or radiation. This success was possible through the use of very high doses of donor bone marrow cells and led to significant clinical improvement in the mice.

What does the future hold? It seems clear that less toxic preparative regimens can be designed and implemented without compromising engraftment. The 2 to 3 log increase in bone marrow cell dose used by Soper et al presents challenges for implementation in humans, but one can envision the use of selected populations such as cord blood as well as stem cells following ex vivo expansion. An encouraging lesson from both studies is that low levels of engraftment (2 percent and 15 percent, respectively) led to successful treatment of both genetic deficiencies. This success is probably explained by selective retention of the wild-type protein, however, and may not apply generally.

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Viral load monitoring in transplant recipients

Stevens et al (page 1165) provide further evidence linking a high-circulating Epstein Barr viral load with the development of posttransplantation lymphoproliferative disorder (PTLD). Several prior reports have identified increased EBV load, as determined in blood lymphocytes, serum, or liver biopsy specimens, at or prior to the time of clinical presentation with PTLD. The present study finds that an elevated whole-blood EBV load can precede the clinical diagnosis and that frequent monitoring is necessary as changes can occur rapidly. An elevated EBV load may be indicative of overimmunosuppression. Adjustments in immunosuppressive dosing or other early interventions to lower viral load might therefore forestall the development of clinical PTLD in monitored patients.

Several questions remain to be answered before proceeding to clinical trials of early intervention, particularly in low-risk transplant recipients. The best assay method, sampling frequency, threshold values, and the effect of antiviral therapy on serum or lymphocyte viral load determinations all need to be elucidated. Of particular concern is the problem of false positive results, as exemplified in the current study, where such a result was found in 2 of 8 control patients. The challenge will be to define a clinical test that is specific enough to justify an intervention that may threaten graft or patient survival in settings where the risk of PTLD is low. Recent progress suggests that reliable, routine monitoring of EBV load in allograft recipients should be feasible and raises the hope that doing so may prevent this frequently fatal complication of transplantation.

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