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Remarks:
•This application was filed on 23.09.2019 as a divisional application to the application mentioned under INID code 62.
•Claims filed after the date of receipt of the application (Rule 68(4) EPC).

(54) ENGRAFTMENT OF STEM CELLS WITH A COMBINATION OF AN AGENT THAT TARGETS STEM CELLS AND MODULATION OF IMMUNOREGULATORY SIGNALING

(57) The present invention provides a clinically applicable method of stem cell transplantation that facilitates engraftment and reconstitutes immunocompetence of the recipient without requiring radiotherapy or chemotherapy, and without development of GVHD or graft rejection. Aspects of the present invention are based on the discovery that the depletion of the endogenous stem cell niche facilitates efficient engraftment of stem cells into that niche. In particular, the present invention combines the use of selective ablation of endogenous stem cells with a combination of antibodies specific for CD117, and agents that modulate immunoregulatory signaling pathways, e.g. agonists of immune costimulatory molecules, in combination with the administration to the recipient of exogenous stem cells, resulting in efficient, long-term engraftment, even in immunocompetent recipients.

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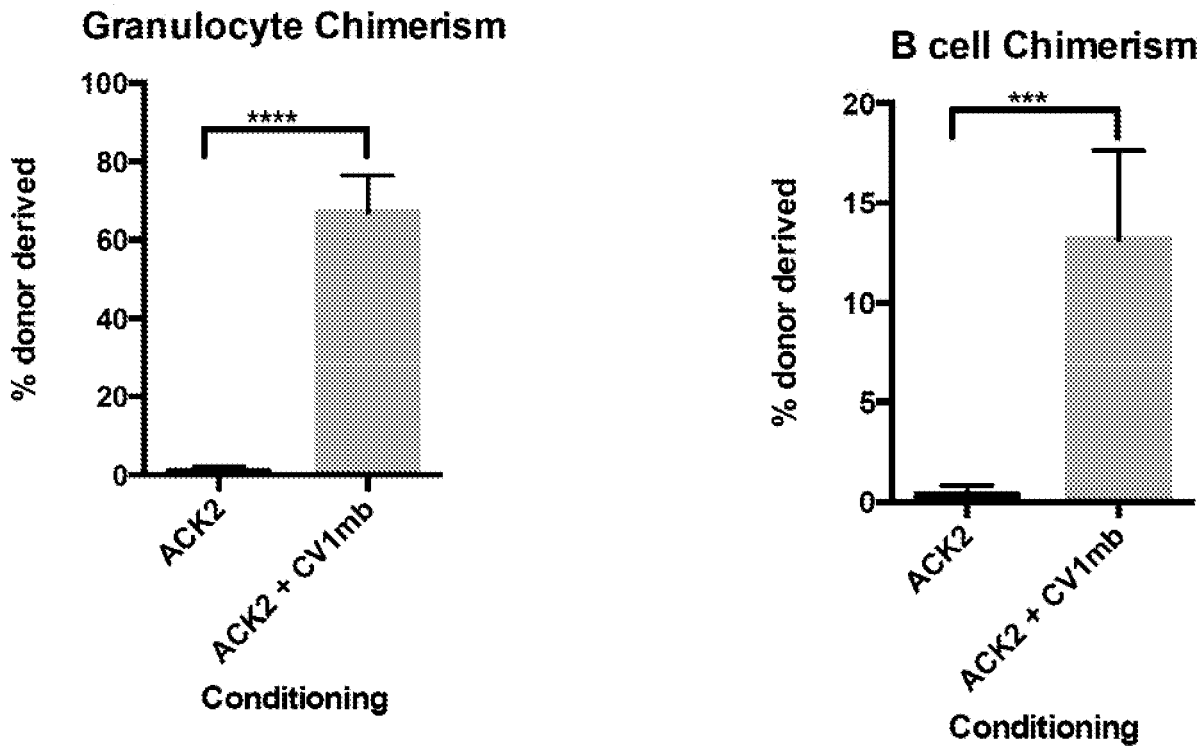
Granulocyte Chimerism
% donor derived
100
80
60
40
20
0
****
ACK2
ACK2 + CV1mb
Conditioning
B cell Chimerism
% donor derived
20
15
10
5
0
***
ACK2
ACK2 + CV1mb
Conditioning

FIGURE 17