December 1, 2007
Issue 8

Focus on Complement

EUROPEAN COMPLEMENT NETWORK

What's inside?

<1> This 8th issue of "Focus on Complement" brings to you: Flash news on the role of complement in nanoparticle vaccination and on a new mouse model in which the involvement of complement in retinal abnormality and visual impairment was demonstrated, two Spotlights on complement teams in the USA and Norway, the first part of a report on novel findings from the 11th European Meeting on Complement in Human Disease that took place last September in Cardiff. All abstracts and invited papers of that meeting are published in a special issue of Molecular Immunology September 2007. This issue also contains the first article in a series of commentaries on unresolved matters in complement biology. The question raised here is: do neurons produce C1q? Please send to the Editors responses and suggestions for new commentaries.

<2> The 22nd International Complement Workshop will be held in Basel, Switzerland between 28 September and 2 October 2008. Please refer to page 12 for details and invitation.

<3> The ICS has constructed a new Homepage at the old address: http://www.complement.org. Please visit the site, click on 'Become an ICS Member' and fill in the requested information online. You can upload your photo. If you were an ICS member before, click on 'Update your info', use your e-mail address as a username and enter your old password. Once inside your data page you can change your username and password. If you encounter any problem, send e-mail to: info@complement.org.

Thanks to our sponsors:

FLASH NEWS

news flash..
The latest in complement research

Vaccination and complement
Reporter: Sakari Jokiranta

Exploiting lymphatic transport and complement activation in nanoparticle vaccines. Reddy ST et al. Nat. Biotechnol. 2007 Oct;25(10):1159-64.

This exciting study shows two novel aspects in modern vaccine development. First, small size of intradermally applied nanoparticles was shown to be important for their transport via interstitial flow into mouse lymph nodes. In vivo only the ultra-small nanoparticles (diameter 25 nm) were efficiently transported to the lymph nodes and there into dendritic cells and macrophages. Second, the ultra-small nanoparticles activated dendritic cells and caused thereby a proper antibody reaction against ovalbumin in vivo only if the particles activated complement. This was studied using wildtype and C3-/- mice that were injected with nanoparticles engineered to activate the alternative pathway efficiently or poorly. Structurally the complement activating nanoparticles had a hydrophobic core of cross-linked polypropylene sulfide and hydrophilic surface corona of copolymerized polyethylene glycol and prolypropylene glycol (Pluronic). The novelty and importance of this study is clearly in combining the nanoparticle vaccine technology and the dendritic cell activation by in situ complement activation on the particles.

Eyesight and complement
Reporter: Sakari Jokiranta

Complement factor H deficiency in aged mice causes retinal abnormalities and visual dysfunction.
Coffey PJ et al. Proc Natl Acad Sci U S A. 2007 Oct 16;104(42):16651-6.

Susceptibility to age-related macular degeneration (AMD) in humans has recently been associated with polymorphisms in several complement proteins, the most frequent being factor H Y402H polymorphism. Since this slowly developing disease has a huge medical, economical, and social impact it would be highly important to obtain a platform to study therapeutic approaches in animals. The authors demonstrate that 2-year-old FH-/- mice have impaired visual acuity, reduced rod responses on electroretinography, autofluorescent subretinal deposits in confocal laser ophthalmoscopy, accumulation of C3 in neural retina, and several changes in retinal histology. Therefore this report is the first rodent model of AMD-type disease although mice do not have a macula. This animal model might prove to be beneficial for both pharmacological AMD research and analysis of complement involvement in AMD.

SPOTLIGHT ON TEAMS - I

John Atkinson's Team

Washington University School of Medicine, St. Louis, MO, USA

Our research team is located at the Washington University School of Medicine in St. Louis, Missouri, USA. In the 1970s and early 1980s, the lab's research interests centered on C4 and C2 in man and mouse, especially their genetics and biosynthesis in this pre-molecular biology era. Since the mid 1980s, the laboratory has focused on identifying and characterizing membrane glycoproteins that regulate complement activation and serve as receptors for immune complexes. Analyzing the structure/function and expression of these proteins, especially CD35, CD46, and CD55, have led us down many interesting paths. We have helped to identify and characterize members of a multigene family of receptors and regulators (the RCA gene/protein cluster at 1q32), identified interactions with several microorganisms (CD46 has been called a pathogen magnet), tried to find new roles for these proteins in reproduction and recently explored a connection to T regulatory cells. Currently, we are also studying poxvirus and flavivirus proteins that mimic human complement regulators, using $Crry^{-/-}$ and other knockout mice to analyze complement homeostasis, and characterizing mutations and polymorphisms in CD46, factor I and C3 that predispose to atypical hemolytic uremic syndrome (aHUS), age-related macular degeneration (AMD) and other human diseases.

Current members of the laboratory who are part of our team but also directing independent projects are Dennis Hourcade (properdin), Claudia Kemper (T regulatory cells), Kathy Liszewski (MCP, viral inhibitors and also our terrific long-standing lab manager), Xiaobo Wu (Crry), Dirk Spitzer (molecular engineering), Paula Bertram (protein production) and Richard Hauhart (CR1, malaria).

The laboratory greatly appreciates and especially thanks Madonna Bogacki and Lorraine Schwartz for all of their assistance in making the "joint" run smoothly (most of the time) and for welcoming students and colleagues to our institution and city. The laboratory thanks the many students and postdoctoral fellows who have contributed so much to these studies and for enlivening the lab (their spirits and reagents still abound). We have also been exceptionally fortunate to collaborate with the many wonderful colleagues both in St. Louis and from around the world!

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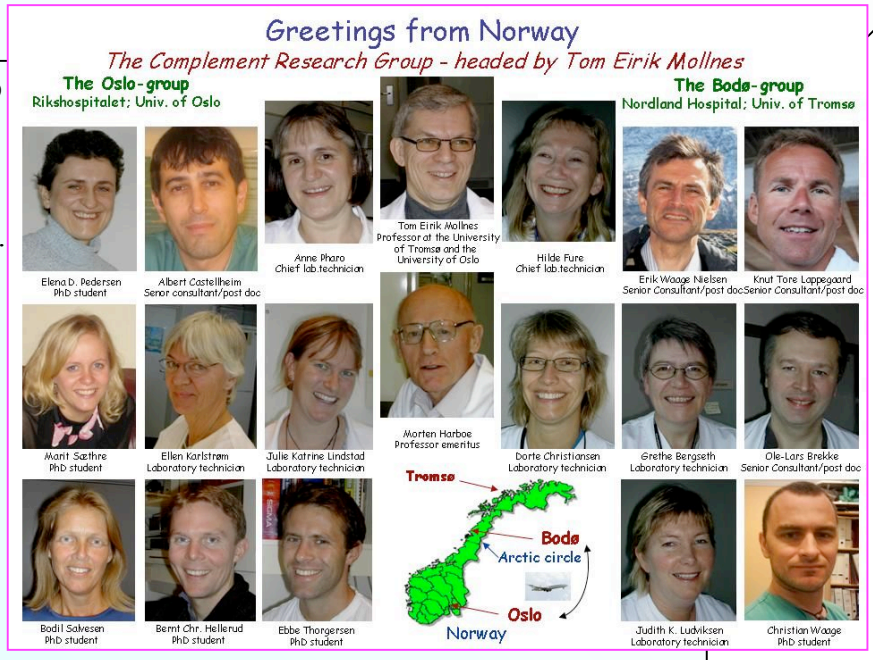
SPOTLIGHT ON TEAMS - II

Tom Eirik Mollnes

University of Tromsø and University of Oslo, Norway



The Complement Research Group headed by Tom Eirik Mollnes is located at two different labs. They are separated by 1200 road kilometers or 1.5 hour flying time. The lab in the north ("The Bodø-Group" on the photo) is at Nordland Hospital in Bodø, a city of 40,000 inhabitants located north of the Arctic Circle in "the land of the midnightsun". The lab is connected to the University of Tromsø, one hour flight north of Bodø. The lab in the south ("The Oslo-Group" on the photo) is in Oslo, the Capital of Norway, at Institute of Immunology, Rikshospitalet and University of Oslo. Mollnes started his research under supervision of prof. Morten Harboe, who has now joined the group as Professor Emeritus.

Our research theme is "The role of Complement in Human Disease". We focus on assay development, activation mechanisms and the interaction of complement with the inflammatory network. In particular, we are searching for secondary inflammatory effects of complement activation. We try to understand the cross-talk between complement and other inflammatory mediators. This will hopefully lead to a better understanding of the role of complement in the pathophysiology of disease and to make it possible to design a rational platform for therapeutic complement modification. Currently all PhD students and postdocs in the group are medical doctors. The technical staff is highly skilled on basic and advanced methods.

We are working in close collaboration with several clinical groups. In order to understand the mechanisms of the "inflammatory network", we suggest that it is crucial to build "scientific networks". Synergy exists between inflammatory mediators in order to obtain specific and enhanced biological effects. Similarly, science will proceed faster if we collaborate and utilize the synergistic effects of our various knowledge, capabilities and talents. Therefore, a main goal for us is to build networks with synergistic effects, locally and across the artic circle. Today, geographic borders should be no obstacle for fruitful collaborations.

Recent years' literature indicates that complement research will expand worldwide in the future. It is our goal to contribute to this progress.

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UNRESOLVED MATTERS

Do neurons produce C1q?

Discussant: Caleb E Finch, PhD (cefinch@usc.edu)
Davis School of Gerontology and USC College
University of Southern Californa, Los Angeles CA USA
Invited by Andrea Tenner

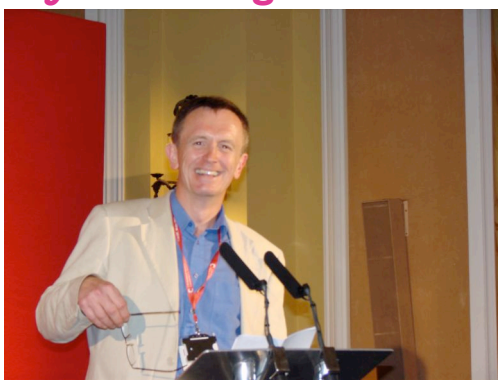
Professor Weihe has shown with beautiful confocal immunocytochemistry that microglia in lentivirus infected monkey brains have increased content of C1q mRNA and C1q protein, whereas C1q was not detected in nearby neurons (Depboylu et al 2005). In other neurodegenerative conditions, we also showed prominent induction of C1q in microglia by in situ hybridization and immunocytochemistry, in Alzheimer brains and in rodent models of deafferentation and excitotoxicity (Pasinetti et al 1992; Johnson et al 1992). However, we also observed C1q grains densely distributed over neuronal layers. Because of the difficulty in resolving microglia within these dense neuronal layers, we studied primary neuronal cultures grown in serum free media to suppress microglia. Single neurons presented clear C1q mRNA signals, which were further induced by excitoxic treatments (Rozovsky et al 1994). Other in situ studies confirmed increased neuronal C1q mRNA in Alzheimer (Shen et al, 1997). Additionally, we showed that the increased C1q protein was synthesized *de novo* by [S35] methionine labeling *in vivo* and that there was correspondingly increased bioactivity in a C1q-dependent hemolytic assay (Goldsmith et al 1997). These reports support findings from the UCIrvine group of Andrea Tenner and colleagues that the increased neuronal C1q protein in early Alzheimer (Fonseca et al 2004; Head et al 2001) is endogenously synthesized. Despite the C1q mRNA in neurons, the neuronal C1q protein, as well as that in senile plaques, could also be synthesized by local microglia, or could be taken up from the blood proteins included in human postmortem tissues that can not be perfused (Goldsmith et al. 1997, Fig 1B). The fog may lift slowly on the cell sources of C1q and other senile plaque proteins. Furthermore, much remains obscure about why neurons express C1q under some circumstances, but also express C-reactive protein (Yasojima et al 2000), which can activate C1q, as well as complement regulators such as apoJ (complement lysis inhibitor) (Rozovsky et al., 1994).

Note added in press: Beth Stevens and Ben Barres of Stanford University and their colleagues reported at the Society for Neuroscience Annual meeting in San Diego (Nov., 2007; Abstract # 131.1) observations of robust induction of C1q synthesis in neurons in postnatal mouse brain as assessed by RT-PCR and immunohistochemistry, but most importantly by in situ hybridization. This induction of neuronal C1q synthesis is dependent on the specific state of local astrocyte differentiation/activation. These findings and their proposed role for the classical complement pathway in synaptic pruning will be described in their manuscript in the Dec. 14th issue of Cell.

The 11th European Meeting on Complement in Human Disease

September 2007 Cardiff, Wales, UK

Part 1 of 2 : Digest of oral sessions, presented by Paul Morgan



Preamble

The 11th European Meeting on Complement in Human Disease, held in Cardiff between 8th and 11th September 2007, provided a feast of excellent science and socialising. The Gods were smiling on the complement community, bringing glorious late summer sunshine for the whole of the meeting! Some 320 delegates were treated to a fantastic scientific programme covering all aspects of clinical complementology.

The teaching day, targeting graduate students, junior post-docs and others new to the field, was held at the School of Medicine. A full house of over 100 was made to work hard in small-group interactive sessions led by a distinguished faculty.

The Meeting Programme comprised 53 oral presentations, 157 posters, three invited speakers and two company presentations. The presentations and posters were divided into eight sessions, each covering a specific area. All the abstracts and accompanying reviews are published in Molecular Immunology (2007) vol. 44, Issue 16. What follows is a very brief summary of each of the oral presentations – an attempt to capture the key messages in a few words. I apologise in advance for inaccuracies and omissions.

Session 1; Complement and Adaptive Immunity

The meeting kicked off with two presentations from Kemper's group, building on their demonstration a few years ago that CD46 was implicated in T cell differentiation and function. They have shown that activation of T cells via CD46 induces a regulatory cell phenotype (cTReg); here they showed that T cells activated in this manner resemble gut-resident T cells in terms of adhesion receptor and chemokine expression profile. These findings raise the possibility that CD46-activated T cells are particularly involved in mucosal immunity in the gut. In a second presentation they described roles of CD46-induced T regulatory cells in controlling B cell responses. Co-culture of cTReg with either naïve or memory B cells caused enhanced antibody production, particularly for IgA and IgM. They described an unpublished association between common variable immune deficiency and deficiency of CD46 expression, and suggested that this might be caused by a loss of the observed effects of cTReg on B cells.

Continuing in the theme of complement-induced defects in T/B cell function, Ghannam and colleagues reported a new case of C3 deficiency. They identified a number of deficits in immune function, including a decreased T cell proliferative capacity, absence of the B memory cell population and reduced antibody responses, and a diminished IL-10 response from cTReg, suggesting a two-way conversation between complement and this cell type.

Reis and co-workers explored the effects of C3 deficiency on monocyte differentiation into dendritic cells (DCs). They examined the expression of multiple markers during differentiation in the presence either of normal serum or C3-deficient serum and found that absence of C3 caused reduced expression of DC-SIGN, HLA-DR, CD80 and CD86, and reduced secretion of multiple cytokines, including TNF, IL-6 and IL-12. Interactions between Toll-like receptors (TLR) and complement were suggested.

Li and co-workers examined the effects of C5a signalling on DC function. They reported that mouse DCs expressed C5a receptor (C5aR) and that C5a was generated locally in cultures of DCs. Blocking of the C5a receptor on DCs diminished capacity to activate T cells and administration of C5a enhanced capacity to activate. DCs from C5aR-/- mice had a much-reduced capacity to activate CD4 T cell responses compared to controls, suggesting an important role for C5a in this interaction.

Interactions between complement and TLRs emerged again in a study of the effects of complement inhibition by low molecular weight dextran sulfate on TLR-induced DC maturation (Spirig et al). Dextran sulfate treatment inhibits complement activation at multiple stages and has diverse other effects, notably on NK cell function. When DC maturation was triggered by the TLR ligand heparan sulfate (released from damaged endothelia), dextran sulfate prevented the maturation. The precise mechanism of this effect was unclear, although a marked reduction in NFkB activation was demonstrated. A role for low molecular weight dextran sulfate in protecting transplanted organs was proposed.

Kohl et al reported studies on the roles of C3a and C5a in models of asthma. C3aR expression was markedly increased in the lungs of C5aR-/- mice compared to controls, and these two receptors had apparently opposite effects in the asthma model. Absence of C3aR signalling caused a decrease in Th2 immunity whereas absence of C5aR signalling caused an increase in Th2 immunity. The critical player in the model was signalling through C5aR. The complexities in the model make it difficult to predict strategies for treatment of asthma in man.

ECN Medal Award Ceremony

At this meeting the ECN Medal was awarded to the late Anders Sjöholm, past ECN President, for his numerous contributions to the fields of complement deficiency and Clinical Complementology. In this picture, his son is receiving the medal from Sakari Jokiranta, ECN Secretary, on behalf of his father. Also on the stage are Lennart Truedsson, who described Anders' accomplishments, and Paul Morgan.

Session 2; Inflammatory diseases, therapeutics and diagnostics

A central role for complement activation in myocardial ischaemia has been accepted for some time but the precise mechanisms of activation are less clear. The Stahl lab has previously suggested that the lectin pathway is important in this respect. In this presentation they explored whether the lectin pathway is particularly relevant in myocardial ischaemia in diabetes. Wild-type and MBL-/- mice were rendered diabetic by treatment with streptozotocin and then subjected to myocardial ischaemia. Diabetic wild-type mice were more susceptible to myocardial injury than non-diabetic controls, and MBL deficiency in diabetic mice protected against injury, implicating the lectin pathway in the disease process.

Holers and co-workers explored the pathways of complement activation driving pathology in a mouse model of arthritis induced using anti-collagen antibodies. They showed that mice deficient in factor B were resistant to disease in this model while mice deficient in either C4, C1q or MBP mice were not. The data unequivocally demonstrate that a functional alternative pathway is necessary and sufficient for disease in this model; this study supports a growing body of evidence that places the alternative pathway amplification loop at the centre of pathology.

Further support for this concept was provided by Mihai et al. in a mouse model of the blistering disease Epidermolysis Bullosa induced by antibodies against Type VII collagen. As in the arthritis study, a panel of complement knockout mice was tested and protection from disease was obtained only in factor B deficiency, implicating the alternative pathway amplification loop in the skin pathology.

The demonstration in 2005 of a strong association of a polymorphism in factor H with age-related macular degeneration (AMD) triggered an explosion of interest in the role of complement in this common and devastating disease. Zipfel et al reported that the disease associated variant of factor H (H402) showed reduced binding to multiple ligands compared to the protective variant (Y402). Importantly, the H402 variant not only bound cell surfaces less well but also showed reduced cofactor activity once bound. AMD might therefore be caused by dysregulation of complement and be responsive to anti-complement therapies.

Tumors evade immune attack in many ways, including increased expression of complement regulators. Neutralising complement regulators on tumors is an attractive strategy to enhance the efficacy of anti-tumor antibodies. Donev described a new strategy for achieving this aim, targeting specific sequences in the promoter region of the CD59 gene that are involved in its over-expression in neuroblastoma. Peptide agents achieved remarkable down-regulation of CD59 in neuroblastoma but did not alter expression in non-neoplastic cells.

Complement activation in the transplanted kidney contributes to graft failure. Lewis and colleagues hypothesised that the C5a/C5aR pathway was involved in graft inflammation and failure. In a mouse model, a specific C5aR antagonist was included in the graft preservation fluid instilled into the donor kidney. Graft survival was significantly extended in the model. Studies in human donor kidneys showed that C5aR expression increased with extended ischaemic time and inversely correlated with graft function. Whether this strategy will improve outcome in human renal transplantation remains to be tested.

Systemic administration of complement inhibitors is an inefficient way of protecting cells and may predispose to bacterial infections and immune complex disease. Targeting the inhibitor to cell membranes should increase efficiency and decrease risk. Smith has pioneered this strategy, developing membrane-associating tags that localise the agent to the cell surface. Success in models has been translated into human trials in renal transplantation. Promising early results require replication in larger studies.

Taylor and colleagues described a new technology for assessing complement activation by therapeutic monoclonal antibodies. Their “Spinning Disc” confocal method enabled real-time monitoring of opsonisation, membrane attack complex (MAC) deposition and killing in cells targeted with antibody and complement. Cells during lethal or non-lethal complement attack threw out elongated membrane projections, termed “streamers”. Production of streamers preceded killing and required MAC formation and could be mimicked by other pore-formers suggesting that it was

triggered by the MAC pores. The study revealed interesting differences in the complement activating properties of different therapeutic antibodies.

Session 3; Complement activation and regulation

With the advent of new variant Creutzfeld-Jacob disease, prion diseases have become a major public health concern. It has previously been suggested that the "infectious" prion proteins bind C1q and activate complement. Here, Dumestre-Perard showed that neither prion monomers nor fragments of the prion protein bound C1q but oligomerised (or surface-immobilised) prion protein did bind C1q and activate complement. The relevance of this observation for prion-mediated pathogenesis is as yet unknown.

As evidence accumulates implicating the lectin pathway in various clinical situations, the need for a simple and specific assay for routine measurement of lectin pathway activity grows. Palarasah et al first showed that treatment of serum with polyanetholsulphonic acid sodium (PAS) ablated activity of the classical and alternative pathways through undefined interactions with C1q and factor D respectively. The lectin pathway survives PAS treatment and can be simply measured by incubation of PAS-treated serum on mannan-coated wells and measuring C3 deposited on the wells. Assays specific for the classical pathway (using human albumin-coated plates reacted with anti-albumin IgG) and alternative pathway (using LPS-coated plates) were described, and used to optimise the concentration of PAS (approx. 0.5mg/ml in serum) used in the lectin pathway assay.

Prechl and co-workers used a protein microarray approach to measure complement activation. The protein antigens were "printed" on the array, and incubated with test antibodies and complement. Specific fluor-labelled secondary antibodies revealed the selective binding of antibody and complement. The system was also used to directly interrogate the complement activating capacity of different antibodies or of other complement-activating substances. Clinical uses in screening for autoimmune or infectious diseases were proposed.

A role for the extracellular matrix (ECM) in complement activation in chronic inflammatory diseases was proposed by Sjoberg et al. Short proteoglycans released from ECM (particularly fibromodulin and osteoadherin) activated complement via both classical and alternative pathways when immobilised on plastic. Direct binding of C1q to these proteoglycans was demonstrated.

Despite many recent innovations, there is still a need for better and simpler assays for the routine evaluation of complement activation in clinical samples. Skjodt et al have generated a panel of monoclonal antibodies and identified several that are specific either for C3c alone or iC3b and C3c. Using a C3c-specific antibody capture system, a specific assay for C3c was generated and validated using CVF and immune complex activated and factor I deficient sera, and by immunoprecipitation from activated serum. This new, simple assay should prove a valuable addition to the tools available for monitoring complement activation in vivo.

Session 4; Complement genetics and deficiencies

Deficiencies of components of the terminal pathway predispose to meningococcal disease. The least common of these, C5 deficiency, may also have other consequences due to loss of the

capacity to generate C5a. Isaac et al presented a large family in which four members, including three siblings, were C5-deficient. All suffered episodes of meningitis. The genetic basis was shown to be the skipping of exon 30 in the C5 gene, a consequence of a point mutation in the relevant splicing site.

A relationship between C4 gene copy number and cardiovascular disease (low copy number correlating with high morbidity) has previously been proposed. Fust et al explored the basis of this relationship. They showed that rare polymorphic changes (of unknown functional effect) in the neighbouring gene encoding the steroid biosynthesis enzyme 21-hydroxylase were strongly associated with the presence of C4B null alleles. Given the importance of 21-hydroxylase in steroid hormone production and the stress response, they propose that the observed association of C4 null alleles with cardiovascular morbidity is a linkage effect.

Complement has long been implicated in the pathology of sepsis but the precise role it plays remains unclear. Lappegard and colleagues used a whole-blood ex vivo sepsis model (incubating with live bacteria) to examine the roles of complement on leukocyte activation. Blood from patients deficient in C2 and, particularly, C5, showed much lower leukocyte activation in the model compared with normal blood. By using a C5a receptor antagonist it was confirmed that several of the leukocyte activation events were highly dependent on C5a, suggesting that such agents might be effective in therapy of sepsis.

As noted above, interest in factor H has exploded, fuelled by links to AMD. Martinez-Barricarte et al looked at the effects of factor H haplotypes and copy-number variation in the factor-H-related genes in eye and kidney diseases. They showed that this genetic region is a hot-spot containing hundreds of SNPs and frequent duplication events. The different factor H haplotypes were shown to be predictive of risk/protection for specific pathologies and several major gene rearrangements, some novel, some previously described, were also found to be predictive of disease.

Ficolin-3 is a member of the lectin family of complement-activating molecules and, like several other family members, shows a very wide inter-individual range of serum concentrations. Munthe-Fogg et al explored the molecular basis of this broad concentration range and identified a polymorphism in the ficolin-3 gene, present with an allele frequency of about 1% in Denmark, that was strongly associated with low serum concentrations in heterozygotes. No homozygotes were found in the population studied. Analysis of recombinant proteins suggested that the product of the minor allele was unstable.

Deficiency of factor I is a rare condition marked by uncontrolled activation of complement and secondary deficiency that predisposes to bacterial infections. Disease is universally severe and difficult to manage. The molecular basis of factor I deficiency is poorly understood. Here, Nilsson et al identified eight mutations in 5 individuals deficient in factor I (two homozygotes, three compound heterozygotes). Mutations were, with one exception, in the LDL-receptor and serine protease domains. Most of the mutations caused decreased secretion of fI;

one generated a truncated protein missing the serine protease domain.

Measuring C4 gene copy number is a useful aid in the assessment of patients with lupus. Available assays are difficult and not well-suited to the routine laboratory. Wu et al described a simple and rapid quantitative PCR method for C4 gene copy. The assay has been validated in over 1000 clinical samples.

Gene copy number variation (CNV) is a neglected aspect of genetic analysis. Yu et al propose that CNV in genes involved in immunity can influence disease susceptibity. They used pulsed field gel electrophoresis to measure C4 gene copy number and deletion of the CFHR3-CFHR1 region in the factor H gene cluster. The latter deletion, known to be protective against AMD, was here shown to be protective against SLE in a large comparative study.

Sections 5-8 will be published in the next bulletin issue...

Final Thoughts

As president of the European Complement Network for the past six years, I have taken great pleasure in watching the European Meeting go from strength-to-strength. It was fitting that my term of office ended with this opportunity to host the meeting in Cardiff and I thank my co-organisers, the guest speakers, sponsors and all the delegates for making it such a success. While the European Meetings on Complement in Human Disease now match the International Complement Workshops for quality (and size!), they remain distinctive with a clear focus on disease and a mission to educate and foster collaboration. These are important distinctions and I hope that the European Complement Network will continue to recognise them and defend these meetings vigorously. The international complement community would be poorer if the European meetings became too much like the International Workshops.

Paul Morgan
Cardiff; October 2007.

Get ready for our next ICW:

XXII International Complement Workshop
Basel, Switzerland
28 September – 2 October 2008

Local Organizing Committee
Prof. Juerg A. Schifferli, University Hospital Basel, Switzerland
PD Dr. Marten Trendelenburg, University Hospital Basel, Switzerland
Prof. Robert Rieben, University of Bern, Switzerland

www.akm.ch/ICW2008

Mark the Date: XXII International Complement Workshop, 28 September – 2 October 2008

Dear Friends,

We invite you to join the Workshop of the community of basic and clinical researchers in complement, who will be reporting their newest findings in Basel.

The Workshop will start with a Welcome Party on Sunday evening, and will be followed from Monday until Thursday by scientific presentations of the best work submitted to the Workshop, Poster presentations and some Lectures relating the basic findings to clinical observations.

The work will be interrupted on Wednesday afternoon to have cultural or sight-seeing activities, and after the final scientific sessions on Thursday, we will have our traditional dinner.

The deadline for abstracts will be appearing on the website in January 2008 (www.akm.ch/ICW2008), but you can expect that it will be around May 2008.

The Workshop will be preceded by a Teaching Day on Sunday, 28 September 2008, which is meant for a maximum of 100 young students or post-docs. The selection of the applicants will be done according to the strict criteria of being at the beginning of their career in our field. The teachers will be mainly members of the ICS board, and we thank them for their spontaneous help.

We would be happy if you could help us making sure that all researchers working in our field are aware of our Workshop, by drawing their attention to the Website (www.akm.ch/ICW2008).

If you have any queries or concerns, please contact the Administrative Secretariat (info@akm.ch), or any of the members of the Local Organizing Committee.

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