Research News

Pre-eclampsia peptide

A study published in the 15 June issue of *Nature* identified a link between pre-eclampsia and neurokinin B (NKB), a member of a family of neuropeptides involved in smooth muscle contraction, vasodilation and activation of the immune system. Pre-eclampsia, characterized by hypertension, proteinuria and edema, affects 5–10% of pregnancies worldwide and is a principal cause of maternal morbidity and death. Page *et al.* found that during human pregnancy, NKB is expressed in the outer regions of the placenta; in third-trimester pre-eclampsia, increased levels were detected in maternal blood. NKB administered to rats intravenously also caused hypertensive symptoms. The exact function of NKB in the disease has yet to be elucidated but may relate to its vasoactive properties. In the meantime, increased NKB levels may provide a predictive test for pre-eclampsia, and antagonists for its receptor could provide a possible treatment for the condition.

Fighting glioma with poliovirus

Researchers have created a genetically modified poliovirus that specifically attacks human malignant gliomas. Malignant gliomas, the most common primary brain tumors, are resistant to conventional therapies, and attenuated variants of pathogenic viruses are now being investigated as new therapeutic strategies. The human poliovirus receptor CD155 is expressed in most malignant human gliomas, making this virus a candidate for targeting glioma cells. However, poliovirus also infects lower motor neurons, causing paralysis. In the 6 June issue of *PNAS*, Gromeier *et al.* described an 'intergeneric' poliovirus chimera in which the internal ribosomal entry site element was exchanged with that of human rhinovirus type 2. The authors demonstrated that this alteration prevents viral propagation in normal neural tissue but allows the virus to replicate in glial tumor cells. Treatment of experimentally induced subcutaneous or intracerebral glioma xenografts in athymic mice with the chimeric poliovirus caused the disappearance of tumors and a significant increase in survival. The authors suggested that polio/human rhinovirus type 2 chimeras may be useful for treating malignant diseases of the central nervous system.

HIV evolution

A phylogenetic analysis of the main group (M group) of human immunodeficiency virus (HIV)-1 has allowed researchers to estimate its year of origin. Extrapolation of the date at which the common ancestor of HIV-1 emerged and the time for its dispersion have been difficult, but unprecedented amounts of HIV sequence information and computational advances have allowed researchers to analyze large sequence sets with sophisticated evolutionary models. Using parallel supercomputers and assuming a constant rate of evolution, Korber *et al.* reported in the 9 June issue of *Science* an analysis of comprehensive full-length *env* sequences from 159 individuals,

along with an independent analysis 66 *gag* gene sequences. The authors estimated the date of the last common ancestor of the HIV-1 M group to be 1931, although they cannot pinpoint exactly when the simian progenitor virus moved between species or which species (human or chimpanzee) was infected at the time of M-group expansion. The study also provides evidence against the theory that HIV-1 was introduced into the human population through simian infectious virus contamination of oral polio vaccines in Central Africa. Understanding the elements that contributed to the rapid dispersion of the HIV-1 M group, which has infected about 50 million people, may help avert future epidemics.

Gulf War Images

A magnetic resonance (MR) spectroscopy study has been used to provide biochemical evidence for neuronal damage in Gulf War veterans. Many Gulf War veterans have experienced 'Gulf War syndrome', a collection of neurological disorders that are similar to primary diseases of the basal ganglia such as Huntington disease, indicating damage to deep

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brain structures. Standard MR imaging of ill veterans, however, has failed to demonstrate any visible changes. In the June 2000 issue of *Radiology*, Haley *et al.* examined ill veterans using MR spectroscopy, which measures the intracellular concentration of protons in small volumes of the brain to detect biochemical abnormalities. They found a reduction in the N-acetylaspartate-to-creatine (NAA/Cr) ratio in the basal ganglia and brainstems of ill veterans, indicating decreased functional neuronal mass. They also found that veterans experiencing the most severe symptoms demonstrated the greatest reduction in NAA/Cr. The authors suggested that the neuronal damage is due to wartime exposure to a variety of chemical agents, and that MR spectroscopy may be used in the diagnosis of 'Gulf War syndrome' and other diseases associated with damage to deep brain structures.

Islet transplantation success

A newly developed transplantation protocol has made it possible for patients with Type I diabetes to achieve sustained insulin independence. Although most Type I diabetics are treated with insulin injections, islet cell transplantation has been pursued as a treatment for patients with uncontrollable serum glucose concentrations. However, this approach has failed in practice, as only 8% of patients receiving pancreatic islet transplantation remain insulin independent for up to 1 year, due to difficulties in obtaining a sufficient number of beta cells and graft rejection. Furthermore, current immunosuppressive regimens include steroids such as glucocorticoids, which induce insulin resistance. In an article to be published in the 27 July *New England Journal of Medicine*, Shapiro *et al.* describe

a glucocorticoid-free immunosuppressive strategy involving drugs that prevent interleukin-2 signaling and T-cell activation. Islet cells isolated from cadaver pancreases were transplanted, through the main portal vein, into seven patients who received the new immunosuppressive drug combination. All seven patients were able to discontinue insulin therapy for an average of 12 months and did not experience acute cellular rejection. The success of this approach creates an attractive area for investigation into tolerance induction, a therapeutic approach that would allow patients receive transplants without undergoing long-term immunosuppression.

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