

# nature REVIEWS

## NATURE REVIEWS MICROBIOLOGY

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When the results of gene-therapy trials for the treatment of severe combined immunodeficiency were published several years ago, there was great excitement among scientists and clinicians. Replacement of the defective gene using retroviral vectors improved immune function in the majority of treated children. But the subsequent development of leukaemia in three patients has shattered this early optimism. In two cases, malignant transformation was associated with the insertional activation of a proto-oncogene *LMO2*, suggesting that, contrary to previously held beliefs, *in vivo* retroviral integration is not a random event. Clearly, to move the gene-therapy field forward, there is an urgent need to understand where and how retroviruses integrate into the human genome, and to develop alternative, safer vehicles for gene introduction.

This month, we tackle both these issues. On page 848, Frederic Bushman and colleagues review recent genome-wide analyses of retroviral integration target sites and suggest ways to modulate site selection to benign locations in the genome. On page 837, Ana Vasileva and Rolf Jessberger detail the characteristics of the adeno-associated virus (AAV). The AAV system shows great potential for targeting gene replacement by homologous recombination, thereby avoiding the risk of insertional mutagenesis.

For most of the world's population, gene therapy is in the realm of dreams — life without basic health care is the unfortunate reality. We focus on this important concern in a new article series, 'CommonHealth of Nations', which reviews the logistics and challenges of aid provision to the developing world. On page 899, Tore Godal asks whether the effectiveness of global aid programmes can be improved by adopting a more holistic approach to the health-aid framework.



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