The question of whether or not human endothelial and epithelial cells persist in grafts transplanted onto SCID mice depends on the type of graft (split skin versus full thickness skin) and location from which the graft is taken. The fate of the graft components is similar to what is observed in the clinical setting of syngeneic skin transplantations performed in patients in order to close defects after skin surgery. Based on the published reports (eg., refs 2–5,7–9) it seems fair to state that split skin grafts usually show persistence of all of the grafts' components. In the case of full thickness skin grafts, epitheliolysis may occur if the grafts are big (>>1cm^2) or extremely thick, such as those derived from lesional psoriatic skin or certain areas of the body such as the back.

Of note, our SCID-human xenogeneic transplantation model[2] is a good tool for studying complex immunological processes such as leukocyte extravasation and T cell homing, as well as human diseases in general and psoriasis in particular. It also provides the option to analyze components other than T cells in the respective diseases such as psoriasis.

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Parker replies — I thank Dr. Boehncke for defining the conditions under which the endothelial and epithelial cells are preserved within xenotransplantated human skin tissue. This important information will enable others to use the xenotransplantation model of psoriasis to greater effect. I would like to point out that while the superficial plexus of vessels is preserved, the deep plexus of vessels is lost in split thickness skin grafts. Thus, as the superficial and deep vascular bed endothelial cells may express different adhesion molecules[8], studies of T lymphocyte homing using xenografted human skin might be complemented by additional studies with deep vascular plexus tissue grafts, as described earlier[8].

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HIV antivirals and immune recovery

To the editor — Now that potent anti-retroviral drugs can control HIV replication for extended periods, the possibility of a concomitant immune reconstitution is raised. In the May issue of *Nature Medicine*, Connors *et al.* reported that antiviral therapy conferred no correction to the disrupted CD4 T cell receptor (TCR) repertoire of HIV infected individuals[1]. Their results showed that CD4 repertoires underwent only minor changes during 6–15 months of anti-viral treatment. We offer an opposing conclusion based on results of our own (Gorochov, G. *et al.* Disordering of CD4 and CD8 T-cell repertoires during progression to AIDS and restoration of the CD4 repertoire by antiviral therapy (manuscript submitted). Gorochov, G. *et al.* TCR- repertoire complexity and evolution of HIV infection: Influence of anti-retroviral regimens including protease inhibitors. 4th Conference on Retroviruses and Opportunistic Infections, Washington DC, USA. Abstr. 110, January 1997). We find that perturbations in CD4 TCR repertoires significantly decrease after 3–6 months of antiviral therapy, and become relatively restored in comparison to seronegative individuals.

There are several possible explanations for this discrepancy. First, we studied 11 patients that underwent a variety of triple anti-retroviral therapies. Restoration of the CD4 repertoire is correlated with efficient therapy, as determined by control of viral replication. Connors *et al.* reported on only three patients. Since their viral loads were only measured down to 10,000 RNA copies per ml it is not clear whether viral replication was well controlled. Moreover, the three patients received antiviral therapy and IL-2 infusions and that combination may affect the CD4 repertoires differently than antiviral therapy alone — the more conventional treatment approach.

Secondly, Connors *et al.* used CD4 samples that were only 90% pure and did not study CD8 samples. It is possible that the CD8 T-cells could covertly contaminate the CD4 TCR profiles, giving the appearance of disruption. Because of similar concerns, we purified CD4 cells to 98%. We suggest that CD4 and CD8 repertoires should be analyzed in parallel to control for overlaps due to contamination. Without such controls, and since strong CD8 oligoclonal expansions are indeed persistent during therapy (unpublished results), even minor CD8 contamination of the CD4 TCR profiles would obscure any CD4 TCR repertoire restoration.

Finally, Connors *et al.* only determined the number of TCR distributions that were "abnormal", by comparing the major peak with its two neighboring peaks, thus ignoring all other possible perturbations. Therefore, their analysis scores only a subset of the changes in repertoire and could underestimate the CD4 repertoire restoration.

Thus, we believe that no clear conclusions regarding CD4 TCR repertoire restoration can be drawn from the paper by Connors *et al.*. We have evidence that reconstitution of the CD4 TCR repertoire is possible, a conclusion that is corroborated by functional and phenotypic data obtained by our group[2]. More studies are necessary to verify whether our encouraging results on this important issue are indeed in-