

Joint Meeting of the British Neuropathological Society and the Société Française de Neuropathologie

18-20 December 2002.
University of Southampton, UK.

It was a fresh frosty sunny December day that welcomed delegates from all parts of Britain and France, from other European countries and from North America to the initial symposium of this conference, 'The Role of Neuropathology in the Post-Genomic Era'. Sebastian Brandner (London) showed how transgenic and knock-out mice are used as models for the study of CNS development and neoplasia, and Dominique Figarella-Branger (Marseille) discussed how progress in the post-genomic era will lead to greater understanding and how one single genetic defect, or even an identical mutation in one gene can lead to different muscle disease phenotypes. Charles Duyckaerts (Paris) gave an erudite account of the development of ideas in neurodegenerative diseases. James Nicoll (Southampton) discussed the results of studies showing that the ϵ allele of the apolipoprotein E gene is associated with poor outcome after several different types of acute brain injury including that due to trauma and intracerebral haemorrhage. The granular osmiophilic deposits surrounding vascular smooth muscle cells that are the pathological hallmarks of CADASIL were described by Marie Magdeleine Ruchoux (Lille). This inherited angiopathy is caused by mutations in the *Notch3* gene in humans and in animal models. David Ellison (Newcastle) grasped the key challenges in tumour biology, by defining how genetic abnormalities affecting the phenotype of tumour cells can be used to devise novel therapies.

Following the symposium, James Lowe (Nottingham) gave his Alfred Meyer memorial lecture, 'Genetic Influences on Regulation of Protein Degradation in the Brain'. He described how intracellular mechanisms involving ubiquitin and the proteasome system were disturbed in dementias such as Alzheimer's disease and Lewy body dementia. He outlined subtle changes in protein expression that give rise to neurofibrillary tangles in Alzheimer's disease and Lewy bodies in Parkinson's disease.

Over the next two days, delegates were treated to a wide array of platform presentations and posters covering advances in many branches of neuropathology and neuroscience. Four contributions were of particular interest.

James Nicoll (Southampton) reported the first neuropathological findings in the brain of a patient from the clinical trial of amyloid ϵ -peptide (A ϵ) immunotherapy for Alzheimer's disease (AN-1792; Elan Pharmaceuticals). The pathology strongly resembles that in mice treated with A ϵ immunotherapy, with patchy loss of A ϵ plaques and some evidence of phagocytosis of A ϵ by microglia. Also present, but not seen in the mouse studies, was a T lymphocyte meningoencephalitis, likely to correspond to the side effect seen in some other patients who received AN-1792. Such observations suggest that immunotherapy can prevent or reverse abnormal accumulation of protein in the human brain and may be relevant to other neurodegenerative disorders (e.g. CJ disease, Huntington's disease) in which proteins accumulate in brain tissue. This highlights a significant role for Neuropathology in assessing the effects of such therapy on the underlying pathological processes.

Gray *et al* (Paris) discussed the pathology of healed 'burnt out' Varicella-zoster-virus (VZV) encephalitis in a 46 year old patient with AIDS treated by Highly Active AntiRetroviral Therapy (HAART). MRI showed multiple necrotic lesions and VZV PCR was positive in the CSF.

Following HAART and high doses of Acyclovir, CD4 cell levels increased, viral load decreased and VZV PCR became negative in CSF. However, he died from bronchopneumonia. Neuropathology showed characteristic 'target-like' lesions of VZV leukoencephalopathy and ventriculitis. But, histologically, the lesions consisted only of necrosis and macrophages with no virus. This case suggests that opportunistic infections for which effective treatment is available may be definitively cured with immunorestitution, and in those patients who die from another cause 'burnt out' pathology may be found.

Foote, Chari, and Blakemore (Cambridge) described repopulation of demyelinated areas of spinal cord tissue by oligodendrocyte progenitor cells (OPCs) even in the presence of astrocytosis. They studied the *taiep* rat which is a long-lived myelin mutant with chronic progressive demyelination, associated with astrocytosis. Thoracic spinal cord was exposed to 40Gy X-irradiation in adult *taiep* rats, to deplete the tissue of OPCs. Repopulation by OPCs was examined at 3 and 28

days, using riboprobes to platelet derived growth factor receptor alpha (PDGFR α), a marker for OPCs. Results showed that the rate of repopulation of OPC-depleted tissue in *taiep* rats was not significantly different from control animals, suggesting that astrocytosis does not affect repopulation of progenitor depleted tissue by OPCs. These findings present a potential therapy for remyelination of areas of demyelination in MS by transplantation of OPCs even in chronic MS lesions with extensive astrocytosis.

Dr. Tibor Hortobagyi, invited by the BNS as a young investigator from Hungary, showed that inhibition of the nitric oxide synthase-poly (ADP-ribose) polymerase activation cascade is neuroprotective in traumatic brain injury and enhances progenitor cell graft survival.

The Conference Banquet took place in the 17th century school building in Winchester College. This gave the opportunity for the more erudite members of the French Society to translate the Latin inscriptions on the walls. Professor Christopher Thompson, Head of the Southampton School of Medicine replied on behalf of the guests and emphasised the key role played by Neuroscience in a modern Medical School.

The meeting was superbly organised by Mrs. Stephanie Birkbeck-Garfield whose fluent French added both charm and utility to the meeting.

● The next meeting of the British Neuropathological Society is in Glasgow 3-5 July 2003 and that of the Société Française de Neuropathologie in Rouen in June 2003.

Professor Roy Weller,
Neuropathology University of Southampton, UK.



Professor Nicholas Kopp,
President of the Société Française
de Neuroradiologie.



Professor Roy Weller (President of the British Neuropathological Society) presenting James Lowe with the impressive Alfred Meyer medal at the end of the memorial lecture.