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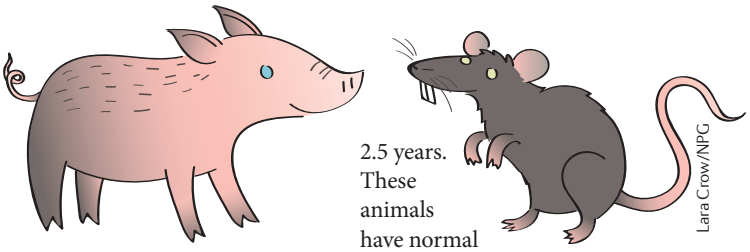
TRANSPLANTATION

Reverse chimerism enables graft acceptance

Induction of reverse chimerism in renal allografts by mobilizing host stem cells from the bone marrow enables long-term graft acceptance in animal models, say Zhaoli Sun and colleagues. These researchers previously showed that the CXCR4 antagonist AMD3100 and low-dose tacrolimus act synergistically to mobilize autochthonous bone marrow stem cells and enable long-term acceptance of rat liver grafts.

Now Sun and colleagues report that treatment with these agents in the first week after kidney transplantation prolonged short-term allograft survival in rats, but death from renal failure occurred at 30–90 days. By contrast, repeat treatment at 1, 2 and 3 months post-transplantation resulted in allograft acceptance and normal serum creatinine levels at 6 months in 11 of 12 recipients.

> “host stem cells recruited to the allograft might promote repair or repopulation of injured tissue”



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Further analyses indicated that the dual therapy resulted in recruitment of host bone marrow stem cells and regulatory T (T_{REG}) cells to the transplanted kidney. Moreover, lymphocytes isolated from the peripheral blood of treated rats or fluorescently labelled T_{REG} cells isolated from treated transgenic mice, suppressed alloimmune responses in mixed lymphocyte reactions.

“These findings suggest that T_{REG} cells downregulate the allogenic immune response after liberation from the bone marrow,” explains Sun. The researchers also hypothesize that host stem cells recruited to the allograft might promote repair or repopulation of injured tissue and improve kidney function.

In a separate study, Sun and colleagues confirmed their findings in immunologically mismatched miniature pigs. They report that three recipient pigs have now survived for 3 years, with no drug therapy for 2.5 years. These animals have normal serum creatinine levels and preserved anti-donor skin graft responses.

“We foresee two potential uses of our chimeric protocol in renal transplantation in the near future: treatment of patients with delayed graft function, and treatment of slowly progressing chronic renal failure following a biopsy showing a salvageable organ,” says Sun. He also suggests that demonstration of host cell repopulation and T_{REG} cells in allografts after stem cell mobilization could serve as an “immunological assay” to facilitate immunosuppression withdrawal in transplant recipients.

Ellen F. Carney

ORIGINAL ARTICLES Hu, X. *et al.* Chimeric allografts induced by short-term treatment with stem cell mobilizing agents result in long-term kidney transplant survival without immunosuppression: I study in rats. *Am. J. Transplant.* http://dx.doi.org/10.1111/ajt.13706 | Cameron, A. M. *et al.* Chimeric allografts induced by short-term treatment with stem cell mobilizing agents result in long-term kidney transplant survival without immunosuppression: II study in miniature swine. *Am. J. Transplant.* http://dx.doi.org/10.1111/ajt.13703