29 BF, C6, and C7 Polymorphisms in Japanese Patients with Chronic Glomerulonephritis

H. Nishimukai[*a], *I. Nakanishi*[b], *H. Kitamura*[c], *N. Iida*[b], *Y. Takeuchi*[a], *K. Mizutani*[d], *T. Shinomiya*[a]

[a] Department of Legal Medicine and [d] 1st Department of Surgery, School of Medicine, University of Ehime; [b] Renal Disease Center, Osaka Prefectural Hospital; [c] Department of Immunology, Center for Adult Diseases, Osaka, Japan

BF subtypes and C6 and C7 types were studied in Japanese patients with various types of chronic glomerulonephritis – IgA nephropathy, idiopathic membranous nephropathy (IMN), and minimal-change nephrotic syndrome (MCNS) – by using isoelectric focusing followed by immunoblotting. There were significant differences in the allele and phenotype frequencies of BF, C6, and C7 between the patient groups and controls. Strong or significant associations between the diseases and the complement types were as follows: (1) IgA nephropathy and C7 5 ($p < 0.001$, RR = 12.7); (2) IMN and BF FA ($p < 0.05$, RR = 2.2); (3) IMN and BF FB ($p < 0.001$, RR = 6.3); (4) IMN and C7 4 ($p < 0.05$, RR = 2.4); (5) MCNS and C6 B2 ($p < 0.05$, RR = 2.7); (6) MCNS and C7 2 ($p < 0.05$, RR = 2.3), and (7) MCNS and C7 5 ($p < 0.001$, RR = 14.2). These complement allotypes may contribute to the pathogenesis of chronic glomerulonephritis.

30 C8 Alpha-Gamma Polymorphism and C8 Hemolytic Activity in Five Siblings with C8β-Deficient Individuals

W. Nürnberger[*a], *I. Michelmann*[a], *V. Wahn*[a], *F. Tedesco*[b]

[a] Zentrum für Kinderheilkunde, Heinrich-Heine-Universität, Düsseldorf, BRD; [b] Istituto di Patologia Generale, Università di Trieste, Italia

Five sibships with C8β-deficient individuals were analyzed. Altogether, 35 persons were studied, 9 of them were C8β-deficient. The C8α-γ polymorphism was analyzed using SDS-PAGE and subsequent immunoblotting [Nürnberger et al, J Immunol Methods 1988;109:257]. Normal individuals (n = 68) showed the polymorphic variant AB (34/68), A (23/68), and B (11/68). All C8β-deficient individuals showed the polymorphic variant A. 8/12 of the obligate heterozygotes (fathers, mothers, children) possessed variant A, 4/12 variant AB. 7/13 of the other relatives possessed variant A, 6/13 variant AB. None of the C8β-deficient individuals or the relatives possessed variant B. The C8-hemolytic activity was tested using standard hemolytic assays. Individual normal sera (n = 28) scattered from 62 to 136% (median 99%) of pooled NHS. C8β-deficient individuals completely lacked hemolytic activity. Obligate heterozygotes had hemolytic activities from 32 to 82% of NHS (median 63%), with 6/12 having less than 62%. The other relatives scattered from 67 to 112% (median 73%) of hemolytic activity in pooled NHS. No association was found (neither in normals nor relatives from C8β-deficient patients) between the C8α-γ pattern and C8 hemolytic activity. However, the polymorphic variant A is overrepresented in the analyzed sibships. These observations support earlier findings [Rogde et al, Ann Hum Genet 1986;50:139] that the genes encoding for C8α-γ and C8β are closely linked on chromosome 1.

31 C6 Polymorphism and C6 Deficiency in Site Strains of the Mutation-Prone Peru-Coppock Mice

A. Orren[*a], *M.E. Wallace*[b], *M.J. Hobart*[c], *P.J. Lachmann*[c]

[a] Department of Immunology, University College of Galway, Ireland; [b] Department of Genetics, University of Cambridge; [c] MIP, MRC Centre, Cambridge, UK.

Peru-Coppock site strains have been developed by sib-mating animals caught at eight sites in the Rimac Valley, Peru, in 1976. They have been shown to have an unusually high tendency to mutation. C6 allotyping of sera from mice of 5 of the site strains showed 3 to possess the common C6A1 haplotype and 2 to have the C6A2B2 haplotype. C6A2B2 has previously only been found in the AKR and RF inbred strains and in no wild mice. In addition, two sublines of site 1 mice

were tested, and one was also found to be C6A2B2. The other site 1 subline lacked both C6 functional and antigenic activity and is thus C6 deficient. This subline has now been designated Peru-Coppock C6Q0. The mice have normal C7 activity, and C7 allotyping has shown them to be C7-2 which is the C7 allotype found in AKR mice. Genetic mechanisms responsible for the C6 deficiency are under investigation.

32 Major Histocompatibility Complex (MHC) Coded Complement Allotypes in AIDS-Kaposi Sarcoma, AIDS-Related Complex/WR5, and in Normal Controls[1]

Georg Plum, H. Krickeberg, C. Bendick, H. Rasokat, G. Mauff*
Departments of Medical Microbiology, Virology, Internal Medicine II, and Dermatology, University of Cologne, FRG

In AIDS-Kaposi Sarcoma (AIDS-KS) and AIDS-opportunistic infections major histocompatibility complex (MHC) associations have been reported for class I and class II genes but not for class III (C2, BF, C4A, C4B). C4 allotypes appear of major immunogenetic relevance for their potential differences in virus-neutralizing potency. In the present study MHC class III allotype frequencies of 30 AIDS-KS and 30 AIDS-related complex (ARC)/WR5 patients and 60 HIV-negative control individuals were compared. All individuals were of West German origin. Diagnosis of ARC and KS (CDC and WR criteria) was done by clinical and laboratory parameters. C2 allotypes were determined by isoelectric focusing and immunoblotting; BF allotypes by agarose gel electrophoresis (AGE) and immunofixation. C4 typing was performed on neuraminidase-treated plasma by AGE immunofixation/haemolytic overlay or immunoblotting using poly- and monoclonal antibodies for C4A/B. Null allele frequencies were corrected by iterative calculation of the Hardy-Weinberg equilibrium. No significant deviation of allele frequencies was observed in the performed tests between KS and ARC patients and normal controls for C2, BF, C4A, and C4B. The results indicate lack of strong MHC class III association with AIDS-KS or ARC. They do not exclude, however, a possible role of deletions and homo/heteroduplications of the investigated complement components, since these could not be determined with the applied techniques. In this respect further investigations are presently under way.

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33 C4A Deficiency, a Genetic Risk Factor for HIV Infection[1]

C. Rittner[a], A. Notghi[a], K. Gutfreund[b], S. Rossol[b], C. Weber[b], P. Everke[a], B. Stradmann-Bellinghausen[a], A. Susemichel-Hüppner[a], G. Ramadori[b], P.M. Schneider[a], G. Hess[b]*
[a] Institut für Rechtsmedizin und
[b] I. Medizinische Poliklinik, Mainz, BRD

67 HIV Patients were studied for the following immunogenetic markers: HLA-A, -B, -C, -DR, C2, BF, C4A, C4B, and C3, DR/DQβ and C4 21-OH RFLPs and C4 α-chains, and were compared with the normal population. Significant deviations were found in HLA-DR, C4A allotype frequencies, C4A gene deletions, and the expression of C4A and C4B α-chains. At the HLA-DR locus, increased frequencies of DR1, DR5(w11), and DR7 were noted with a decrease of DRw6. In C4A allotyping, a significant high proportion of Q0 alleles, reflected in the number of C4A gene deletions ($p = 0.0008$), was observed. The α-chains in sodium dodecyl sulfate gels [Roos et al., Nature 1982] showed a weaker expression (C4A < C4B) compared with the controls, independent of the stage of the disease (T4 > 400 vs. < 400 cells/μl or Walter Reed 0–2 vs. 3–6, respectively). The inherited C4A deficiency and HLA-DR1, DR5, and DR7 may be risk factors for seroconversion and not for the progression of the disease. All patients possessed at least one of these factors, whereas 27% of normal population lack all ($p = 0.0001$). We conclude that AIDS exhibits immunogenetic characteristics which have been described previously for some slow-virus and autoimmune diseases.

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34 Formal Genetics, Po
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S. Rogde, B. Mevåg*
J. Sodetz
Institute of Forensic
Department, Riksho
Norway, and Depart
School of Medicine,
Carolina, Columbia,

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35 C8A and C8B Polym

S. Rogde, P. Teisbe*
Institute of Forensic
Department, Riksho
Norway

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C8AA 0.59, C8AB 0.41,

36 Complement C2, BF,
Leprosy and Healthy

J. Santamaria, Iara*
A. Ragiotto, N.P. Ali
University Hospital,
Curitiba, Brazil, and
Microbiology, Colog

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