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Issue 19

Focus on Complement

A newsletter of the International Complement Society

EUROPEAN COMPLEMENT NETWORK

About this issue & More

What's inside?

<1>Two flash news items, are presented by Dr. Michael Pangburn: **(a)** the role of C5aR in dendritic cells and T cells, and **(b)** Complement-dependent transport of antigens into B cell follicles.

<2> Dr. Michael Pangburn also presents a complement team from U. Chicago. The Editorial Board of "FoC" would like to thank Dr. Pangburn for his timely contributions.

<3>A post conference message from the local organizing committee of XXIII ICW, is also included. Although we plan to post pictures from the meeting on the XXIII ICW website latest by the end of September, we have included few pictures in this issue of "FoC" for your enjoyment. David Habiel, a graduate student in Richard Kew's lab at Stony Brook, took these pictures. To see more pictures, visit the ICW 2010 website at:
http://www.hsc.stonybrook.edu/ics2010/

FLASH NEWS

C5aR Role in DC & T cells -*Reporter* : M. Pangburn

C5 Receptor-deficient dentritic cells promote induction of Treg and Th17 cells. Weaver DJ, ES Reis, MK Pandey, G Köhl, N Harris, C Gerard, and J Köhl. Eur. J. Immunol 40:710-721, 2010.

Recently, publication after publication has demonstrated the extent to which complement controls adaptive immune responses. In this paper, another landmark, Weaver and Köhl have shown that the complement-derived peptide C5a determines the outcome of T-cell differentiation. The paper shows that C5aR activation on dendritic cells (DC) provides a critical innate immune signal that regulates differentiation of naïve T cells into Th1, Th17 and Treg. C5aR+/+ dendritic cells stimulated by a TLR2 ligand induce naïve CD4+ Th cells to undergo differentiation to Th1. Without C5aR co-signaling T-cells differentiate into Th17 and Treg cells. Other work by these authors has recently shown that C5aR on macrophages regulates their responses to TLR stimulation. Others have shown that the C3aR has a powerful influence on responses of DC and in the absence of C3aR, DC lose their capacity to induce Th1 in favor of Treg. Indeed, a child identified with a complete lack of C3 was demonstrated to be largely incapable of mounting any adaptive immune cell responses (J. Immunol. 181:5158, 2008). Clearly, this paper by Weaver and all the other recent contributions in this area will change how the textbooks describe both complement and adaptive immunity.

Transport of Antigens -*Reporter* : M. Pangburn

Complement-dependent transport of antigen into B cell follicles. Gonzalez SF, V Likacs-Kornek, MP Kuligowski, LA Pitcher, SE Degn, SJ Turley, and MC Carroll. J. Immunol. 185:2659-2664, 2010.

Although this is a brief review, it refers to a series of studies by the authors and many others showing (sometimes in the most dramatic fashion possible - real-time *in vivo* movies) the migration patterns of antigenic materials as they pass through and are processed by peripheral lymph nodes. The receptor complexes CD21/35 and CD11b/18 participate in the capture of antigens tagged with C3b/iC3b/C3d for presentation to follicular dendritic cells in the B-cell compartment of lymph nodes. These C3-Ag complexes travel down conduits to educate naïve B cells. The authors also describe how complement-tagged viruses and SIGN-R1 are involved in the processing of bacteria and influenza virus in lymph nodes. Understanding how this complex, three dimensional apparatus selects and processes antigens is critical to understanding adaptive immunity, vaccine design and the role of complement in both.

SPOTLIGHT ON TEAMS - I

COMPLEMENT IN "THE WINDY CITY"— CHICAGO

Complement research at the University of Chicago has an interesting and long history. In the early 1980's, M. Ed Medof began his work that would span the next several decades. Around the time Ed moved from Chicago to join Victor Nussenzweig in New York, Rick Quigg began his fellowship with David Salant in Boston. Because products of complement activation are deposited in a variety of human glomerular diseases, his work concentrated on the pathobiology of complement in glomerular diseases. Rick's first faculty position was at the Medical College of Virginia, where he greatly benefited by his close association with Shaun Ruddy, from whom he learned the nuances of complement chemistry. He then moved to the University of Chicago in 1994 to continue where Ed left off.

Because the kidney disease models were in the rodent, early research in the Quigg lab was directed towards dissecting the rodent complement system and regulators, work that was greatly benefited by close collaborations with V. Mike Holers and B. Paul Morgan, eminent complement biologists/scientists with similar interests. The Quigg lab went on to dissect the roles for complement regulation by Crry, DAF, and factor H, and complement activation and effects through C3aR and C5aR in disease states such as lupus nephritis and acute renal failure.

Since the late 1990's, the Quigg lab has included Drs. Jessy Alexander and Lihua Bao, who have become complement biologists par excellence. Jessy has shown that factor H in rodents is the platelet and podocyte immune adherence receptor, where it serves as the analogue to CR1 on human erythrocytes and podocytes. Lihua has described the roles for complement in lupus nephritis, and more recently, she has shown that autoimmunity to podocytes occurs when T cells lack DAF, leading to the significant human disease, focal glomerulosclerosis.

The Quigg lab continues to examine how complement activation and its regulation affect kidney diseases, and the therapeutic potential of interrupting this system. The roles the complement system play in autoimmune kidney diseases continue to expand - it appears the more we understand about the complement system, the more complicated it really seems to be - overall, a good thing, as it makes the work exciting on a daily basis.

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The XXIII International Complement Workshop-2010- Souvenirs from the "Big Apple"- New York:

How time flies! It seemed only yesterday that we were in Basel and were delighted to learn that we would host the XXIII ICW in New York. Now, the XXIII ICW has come and gone and is already a distant memory; and everyone is looking forward to the XXIV ICW in Crete in 2012. Although previous organizers, such as Jürg Schifferli in Basel, Wen-Chao Song in Beijing, and Carl-Wilhelm Vogel in Honolulu and their predecessors have done outstanding jobs in organizing the previous Workshops, it is only now— from first-hand experience — that we could understand what a formidable task it is to organize such a meeting. Therefore our kudos goes to all the previous and future organizers not only of the International Workshops, but also of the European Complement in Health and Disease.

The meeting in NY was dedicated to the many great complementologists who preceded us and to the young and talented investigators who *are* the future of our field. Therefore, we were particularly delighted to see a record number of young investigators attending the XXIII ICW. Despite the global economic hardships, we were also pleasantly surprised to see a robust number of established investigators who came from distant corners of the globe to grace the meeting. We would like to seize this opportunity to thank all who participated especially the Chairs, speakers, Teaching Day lecturers and abstract presenters for making the XXIII ICW a very successful meeting indeed. Special thanks also goes to the keynote speakers— Dr. Michael M. Frank, who gave the Hans Müller-Eberhard Memorial Lecture; Dr. Allen P. Kaplan, who gave the Clinical lecture; and Dr. Betty Diamond, who gave the keynote address.

The final tally of participants was 414 of which 236 were established investigators and 149 young investigators and 29 guests. Not included in the total tally are 17 guests representing our corporate sponsors and exhibitors, without whose support the meeting could not have been realized.

The Teaching Day, run by Ellinor Peerschke, was perhaps the star of the show as it was attended by more than 120 participants—more than twice the expected number—and was taught by some of the outstanding leaders in the field. Based on the survey that was taken after the end of the session, the Teaching Day appears to generate a lot of interest and will remain a mainstay of future ICWs.

We would also like to take this opportunity to express our heart-felt gratitude to all those who took the time to write to us kind words of praise and encouragement. It meant a lot to us. We intend to put selected pictures that were taken during the 5-day meeting on the XXIII ICW website (http://www.hsc.stonybrook.edu/ics2010/) within the next couple of weeks. In the meantime, here are some pictures for you to enjoy:


August 5th in the
Wintergarden Room


EXIT
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Complement Reagents Corner

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