EMBODY 2000

European Meeting on Biomarkers of Organ Damage and Dysfunction

Cambridge, UK 3-7 April 2000

Final Programme and Abstract Book

Scientific Programme

Wednesday 5th April

Parallel Symposia (continued)

14.00 – 15.30 **Auditorium:**
Markers in acute hepatic failure
Chairperson: Dr A Gimson, UK

14.00 Prognosis and Management. *Dr F Larsen, Denmark*

14.30 Artificial Liver Support. *Dr R Hughes, UK*

15.00 - 15.30 **Free communications**

15.00 The monoethylglycinexylidide (MEGX) test as a marker of hepatic dysfunction in septic patients with pneumonia. *Dr AA Igonin, Russia*

15.15 Neuronal and glial markers and their relation to the development of intracranial hypertension in patients with fulminant hepatic failure. *Dr GI Strauss, Denmark*

14.00 – 15.30 **Umney Theatre:**
Markers of regulation and response
Chairperson: Prof N Fausto, USA

14.00 Cytokines and signalling in inflammation. *Prof Heinrich, Germany*

14.30 Responses to viruses and self. *Prof M Manns, Germany*

15.30 Coffee break & poster viewing

Parallel Symposia

16.00 – 17.30 **Auditorium:**
Markers of hepatic fibrosis and chronic end-stage disease
Chairperson: Dr G Alexander, UK

16.00 Liver Fibrosis. *Prof M Arthur, UK*

16.30 Progress for hepatic fibrosis and chronic end-stage disease. *Prof M Burdelski, Germany*

17.00 - 17.45 **Free communications**

17.00 Serum type III procollagen peptide (PIIINP): a biomarker of hepatic fibrogenesis in psoriasis. *Dr A Smith, UK*

17.15 Importance of positron emission tomography for strategy in liver resection of primary and secondary liver tumours. *Dr B Boehm, Germany*

17.30 A novel system for the determination of a panel of tumour markers based on a biochip technology. *Dr CM Pope, UK*

16.00 – 17.30 **Umney Theatre:**
Markers of gastrointestinal disease
Chairperson: Prof H Hodgson, UK

16.00 Abdominal tumours. *Dr N Wright, UK*

16.30 Malabsorption. *Prof PJ Ciclitira, UK*

17.00 Pancreatic abnormalities. *Prof PG Lankisch, Germany*

17.30 - 18.00 **Free communications**

17.30 Matrix metalloproteinase 2,9 and tissue inhibitors of metalloproteinase-1 and 4 are increased in the vitreous humour of diabetic patients compared to non-diabetic subjects. *Dr BH Patel, UK*

17.45 Biochemical evaluation of patients with acute pancreatitis.
Dr S Ignjatović, Yugoslavia

Wednesday 5th April

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Cytokines and signaling in inflammation

Prof PC Heinrich, Aachen, Germany.

Cytokines play an important role in the communication between cells of multicellular organisms. As intercellular mediators, they are key players in the control of the immune response during infections, inflammatory joint, kidney, vessel and bowel diseases or neurological and endocrinological autoimmune diseases. Cytokines have been classified, on the basis of their biological responses, into pro- and anti-inflammatory cytokines. The group of pro-inflammatory cytokines comprises IL-1, TNFα, IL-8, interferon γ; anti-inflammatory cytokines are IL-4, IL-10, IL-13, TGFβ. Pro- as well as anti-inflammatory properties have been described for the so-called IL-6-type cytokines including IL-6, IL-11, leukaemia inhibitory factor, oncostatin M, ciliary neurotrophic factor and cardiotrophin. This latter subfamily was found to signal through the activation of Janus tyrosine kinases (Jaks) and the transcription factors of the STAT (signal transducers and activators of transcription) family. The Jak/STAT pathway involves the dimerization of the signal transducers gp130, LIF-R, OSM-R, their tyrosine phosphorylation, recruitment of STAT factors and the tyrosine phosphatase SHP-2, translocation of tyrosine- and serine-phosphorylated STAT-dimers to the nucleus and binding of STATs to enhancer sequences of respective target genes resulting in transcriptional activation.
In this presentation, emphasis will be placed upon mechanisms of termination and modulation of IL-6-type cytokine signalling, i.e. (i) the role of the tyrosine-phosphatase SHP-2 counteracting acute phase protein (APP) induction; (ii) the role of SOCS feedback inhibitors in APP synthesis; (iii) the importance of different half-lives of the signalling molecules gp130, Janus kinases, SHP-2, STATs and SOCS; (iv) internalization of the receptor complexes (constitutive internalization of gp130 due to a di-leucine motif within the cytoplasmic tail). Finally, new data on the cross-talk between MAP kinases and the Jak/STAT pathway will be presented.

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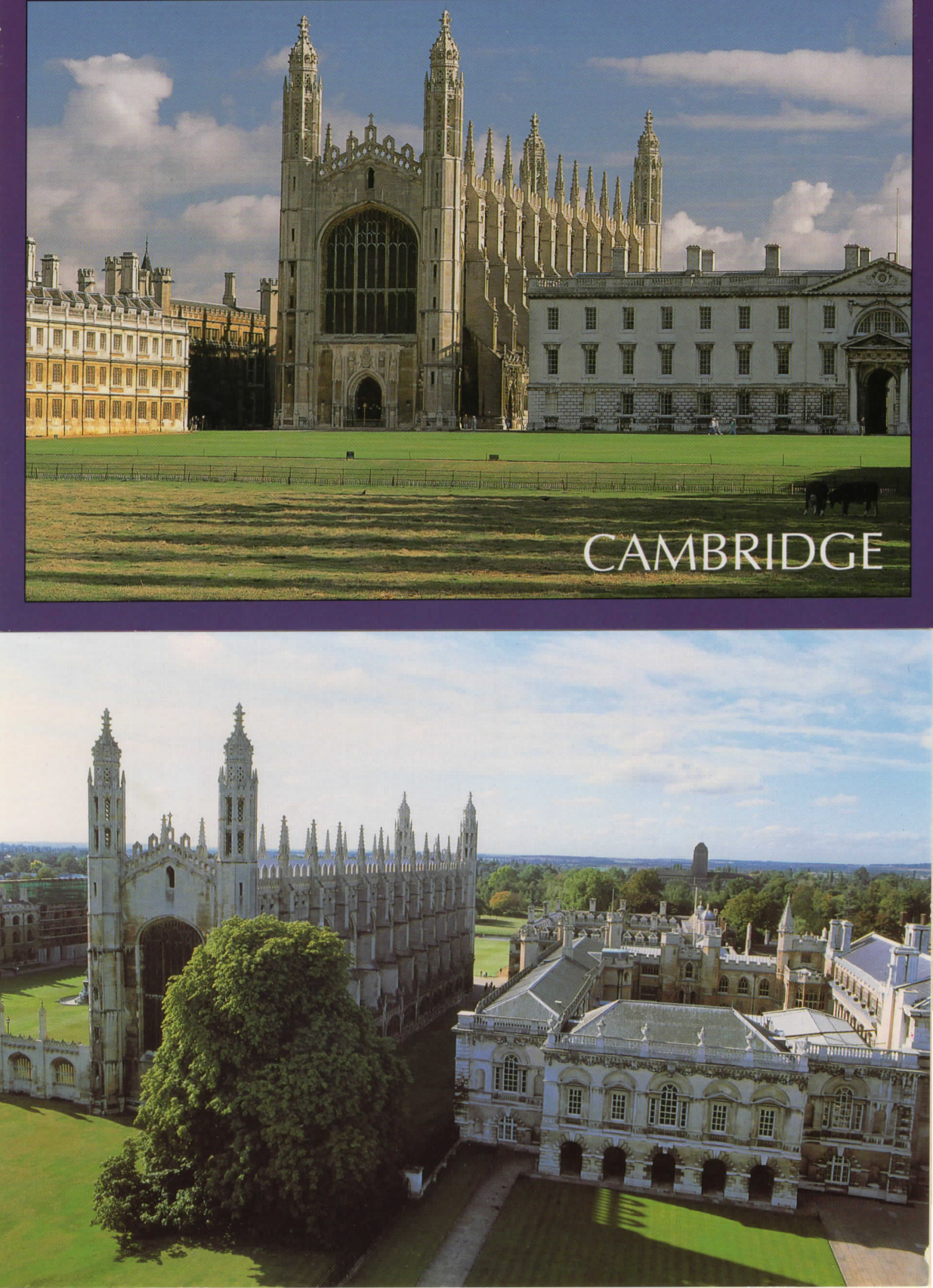
Responses to viruses and self

Prof MP Manns, Hannover, Germany.

Microbial agents are thought to be triggers for autoimmune liver disease beside predisposing genetic factors such as MHC class I-III genes. There are 3 main theories how viruses might cause autoimmune reactions:
Potentially autoreactive lymphocytes present in an anergic status in many individuals might be activated by means of molecular mimicry. Epitopes shared by viral proteins and cellular autoantigens may lead to a loss of the peripheral tolerance against these self proteins.
The second possibility is bystander activation through release of pro-inflammatory cytokines and chemokines. Organ-specific inflammation caused by the virus may thereby co-stimulate autoreactive lymphocytes.
The third possibility represents the unspecific stimulation by viral super-antigens of large T-cell subsets. The activated T-cells might gain access to the target tissue and initiate a self-perpetuating autoimmune reaction. Although seen in mice, so far there is no evidence for an involvement of superantigens in human autoimmune diseases. Apart from this, several viral proteins may interact with different components of the immune systems thereby modifying immune responses as shown for adenoviral proteins.
While the mechanisms described above might contribute to or cause autoimmune diseases with tissue destruction, other immunological reactions against self-proteins might just represent epiphenomena. Antigens released by viral or immune mediated tissue destruction can trigger an immune response to tissue specific antigens without subsequent destruction of tissue. They might be seen as markers for ongoing tissue damage. While little is known about cellular immune responses in autoimmune liver disease, the humoral autoimmune reactions are well characterised. Hepatitis A, hepatitis B, hepatitis C, herpes simplex and Epstein-Barr-virus have been implicated in the onset of autoimmune hepatitis, and a mechanism of molecular mimicry has be suggested for the humoral immune response on the basis of sequence homology between viral and hepatocyte proteins and on the basis of antibody cross-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