

In-vivo model of human stem cell rejection in NSG mice

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T cell alloreactivity against human CD34⁺ cells was tested for the first time in-vivo in a NOD/SCID γ -null (NSG) mouse model. Human allogeneic blood CD3⁺ T cells were co-transplanted with allogeneic cord blood CD34⁺ cells in sublethally irradiated mice. At 6 weeks post transplant, marrow and spleen cells were harvested and analyzed by flow cytometry. Independently of high or low CD3:CD34 cell ratio of the graft, all the mice showed a reduced overall number of huCD45⁺ cells in the marrow ($p=0.0001$) compared to control. Stem cell graft failure was documented by detecting only the engraftment of human CD4⁺ and CD8⁺ T cells and no myeloid or B cells in the marrow and spleen. Only when mice were transplanted with a very low CD3:CD34 cell ratio (0.1:1) a mix chimerism of huCD45⁺ T, B and myeloid cells was observed. To investigate whether a single T cell population could cause stem cell rejection, mice were transplanted with selected CD3⁺CD4⁺ or CD3⁺CD8⁺ T cells and CD34⁺ cells at 1:1 ratio. Rejection was observed in 100% of mice transplanted with human CD3⁺CD4⁺ cells. Instead, mice transplanted with human CD3⁺CD8⁺ cells showed a mixed chimerism of T, B and myeloid cells both in marrow and spleen. Spleen CD4⁺ cells proliferated in mixed leukocyte cultures after stimulation with CD34⁺ cells, whereas spleen CD8⁺ cells were unresponsive. These results show that alloreactive CD4⁺ T cells serve an important role in stem cell rejection while CD8⁺ T cells appear to facilitate immune tolerance.

Biography

Damiano Rondelli obtained his MD and training in hematology from University of Bologna, Italy. He started his research in stem cell transplantation at the Fred Hutchinson Cancer Center in Seattle, WA before joining the faculty of University of Bologna in 1995. In 2002 he moved to the University of Illinois at Chicago where currently is a Professor of Medicine and Director of the Blood and Marrow Transplant Program. He had published more than 100 full papers in peer-reviewed journals.

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