah Dunn-Walters, Reader in Immunology, Department of Immunobiology, King's College London School of Medicine, UK
A diverse B cell repertoire is essential in order to increase the chances of being able to recognise foreign antigen. At the same time the repertoire has to avoid carrying specificities for self antigens. Older people are more prone to infection, less able to respond well to vaccine and generally have more autoantibodies in their blood. We will discuss this in the context of our findings on B cell repertoire changes with age, and different types of B cells that respond to different types of antigen challenge.

11:00 – 11:30 **Effects of ageing on antigen sampling in the mucosal immune system**

Dr Neil A Mabbott, The Roslin Institute & Royal (Dick) School of Veterinary Sciences, University of Edinburgh, UK
The gastrointestinal tract is continuously exposed to large amounts of commensal and pathogenic microorganisms. As well as mounting an effective immune response against food-borne pathogens, the mucosal immune system must also recognise the harmless antigens (Ag) associated with food and commensals and generate immunological tolerance against them. The transcytosis of Ag across the follicle-associated epithelium (FAE) of Peyer's patches by M cells is important for the induction of efficient immune responses to mucosal antigens. The mucosal immune response is compromised by ageing, but effects on M cells were unknown. We show that M-cell density in the FAE of aged mice was dramatically reduced. As a consequence, aged Peyer's patches were significantly deficient in their ability to transcytose particulate lumenal antigen across the FAE. Ageing specifically impaired the expression of Spi-B and the down-stream functional maturation of M cells. Ageing also dramatically impaired CCL20 expression by the FAE. As a consequence, fewer B cells were attracted towards the FAE, potentially reducing their ability to promote M-cell maturation. These data show that ageing dramatically impedes the functional maturation of M cells, revealing an important defect in the mucosal immune system's ability to sample lumenal antigens.

11:30 – 12:00 **Speakers' photo then mid-morning break and poster exhibition and trade show**
Please try to visit all the exhibition stands during your day at this event. Not only do our sponsors enable Euroscicon to keep the registration fees competitive, but they are also here specifically to talk to you.

12:00 – 12:30 **Para-inflammation and Age-related Macular Degeneration**
Dr Heping Xu, Centre for Vision and Vascular Science (CVVS) Queen's University Belfast Institute of Clinical Science, Ireland
Para-inflammation is an immune response to chronic noxious stimuli at a low magnitude that lies between the basal homeostatic state and overt inflammation. The physiological role is to maintain tissue homeostasis and functionality. Dysregulation in the para-inflammatory response underlies many chronic diseases such as diabetes, atherosclerosis and various age-related degenerative disorders. The nature of retinal para-inflammation under normal ageing conditions and the role of dysregulated or maladapted para-inflammatory response in age-related macular degeneration will be discussed.

12:30 – 13:00 **Lymphocyte proliferation, ageing and the regulatory proteolysis of key proteins.**
Professor Jacek Witkowski, Department of Pathophysiology, Medical University of Gdansk, Poland
Cells control the activities of their proteins by limited regulatory proteolysis (LRP). The 'calpain-calpastatin system' (CCS) regulates the activities of signal transduction molecules, receptors, transcription factors and elements of cell division 'machinery' known to be modified by ageing, and thus is an important object in the study of immunosenescence and longevity. We have recently launched an international project (CALPACENT®) aiming at defining the role of CCS in the wellbeing of the immune systems in centenarians. We will discuss the results obtained so far in the context of dwindling performance of ageing immune system and of current understanding of cellular LRP.

13:00 - 13:30 **Effects Of Melatonin On The Age-Dependent Dysregulation Of The Nf-Kb/Nlrp3 Activation During Sepsis**
Mr. Huayqui Volt Valdivia, Biomedical Research Center, University of Granada, Spain
The age-related changes of the immune system involve a persistent proinflammatory state. This subclinical and chronic inflammation contributes further to enhance the susceptibility of the elderly patients to several acute and chronic inflammatory diseases, including sepsis and ageing itself. The recent discovery of the NF-kB/NLRP3 connection during the innate immune response to inflammatory signals leads to explore the activation of this pathway during ageing in a mouse model of sepsis. The lack of an effective treatment of this disease supports the look for new molecular targets and/or drug therapy. We explored whether the anti-inflammatory actions of melatonin can protects against NF-kB/NLRP3 activation. Our results support NLRP3 inflammasome as a novel molecular signaling pathway during sepsis and indentify it as a main target

for the anti-inflammatory action of melatonin. Due to the age-dependent reduction in the endogenous melatonin production, the relation between melatonin reduction and increased inflammatory response with age is discussed.

13:30 - 14:30 **Lunch, poster exhibition and trade show**

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14:30 - 15:00 **Discussion session**

This discussion session is an informal question and answer session. This is an ideal opportunity to get advice and opinion from experts in this area. This session is not for questions about specific talks, which can be asked after the speakers session, but for discussing either general topics or specific issues.
There are three ways you can ask questions:

1. Before the session you can *submit your question to Euroscicon staff* at the registration desk,
2. Before and during the session you can *submit a question or comments, by email*, which will be provided on the day
3. During the session you can *put your hand up* and join in

15:00 – 15:30 **Ageing of the immune system – Role of CMV for Coronary Heart Disease**

Professor Ioakim Spyridopoulos, Chair of Cardiovascular Gerontology, Hon. Consultant Interventional Cardiology, Newcastle University and Freeman Hospital, UK
While human cytomegalovirus (CMV), a herpesvirus that is never cleared from individuals following primary infection, is deemed harmless in immunocompetent people, there is mounting evidence that it adversely affects human lifespan linked to a higher incidence of coronary heart disease (CHD) in seropositive individuals. This talk will look into the potential link between an ageing immune system, cytomegalovirus infection and progression of atherosclerosis. It will attempt to link cellular changes in the CD8 T cell compartment secondary to CMV, telomere biology and inflammation with the pathophysiology of coronary artery disease.

15:30 – 16:00 **Afternoon Tea, last poster session and trade show**

16:00 – 16:30 **Old before our time? Cytomegalovirus establishes the rudimentary signs of an ageing immune system even in young and healthy adults.**

Dr James Turner, Lecturer, Department for Health, University of Bath, Bath, UK.
Ageing is associated with a decline in immune competence termed immunosenescence. In the elderly, this process has been associated with increased susceptibility to infection, accelerated cognitive decline, frailty and increased mortality. It has become clear that many features of an ageing immune system are determined by Cytomegalovirus (CMV) infection. Until recently, it remained largely unexplored whether CMV drives immunity towards a senescent profile in young and healthy adults. In this talk I will present the results of a recent investigation, whereby several hallmarks of immunosenescence were assessed in a chronologically young population of healthy university students.

16:30 – 17:00 **Insights into maintaining Immunsurveillance in Advanced Age: Killer Inhibitory Receptors (KIR) haplogroups A and B track with Natural Killer Cells and Cytokine Profile in Oct/Nonagenarians in Belfast Elderly Longitudinal Free-living Aging Study (BELFAST)**

Dr Irene Maeve Rea, Senior Lecturer and Consultant Physician Geriatric Medicine , Queens University Belfast and Belfast Health and Social Care Trust, Northern Ireland
Natural Killer cell (NK) populations, Killer Cell receptor complexes (KIRs) and associated cytokine profiles are highly

effective collaborators in controlling, patrolling and protecting our immune landscape.The intrinsic and extrinsic factors that shape human NK cell diversity remain incompletely understood. In dissecting out elements of this immune landscape we have reported relationships between NK cells and NK-related subsets, KIR A and B haplogroups and cytokines as in subjects from the BELFAST study. The findings across the 3 interacting domains are exploratory but may serve to stimulate debate and encourage replication studies to improve our understanding about the immune signatures of those who live successfully into their 90s.

17:00 **Chairman's Summing Up and Close of Meeting**

Registration Website: https://www.regonline.co.uk/AgeingImm2014

Meeting reports from this event will be published by *Expert Review of Clinical Immunology* and by *HONNAO* publishing

Keywords: B cells, repertoire, antibody genes, immunity, Ageing, para-inflammation, age-related macular degeneration, microglia, complement, Ageing, Cardiovascular, Telomeres, CD8 T lymphocytes, Cytomegalovirus, Immunosenescence, Cytomegalovirus, Vaccination, Interleukin-6, CD8+ T cells, Natural Killer Cell, Killer Inhibitory Receptor Haplogroup, Cytokine, longevity, Octo/nonagenarians, immunosenescence, T cells, calpain, cell cycle

About the Speakers

Deborah Dunn-Walters is Reader in Immunology at King's College London, with extensive experience in B cell repertoire analysis, and molecular events involving the immunoglobulin gene during B cell development. She combines traditional molecular biology techniques with novel mathematical analyses to devise new ways of investigating the humoral immune system. She is particularly interested in research that aims to improve the health of older people.

Heping Xu graduated in medicine from Hengyang Medical College, China in 1987. He completed his ophthalmology training in XiangYa Hospital and obtained his PhD in vision science from Hunan Medical University in 1994. He carried out his post-doc training, first in cell biology in Japan (1997-2000), and then in ocular immunology at the University of Aberdeen (2000-2004). Dr Xu was awarded a Research Council UK (RCUK) fellowship in 2005, and was promoted to Senior RCUK fellow in 2008. Dr Xu moved to the Centre for Vision and Vascular Science, Queen's University Belfast in 2009 as a Senior Lecturer, and was promoted to Reader in 2011. Dr Xu's research is centred on the immunopathogenesis of sight-threatening retinal diseases, including uveoretinitis, age-related macular degeneration and diabetic retinopathy.

Jacek M. Witkowski is a professor of cell biology, immunology and biogerontology, and over last decade heads the Department of Pathophysiology, Medical University of Gdansk, Poland. His group was the first to report the aging-related modulation of many human T cell features, including decreased membrane potential and Na-K ATPase activity, accumulation of regulatory T cells expressing low numbers of CD4, and reduced expression and glucuronidase activity of Klotho. Currently they investigate the determinants of modified human immune cells' behaviour during physiological aging, longevity, and age-related pathologies. Recently his group had reported reduced amounts of calcium-activated proteases (calpains) in elderly lymphocytes.

Huayqui Volt Valdivia received his Biology degree in 2008 from the University of Granada (Spain). He finished the Master in Advanced Biotechnology in the Autonomous University of Barcelona (Spain) in 2010, working on the aerial dispersion, Stemphylium vesicarium reservoirs and impact on the agricultural ecosystem microbiota, under the supervision of Dr. Núria Gaju Ricart. During 2009, he worked in the Public Health Laboratory of the Health Ministry in Ibiza and Formentera (Spain), where he carried out the microbiological and chemical analysis of food and water. In 2011, he joined to the research group

CTS-101: Intercellular Communication at the Biomedical Research Centre of the University of Granada, where he is currently doing the experimental research to obtain his PhD degree under the direction of Professor Dario Acuña-Castroviejo. His main work is the regulation of the innate immune response during aging and the involvement of RORalpha receptors and melatonin in this response.

Ioakim Spyridopoulos has received his Medical degree in 1992 at the University of Hannover, Germany. He has been a postdoctoral fellow at TUFTS University in Boston/MA from 1995-1997. Further research stays at Tübingen University and Frankfurt University have added to his work on atherosclerosis research. Following his appointment as Hon. Consultant in Interventional Cardiology at the Freeman Hospital at Newcastle Upon Tyne Trust in 2008 he was also appointed Chair of Cardiovascular Gerontology with Newcastle University. His main research field is "Inflammaging" in cardiovascular system, especially in the context of coronary heart disease. He is supported by the British Heart Foundation and the NIHR Biomedical Research Centre.

James Turner undertook a PhD between 2007-2010 at the University of Birmingham. His thesis covered topics including immunosenescence, oxidative stress and exercise. James remained in Birmingham to undertake two post-doctoral research positions; first between 2011-2012, characterising T cell responses to novel leukaemia antigens, and second, from 2012-present, conducting research towards producing a prophylactic Epstein-Barr Virus vaccine. From September 2013, James became employed as a Lecturer in the Department for Health at The University of Bath, where he will lead a programme of research that spans the domains of physical activity, immune competence, and ageing.

I Maeve Rea, Senior Lecturer/Consultant Physician in Geriatric Medicine at Queens University Belfast, was educated at Queens University and did postgraduate research in immune-genetics at Stanford University with Prof Rose Payne. She teaches widely in the Undergraduate Medical curriculum and within her Health Service remit, she provides a clinical service to Elderly people, with a special interest in patients over 90 years of age. Dr I Maeve Rea has a long-time research interest is in healthy ageing and set up and co-ordinates a longitudinal study of octo/nonagenarians, Belfast Elderly Longitudinal Free-living Ageing STudy (BELFAST) and is a Prinicpal Investigator in the Genetics of Healthy Ageing Study (GeHA), which is contributing to understanding the genetic, immunological, cardiovascular and nutritional factors contributing to good quality ageing.

POSTER PRESENTATIONS

FUNCTIONAL CELLULAR IMAGING OF IMMUNE RESPONSES DURING AGEING USING INTRAVITAL MULTIPHOTON MICROSCOPY

M. Pattison, K. Renault, N. Mabbott, B. McColl
The Roslin Institute, The University of Edinburgh, Easter Bush, Midlothian, EH25 9RG

The immune system protects us against bacteria, viruses and other pathogens, and if compromised can result in susceptibility to infection. Immunosenescence refers to age-related immune impairments in immune function that may contribute to increased prevalence and severity of infectious disease in the elderly. Despite increasing understanding of molecular and cellular age-related immune alterations, knowledge is incomplete, particularly on dynamic and functional cellular changes. Multiphoton microscopy is a technique optimised to visualise and quantify dynamic cell behaviour *in vivo* under near physiological conditions. Our aim is to use multiphoton *in vivo* imaging of ageing mice to study how age affects important immune responses *in situ*. The development of multiphoton technology has enabled the *in vivo* visualisation of cells and molecules deep within intact, dense tissues, making it ideally suited for imaging lymphoid tissues. To date,

multiphoton microscopy has enabled us to visualise important immune events in lymphoid tissues, including antigen capture and transport, interactions between immune cell populations, and lymphocyte proliferation and egress into the periphery[1-4]. We are developing methods to investigate the structural and cellular changes in lymphoid tissues during ageing, with focus given to imaging the dynamic interactions between antigen and lymphoid cells that influence antigen trapping, trafficking and effector responses. Initial studies have immunohistochemistry and flow cytometry to define key structural and cellular changes occurring at 4, 12 and 22 months of age. This information will be used to identify selected cell populations of interest. The effect of ageing on dynamic activity of these cell populations and trafficking of antigen necessary for response to pathogen challenge will then be determined using multiphoton *in vivo* imaging. An improved understanding of how ageing affects functional activity in the immune system may reveal novel targets for intervention to alleviate age-related immune dysfunction and possibly lighten the medical burden of ageing. 1. Swirski, F.K., et al., *Identification of Splenic Reservoir Monocytes and Their Deployment to Inflammatory Sites.* Science, 2009. 325(5940): p. 612-616. 2. Phan, T.G., et al., *Immune complex relay by subcapsular sinus macrophages and noncognate B cells drives antibody affinity maturation.* Nature Immunology, 2009. 10(7): p. 786-U153. 3. Arnon, T.I., et al., *Visualization of splenic marginal zone B-cell shuttling and follicular B-cell egress.* Nature, 2013. 493(7434): p. 684-8. 4. Heesters, B.A., et al., *Endocytosis and recycling of immune complexes by follicular dendritic cells enhances B cell antigen binding and activation.* Immunity, 2013. 38(6): p. 1164-75.

EFFECTS OF MELATONIN ON THE AGE-DEPENDENT DYSREGULATION OF THE NF-kB/NLRP3 ACTIVATION DURING SEPSIS

H. Volt, C. Doerrier, J.A García, L.C López, G. Escames, D. Acuña-Castroviejo.
Centro de Investigación Biomédica, Parque Tecnológico de Ciencias de la Salud, Avda. del Conocimiento s/n, 18100 Armilla, Granada, Spain.

Immunoaging, a term describing age-related changes of the immune system, involves a persistent proinflammatory state coursing with cardiac and energy metabolism alterations. This subclinical and chronic inflammation contributes further to enhance the susceptibility of the elderly patients to several acute and chronic inflammatory diseases, including sepsis and ageing itself.

The lack of an effective treatment of sepsis and septic shock supports the look for new molecular targets and/or drug therapy. The recent discovery of the NF-kB/mitochondrion/NLRP3 connection during the innate immune response to inflammatory signals lead to explore the activation of this pathway during ageing in a mouse model of sepsis. In this experimental model we also explored whether the anti-inflammatory actions of melatonin can protects against NF-kB/NLRP3 activation. Eighteen months-old C57BL/6J mice were grouped into three experimental groups: a) control group; b) septic group, in which sepsis was induced by cecal ligation and puncture (CLP), and c) septic group treated with melatonin. Mice received a total dose of 90 mg/kg melatonin. Mice were sacrificed 8 hrs after induction of sepsis, and their hearts were collected and processed immediately for mitochondrial respiration, or frozen to -80 °C to further analysis. The expression and levels of key molecules involved in NF-kB/NLRP3 signaling pathway were analyzed by RT-PCR and Western-blot, respectively; DNA-binding capacity of NF-κB p65 subunit was assessed by ELISA, and cytosolic oxidative stress was measured spectrophotometrically. The data obtained from aged mice were compared with three months-old mice. Our results show the existence of a basal pro-inflammatory process that increases with age, which depended on the activation of both NLRP3 inflammasome and NF-kB. These changes were accompanied by the enhanced proinflammatory cytokines (IL-1β, TNF-α), and enzymes (iNOS) expression, as well as mitochondrial failure. We also show that these markers of the innate immunity further increased with sepsis. Melatonin administration absolutely prevented the NF-kB-dependent inflammatory response by increasing the nuclear level and deacetylase activity of Sirtuin-1. Furthermore, melatonin restored the cellular redox balance and mitochondrial function in septic mice, leading to NLRP3 inflammasome inactivation. These results support NLRP3 inflammasome as a novel molecular signaling pathway during sepsis and indentify it as a main target for the anti-inflammatory action of melatonin. Due to the age-dependent reduction in the endogenous melatonin production, the relation between melatonin reduction and increased inflammatory response with age

is discussed. *Supported by grants # PI08-1664 andRD12/0043/0005 (ISCIII, RETICEF, Spain).*

HUMORAL AND CELLULAR IMMUNE RESPONSES TO PRIMARY JAPANESE ENCEPHALITIS VACCINATION IN THE ELDERLY COMPARED TO THE YOUNG

A. Wagner[1], E. Garner-Spitzer[1], J. Jasinka[1], M. Paulke-Korinek[1], M. Hofer[1], K. Stiasny[2], F. X. Heinz[2], H. Kollaritsch[1], U. Wiedermann[1*]

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Background: Immunosenescence includes reduced B and T-cell responses in the elderly population. It has been shown that booster vaccination is less effective in the elderly compared to the young. However data on the efficacy of primary immunisation in the elderly is still sparse. In a monocentric, open label, phase IV study we investigated humoral and cellular immune responses to primary (JE) vaccination in young (18-40 years old) compared to elderly participants(>60 year old). **Methods:** Participants (n=30 per group) received a primary course of a vero-cell based adjuvanted Japanese Encephalitits vaccine. Neutralising antibody titers (NT) were measured in serum samples taken before vaccination, one and five weeks after the second vaccination. PBMC´s were taken before and one week after the second vaccination to analyse different T- and B-cell subsets and cytokine production upon JE-antigen restimulation. **Results:** Elderly participants displayed JE-NT´s were significantly lower than in the younger participants. Furthermore 13% of young (mean age 24.3 y) versus 47% of the elderly (mean age 68.8 y) participants were low-responders not mounting sufficient JE-specific antibody levels (NT <1:20). Reduced humoral immune responses were associated with altered cytokine production (IFN-g, IL-2) in vitro and higher numbers of regulatory T cells in the elderly study population. Additionally, higher frequencies of late-differentiated effector and effector memory cells were detected in the elderly, correlating with CMV seropositivity. **Conclusion:** In our study humoral and cellular immune responses to primary JE vaccination were significantly reduced in the elderly compared to young participants. Therefore primary vaccination in the elderly may require different vaccination strategies to ensure sufficient immunity such as modified vaccination/booster schedules, careful selection of adjuvants and if possible encouraging primary vaccination before the age of 60.

DETECTION OF INFECTION IN FRAIL ELDERLY: A CHALLENGE

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Background

Signs and symptoms of infection in the frail elderly is often atypical, while specific ones are missing, causing a delay in diagnosis and treatment. These atypical signs are observed as absence of fever, weakness, falling, weight loss, physical dysfunction and cognitive decline. Lack of fever is probably related to a lower baseline temperature, due to physical and cognitive decline and a low body mass index. In this poster we illustrate the challenge of detecting infection in an elderly nursing home resident (NHR). **The story of Mr Nelson** Mr Nelson is 83 years old nursing home resident (NHR). He has been living at the nursing home for two years due to progressing dementia. He is also diagnosed with chronic obstructive pulmonary disease (COPD) and pulmonary cancer. He is on daily medication with sedatives, antidepressants and paracetamol 1 g three times a day. He is vaccinated against influenza and pneumonia. He is well nourished, but has a severe physical disability and can only manage to eat by himself and tell when he needs the toilet. He has a severe cognitive decline and is assessed as having chronic pain. He normally does not behave with delusions, hallucinations, is not unrestrained or euphoric and his appetite is normal. He often shows severe aggressiveness and irritability and is assessed as having a mild depression, mild anxiety, moderate apathy and abnormal motoric behaviour. His baseline body

temperature is 36,6°C in the ears and 36,9°C rectally .During the last year, three events with suspected infection are documented in his record. Figure 1 shows a summary of the documentation of his second infection. The figure illustrates that the nursing assistants (NA) early on document that he does not feel well, expressed as *"expression in the eyes", less appetite, lethargy and general signs of illness*". They also observed respiratory symptoms. Day six the registered nurse (RN) informs the general practitioner (GP), who takes no further action. There are no more documentation about Mr Nelsons' condition until evening day 16, when the RN order paracetamol due to fever. The condition worsens and Mr Nelson dies on day 24. **Comment** Mr Nelson was participating in a study of signs and symptoms of infection in nursing home resident. Therefore, on day two blood sampling and analysis of C-reactive protein (CRP), white blood cells (WBC) and inflammatory cytokines Interleukin (IL) IL-1β, IL-1RA, IL-6, IL-8 and Il-10 were performed. The analysis revealed a CRP of 158, a WBC of 14,4 and changed levels of IL-1RA, IL-6, IL-8 and Il-10, indicating an ongoing bacterial infection. It is quite clear from nurses and doctors documentation that fever, in the sense of X degrees, is essential for further action. **Clinical implications** NHR are more likely to suffer from acute infections due to general frailty and physical incapability. The most frequent infections are urinary tract and lower respiratory tract infections. Among very old women the presentation of urinary tract infection has been associated with delirium, which is associated with increased mortality. Male gender and physical impairment have been found to be associated with higher mortality rate in pneumonia, with the highest rate occurring in NHR. Pneumonia is also related to increased mortality in individuals with advanced dementia and chronic obstructive pulmonary disease (COPD). The story of Mr Nelson is not unusual. It illustrates the complexity of assessing frail elderly with physical and cognitive decline. One clue may be to listen to NAs observation of changed condition.

PETRI NETS COMPUTER MODEL OF IMMUNE SYSTEM OPENS OPPORTUNITY TO STUDY EFFECTS OF AGEING, AUTISMS AND FEVER

A. Gogolinska*, W. Nowak

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Petri nets (PN) are one of several mathematical modeling languages developed for the description of distributed systems. They provide a framework to create large models of complex systems. A Petri net consists of two types of nodes: transitions, which represent events, for example a chemical reaction, and places which represent objects, for example chemical compounds. We have used that tool to create a model of the Immune System (IS). Our model consists of four parts: the reaction of DC cell, the Th lymphocytes activation, the cellular response, the humoral response and the reaction of macrophages. The model is relatively elaborated, it contains about 100 places and 100 transitions [1]. We used this PN model to study a few phenomena: effects of fever, autism and ageing on the IS. Events which are associated with the fever [2] were recognized in the model and weights of transitions corresponding to those events were increased. PN modeling shows that this results in a better efficiency of the IS and faster defeat of the infection. Autism Spectrum Disorder (ASD) seems to have connection with the IS - for example levels of some cytokines are elevated in autistic patients [3] and fever improves condition of autistic children [4]. Correlation between levels of cytokines, autism and fever were studied using the Petri net model of IS [1]. Ageing has a big impact on the IS. In elderly people numbers of native T and B cells are decreased, also activation rate and production of some cytokines by T cells are reduced. On the other hand the numbers of memory T and B cells are elevated [5]. Those phenomena were added to our PN. The impact of ageing on the IS performance was checked during a dynamical simulation of an infection within the PN model. The results of mathematical modeling of fever, autism and ageing will be presented in the poster. We show that this informatics approach provides useful tool for relatively easy and fast modeling of different aspects of IS physiology. 1. Gogolinska, A. and W. Nowak, Petri Nets Approach to Modeling of Immune System and Autism, in Artificial Immune Systems, C. Coello Coello, et al., Editors. 2012, Springer Berlin Heidelberg. p. 86-99.

2. Hasday, J.D., K.D. Fairchild, and C. Shanholtz, The role of fever in the infected host. Microbes and Infection, 2000. 2(15): p. 1891-1904. 3. Ashwood, P., et al., In Search of Cellular Immunophenotypes in the Blood of Children with Autism. PloS one,

2011. 6(5): p. e19299. 4. Curran, L.K., et al., Behaviors associated with fever in children with autism spectrum disorders. Pediatrics, 2007. 120(6): p. e1386. 5. Larbi, A., et al., Aging of the immune system as a prognostic factor for human longevity. Physiology, 2008. 23(2): p. 64-74.

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This meeting was organised by Euroscicon (www.euroscicon.com), a team of dedicated professionals working for the continuous improvement of technical knowledge transfer to all scientists. Euroscicon believe that they can make a positive difference to the quality of science by providing cutting edge information on new technological advancements to the scientific community. This is provided via our exceptional services to individual scientists, research institutions and industry.

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