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EUROPEAN COMPLEMENT NETWORK

ABOUT THIS ISSUE & MORE

What's inside?

<1> Two flash news, are presented by Dr. Sakari Jokiranta on:
(a) Factor H and oxidative stress; (b) Eculizumab in the treatment of dense deposit disease- a compilation of three articles published back-to-back in the New England J. of Med.

<2> No "Complement Teams" are presented in the present issue.

<3>. A reminder of important dates of the fast approaching XXIV International Complement Workshop (ICW) in Crete.
www.complement2012.org

<4>. This issue also highlights a recent recognition of an ICS member- Dr. Jane Salmon.

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FLASH NEWS

Factor H and Oxidative stress-Reporter: S. Jokiranta

Complement factor H binds malondialdehyde epitopes and protects from oxidative stress. D. Weismann, K. Hartvigsen, N. Lauer, K. L. Bennett, H. P. N. Scholl, P. Charbel Issa, M. Cano, H. Brandstätter, S. Tsimikas, C. Skerka, G. Superti-Furga, J. T. Handa, P. F. Zipfel, J. L. Witztum, and C. J. Binder. *Nature* 2011; 478: 76-81.

This article describes binding of factor H to malondialdehyde (MDA) -epitopes and links the findings to pathogenesis of age-related macular degeneration (AMD). Malondialdehyde-epitopes are oxidation-specific epitopes that act as danger-associated signals for the immune system. The epitopes are generated, for example during apoptosis and tissue injury and lead to enhanced inflammation. In this article the authors used a proteomic approach to detect which human proteins bind to these epitopes and identified factor H as a main MDA-binding protein. It was shown that binding of factor H to these epitopes leads to reduced complement activation and attenuated inflammation. The binding sites on factor H were identified on domains 7 and 20 and, interestingly, the authors show that AMD-associated polymorphism in factor H domain 7 (Y402H) lead to reduced binding to the MDA-epitopes. The authors suggest that reduced binding of FH to MDA-epitopes explains the enhanced inflammation in the eye during pathogenesis of AMD. This paper is potentially very important since it provides a novel explanation on the association between factor H polymorphism and AMD and, although not mentioned in the article, might be a basis for new insights into the role of certain factor H mutations in endothelial cell injury in atypical haemolytic uremic syndrome, too.

Eculizumab in dense deposit disease-S. Jokiranta

Eculizumab in a Patient with Dense-Deposit Disease. Daina, M. Noris, and G. Remuzzi. *N Engl J Med* 2012; 366: 1161-3.

Eculizumab for the Treatment of Dense-Deposit Disease. M. Vivarelli, A. Pasini, and F. Emma. *N Engl J Med* 2012; 366:1163-5.

Eculizumab and Refractory Membranoproliferative Glomerulonephritis. S. Radhakrishnan, A. Lunn, B.M., M. Kirschfink, P. Thorner, D. Hebert, V. Langlois, F. Pluthero, and C. Licht. *N Engl J Med* 2012; 366:1165-6.

These three patient cases were published in the same issue of the journal. In all the articles, the authors describe the effect of inhibition of terminal complement cascade by anti-C5 antibody eculizumab in treatment of one patient with membranoproliferative glomerulonephritis (MPGN), also called dense-deposit disease (DDD). All the patients had low plasma C3 level and evidence of the activation of the terminal complement cascade as either plasma sC5b-9 level was markedly increased or C5b-9 complexes were detected in kidney biopsy. One of the patients had suffered from MPGN for years while the others were recent cases. The effect of eculizumab was clearly beneficial in all the cases. In one of the articles (Daina et al.) it was also mentioned that two more patients with DDD have been treated with eculizumab, and the one who benefitted of the treatment showed increased plasma sC5b-9 level. The results together indicate that (1) the terminal pathway activation is important in pathophysiology of DDD in humans, (2) inhibition of complement activation is beneficial at least in some of the DDD patients, and (3) detection of elevated plasma sC5b-9 might be used to select the patients for this treatment.

ANNOUNCEMENT



Dear Colleagues,

The **XXIV International Complement Workshop** will be held on **October 10-15, 2012**, on the scenic island of **Crete, Greece**. It will serve as a timely and lively scientific platform to share the latest research updates, discuss emerging trends and concepts in the field, meet current and future collaborators, and get inspired by new ideas. Submitted abstracts will be peer-reviewed and selected for either an oral presentation in the top-modern conference center, or for the poster sessions. In addition to the scientific highlights, the Greek sun, cuisine, and cultural attractions will certainly contribute to a relaxed and unforgettable workshop experience. The regular registration package will include wonderful room accommodations in a 5-star hotel—located directly on the banks of the Mediterranean Sea—, breakfast, lunch, dinner, and coffee breaks, as well as a social program including trips to Cretan highlights and, of course, some dancing.

Rarely before has the field of complement research seen such dramatic changes and exciting developments than during the past decade. Driven by seminal discoveries ranging from molecular to clinical aspects, and fueled by recent progress in the therapeutic intervention in complement-mediated diseases, novel insights into the function of complement appear at an increasingly rapid pace. New players in the network have been discovered, and several functional aspects have been redefined or extended, recently. At the same time, we are coming to realize that the physiological spectrum of complement by far exceeds host antimicrobial defense and that the complement network is highly intertwined with a variety of bodily systems. Open and vivid scientific discussions, the integration of new research ideas and talents, and the interaction with peripheral fields can further drive complement research to new horizons.

The keynote speakers of the meeting are:

Alberto Mantovani, M.D. Professor, University of Milan Scientific Director, Istituto Clinico Humanitas.

Hans J. Müller-Eberhard Memorial Lecture: *The humoral arm of innate immunity: recurrent themes and regulatory pathways*

Shankar Subramaniam, Ph.D. Professor and Chair Department of Bioengineering, University of California, San Diego.

Systems Biology and Innate Immunity

Joe Nadeau, Ph.D. Director of Research and Academic Affairs of the Systems Biology Institute, Seattle.

Tipping complex systems from disease to health: genetic and dietary influences on metabolic disease, cancer and inflammation

Additional speakers will be selected from the submitted abstracts

The deadline for receipt of abstracts, early registration, and hotel reservations is **July 10, 2012**. Please note that the cost of the registration fee is **575 Euro** and hotel accommodations from **85-110 Euro/night**.

Additional information will be sent only to people who respond to this announcement and pre-register on-line. For your convenience and to expedite the communication process, registration materials, including abstract and hotel reservation forms, are available on the web site. Information on Crete, travel to Greece, hotel accommodations, etc. is also available on the web site. Updated information will be available through this site.

<http://www.complement2012.org> or <http://www.aegeanconferences.org>

To pre-register to the conference please visit:

<https://www.aegeanconferences.org/registOpen.do?method=open>

To encourage the participation of young scientists, the following **Trainee Travel Awards** will be available to offset a portion of the travel expenses to the Conference:

- [Trainee Travel Awards](#)
- [The Lambris Complement Training Award \(LCTA\)](#)
- [Young Investigator Awards for Research in Complement](#)

For more information please visit the workshop's website.

We look forward to welcoming you in Crete for a scientifically stimulating and socially enjoyable meeting.

Best personal regards,

Local Organizing Committee

John D. Lambris (www.lambris.com)

University of Pennsylvania, USA

Chair of the Organizing Committee

George Hajishengalis

University of Louisville, USA

Daniel Ricklin

University of Pennsylvania, USA

Program Committee

The Program Committee will consist primarily of ICS Board members (see www.complement.org), and possibly a few ad hoc members. The committee will select the abstracts for presentation, travel awards, and the keynote speakers. The Chair of the Program Committee is the current President of the ICS, **Dr. Paul B. Morgan**, University of Wales College of Medicine. The other members are as follows:

Michael Pangburn, Past President (*University of Texas Health Sci. Ctr., USA*)

Berhane Ghebrehiwet, Secretary (*Stony Brook University, USA*)

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Santiago Rodriguez de Cordoba (*Centro de Investigaciones Biologicas, Spain*)

Wenchao Song (*University of Pennsylvania, USA*)

RECENT AWARDS AND RECOGNITION of ICS MEMBERS

Jane E. Salmon, M.D. - received the 2012 Virginia Kneeland Frantz Award for Distinguished Women in Medicine awarded by the Columbia University College of Physicians & Surgeons Alumni Association.

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- XXIV International Complement Workshop Greece October 10-15.

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