resistance are intellectually satisfying, although many questions remain unanswered. Nod2 expression is restricted to monocytes and macrophages, but it is unclear how Nod2 defects affect the excessive inflammatory symptoms seen in CD patients. Nod2 signaling might regulate the induction of cytokines (via NF-κB) that control the inflammatory response. It is also possible that Nod2 mutations in the LRRs change pathogen recognition patterns. A related Nod1 protein is expressed on epithelial cells of the gastrointestinal tract and has been shown to respond to LPS by inducing the NF-κB pathway. Thus, the intracellular Nod-like proteins appear to mirror the Toll-like receptors on the cell surface, which also detect bacterial LPS. Bacterial recognition by the Nod LRRs, followed by signal transduction, links the innate response to pathogen components to the control of the inflammatory response. These discoveries provide an instructive example of how a Nod from a plant can point us in the right direction for studying human disease susceptibility.

1 Hugot, J.P. *et al.* (2001) Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. *Nature* 411, 599–603
2 Ogura, Y. *et al.* (2001) A frameshift mutation in *Nod2* associated with susceptibility to Crohn's disease. *Nature* 411, 603–606

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Beneficial autoimmunity in traumatic brain injury

Traumatic brain injury or stroke-mediated primary central nervous system (CNS) damage is followed over the following few days by a self-propagating, slower, secondary damage, in which additional neurons die and the affected brain area is considerably enlarged. Neuroscientists have therefore striven to find effective strategies for minimizing the secondary damage, for which a relatively longer therapeutic time window might be available. Several lines of evidence suggest that immune activation, in particular elevated local levels of cytokines, adhesion molecules, prostanoids and inducible nitric oxide synthase, participate in the secondary damage. Hence, recent drug trials have targeted the immune system, seeking to reduce secondary traumatic brain damage by restraining the immune system. So far, results from such trials are not encouraging.

New observations from Michal Schwartz and her colleagues[1] might explain why such strategies have so far been disappointing. These authors have recently shown that active or passive immunization with CNS myelin-associated self-antigens can reduce the secondary neuronal loss, indicating that certain aspects of immune activation, in particular those involving autoimmune T-cell-mediated recruitment of macrophages, are beneficial for lessening secondary damage following CNS trauma[2–4]. The new studies illuminate the beneficial role of immune activation for reducing secondary brain injury by showing that it is a physiological process. Less optic nerve damage occurred in rats that underwent an earlier unrelated injury to their spinal cords. Moreover, optic nerve injury was more severe (40% less surviving neurons) in rats lacking mature T cells (thymectomized at birth), and less severe in transgenic mice over-expressing a T-cell-receptor for myelin basic protein (MBP). In addition, improved functional recovery from spinal cord injury was observed in rats receiving passive transfer of MBP-activated splenocytes from spinally injured rats.

Altogether, the new observations present a compelling new picture of beneficial immune system activation, potentially capable of reducing secondary damage following traumatic CNS injury when properly tuned and trained. As well as being more theoretically appealing from the evolutionary perspective – an immune system doing more harm than gain was not very persuasive to begin with – the new study points towards practical use of immune activation, namely, passive or active immunization, for reducing secondary neuronal cell death following CNS injury. However, it is plausible that such beneficial immune activation is insufficient, owing to the immune-privileged character of the CNS. Eventually, patients at high risk of recurring cerebral strokes, and possibly vascular dementia patients, could benefit from fine-tuned active immunization with CNS auto-antigens, and brain trauma patients could recover better with similar passive immunization protocols. Evidently, the new study opens exciting new routes for immune intervention in the neurotrauma ward.

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2 Schwartz, M. and Kipnis, J. (2001) Protective autoimmunity: regulation and prospects for vaccination after brain and spinal cord injuries. *Trends Mol. Med.* 6, 252–258
3 Schwartz, M. and Moalem, G. (2001) Beneficial immune activity after CNS injury: Prospects for vaccination. *J. Neuroimmunol.* 113, 185–192
4 Schori, H. *et al.* (2001) Vaccination for protection of retinal ganglion cells against death from glutamate cytotoxicity and ocular hypertension: Implications for glaucoma. *Proc. Natl. Acad. Sci. U. S. A.* 98, 3398–3403

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In Brief

A model for sudden infant death syndrome

A new 'knockout' mouse model has been developed that could provide insight into the mechanisms responsible for cases of sudden infant death syndrome (SIDS). Researchers from Wake Forest University School of Medicine engineered the animals to contain no functional copy of the gene *MTP*, which encodes mitochondrial trifunctional protein. Their results, published in July's *Journal of Clinical Investigation*, revealed a crucial role for the gene in foetal development and survival. Newborn mice were noted to have stunted growth, low blood-sugar levels, and died suddenly within 36 hours of birth. The missing gene is vital in the metabolism of fatty acids and it is believed that accumulation of fatty acids leads to fatal toxicity in the knockout infants. It remains to be proven if similar deficiencies in fatty acid metabolism contribute to the tragic cases of human SIDS. *PoN*

