Microchimerism maintains deletion of the donor cell-specific CD8+ T cell repertoire

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Rare cases of stable allograft acceptance after discontinuation of immunosuppression are often accompanied by macrochimerism (> 1% donor cells in blood) or microchimerism (< 1% donor cells in blood). Here, we have investigated whether persistence of donor cells is the cause or the consequence of long-lasting CTL unresponsiveness. We found that engraftment of splenocytes bearing a single foreign MHC class I-restricted epitope resulted in lifelong donor cell microchimerism and specific CTL unresponsiveness. This status was reversed in a strictly time- and thymus-dependent fashion when the engrafted cells were experimentally removed. The results presented herein show that microchimerism actively maintains CTL unresponsiveness toward a minor histocompatibility antigen by deleting the specific repertoire and thus excluding dominant, T cell extrinsic mechanisms of CTL unresponsiveness independent of systemically persisting donor cell antigen.

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