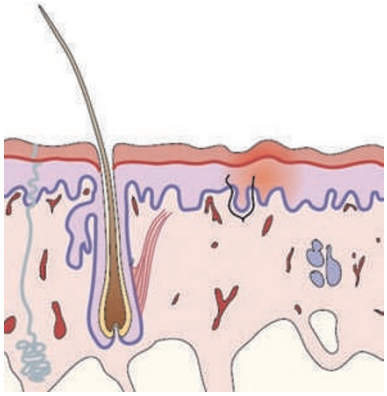
IN BRIEF



WOUND REPAIR

Stress-mediated increases in systemic and local epinephrine impair skin wound healing: potential new indication for beta blockers

Sivamani, R. K. *et al. PLoS Med.* **6**, e1000012 (2009)

Major burn injury leads to the release of stress hormones — most notably cortisol — which impair wound healing. Sivamani and colleagues have identified an alternative pathway, whereby stress-induced increases in epinephrine levels resulted in β2 adrenergic receptor (β2AR) activation on keratinocytes. This leads to downregulation of the Akt pathway, accompanied by a stabilization of the actin cytoskeleton and an increase in focal adhesion formation, which results in a non-migratory cell phenotype. In mice, β2AR antagonists — currently in clinical use — enhanced wound closure, suggesting that these drugs could be a new, low-cost approach for wound repair.

HIV

Phase 2 gene therapy trial of an anti-HIV ribozyme in autologous CD34$^+$ cells

Mitsuyasu, R. T. *et al. Nature Med.* **15**, 285–292 (2009)

This paper describes the first Phase II clinical trial of cell-delivered gene transfer in HIV treatment. HIV-1-infected adults received a *tat–vpr*-specific anti-HIV ribozyme (OZ1) or placebo, delivered in autologous CD34$^+$ haematopoietic progenitor cells. Although there was no difference in viral load between the OZ1 and placebo group at the primary end point, CD4$^+$ lymphocyte counts were higher in the OZ1 group throughout the study, and there were no OZ1-related adverse events. So, this indicates that cell-delivered gene transfer is safe and biologically active in individuals with HIV.

IMMUNE REGULATION

Protection from lethal Gram-negative bacterial sepsis by targeting Toll-like receptor 4

Roger, T. *et al. Proc. Natl Acad. Sci. USA* **106**, 2348–2352 (2009)

Donor Toll-like receptor 4 contributes to ischemia and reperfusion injury following human kidney transplantation

Kruger, B. *et al. Proc. Natl Acad. Sci. USA* **106**, 3390–3395 (2009)

These two papers highlight how Toll-like receptor 4 (TLR4) could be a therapeutic target in immune-related disorders. Roger and colleagues validated the concept of TLR4 signalling pathways as a crucial upstream event in the pathogenesis of Gram-negative bacterial sepsis. Anti-TLR4 antibodies inhibited intracellular signalling, reduced cytokine production and improved survival in experimental models of Gram-negative bacterial sepsis. Importantly, antibodies administered as long as 13 hours after the onset of infection were effective, making inhibition of TLR4 an attractive approach for anti-sepsis therapy. Kruger and colleagues investigated the role of TLR4 in delayed graft function, which can lead to renal failure and reduced allograft survival following kidney transplantation. They provided evidence that TLR4 produced by donor kidneys contributes to the development of ischaemia–reperfusion injury — which leads to delayed graft function — following human kidney transplantation. So, TLR4 antagonists could be developed as therapies aimed at preventing delayed graft function.