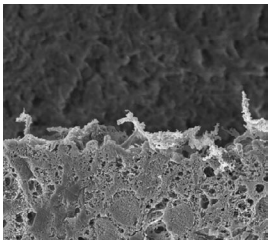
Dual role for p22^{phox} in host defense and inner ear development

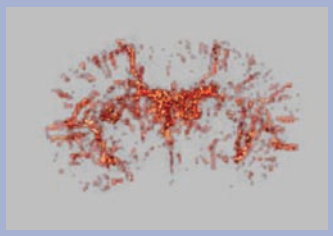


The production of superoxide by phagocyte NADPH oxidase is crucial in the fight against infection with microorganisms. Its superoxide-producing cytochrome core comprises heterodimers of p22^{phox} and gp91^{phox}, and inactivation of either component in humans leads to a severe immune disorder known as chronic granulomatous disease (CGD). Although a mouse model of gp91^{phox} deficiency has been described, the study of p22^{phox}-dependent immune deficiency has been stifled by the lack of an animal model. In this issue (pages 1176–1185), Nakano and colleagues have identified the nmf333 mouse strain, produced at The Jackson Laboratory, as the first animal model of p22^{phox} deficiency. Surprisingly, nmf333 mice were found to have a severe balance disorder in addition to a CGD-like immune defect. Further investigation revealed that the balance disorder was caused by the aberrant development of vestibular gravity-sensing organs due to inactivation of an NADPH oxidase in the inner ear. These data led the authors to propose that vestibular development is controlled by an NADPH oxidase and that patients with the form of CGD caused by a p22^{phox} deficiency may have unrecognized symptoms of a balance disorder.

Timing is of the essence for IL-7 therapy

An inability to induce potent CD8$^+$ T cell responses has hampered the development of vaccines to protect against infection with a number of viruses, including HIV and HCV. Developing approaches to boost vaccine-induced CD8$^+$ T cell responses is therefore an area of intensive investigation, and IL-7 has received much attention because of its crucial role in the generation and maintenance of memory CD8$^+$ T cells. In this issue (pages 1027–1039), Nanjappa and colleagues have shown that IL-7 enhanced the number and function of memory CD8$^+$ T cells in mice only if it was administered during the contraction phase of the immune response mounted after mice were infected with either lymphocytic choriomeningitis virus or vaccinia virus or were administered a DNA vaccine. Importantly, CD8$^+$ T cells from mice treated with IL-7 during the contraction phase exhibited more efficient memory responses and improved viral control. These data indicate that the timing of IL-7 therapy, relative to immune response initiation, is important in determining whether it has a beneficial effect on the antiviral CD8$^+$ T cell response, and as such have important clinical implications for the use of IL-7 to boost CD8$^+$ T cell memory following vaccination.

A new look inside the brain



Cerebral malaria (CM), which kills over 3 million individuals a year, is caused by infection with *Plasmodium falciparum*. Platelet sequestration in the brain, through adherence of the platelet-specific glycoprotein IIb/IIIa receptor (GPIIb/IIIa) to fibronectin of the cerebral microvasculature, has a crucial role in the pathogenesis of CM. A new way to detect platelet accumulation in the microvasculature of the mouse brain before the emergence of clinical signs of the disease has now been developed by von zur Muhlen and colleagues (pages 1198–1207). A single-chain antibody specific for the ligand-induced binding sites (LIBS) of GPIIb/IIIa receptors, which are exposed upon platelet activation, was conjugated to microparticles of iron oxide (LIBS-MPIO). Using LIBS-MPIO as the contrast agent, it was possible to detect by MRI activated platelets in the brain of mice 6 days after they were infected with *Plasmodium berghei*. At this time point after infection, clinical symptoms of the disease had not appeared, and activated platelets in the brain could not be detected by conventional MRI. These data led the authors to suggest that targeted contrast agents such as LIBS-MPIO might provide useful for diagnostic, mechanistic, and therapeutic studies.

HOXA11 shows its strength

The quality of life of millions of women is negatively affected by pelvic organ prolapse (POP) — the downward descent of the pelvic organs, causing symptoms such as urinary incontinence. In women with POP, the uterosacral ligaments (USLs), the main supportive structures of the uterus and vagina, are attenuated. Although changes in the content and quality of collagen in the USLs have been associated with POP, no molecular mechanism(s) underlying this disorder has been described. However, Connell and colleagues have now shown in mice that the protein encoded by the homeobox gene *Hoxa11* is an essential molecular factor for the development of USLs, leading to the suggestion that changes in HOXA11-regulated pathways might weaken USLs and thereby cause POP (pages 1050–1055). It was shown that mice lacking Hoxa11 had no USLs and that *HOXA11* expression was markedly decreased in the USLs of women with POP. The USLs of women with POP also expressed decreased levels of the genes encoding collagen type I and collagen type III as well as increased levels of the gene encoding MMP2, a mediator of ECM degradation. Further in vitro analysis indicated that the mouse *Hoxa11* gene increased expression of the gene encoding collagen type III and decreased expression of the gene encoding MMP2, thereby defining a new molecular mechanism regulating the mechanical strength of USLs.