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Impact of Mismatching for Minor Histocompatibility Antigens on the Occurrence of Graft-Versus-Host Disease

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The results in human bone marrow transplantation are still not fully satisfactory. Despite the selection of HLA identical siblings as bone marrow donors for patients with severe aplastic anemia or hematologic malignancies, Graft-versus-Host Disease (GvHD) occurs in approximately 20-70% of the patients depending on their age. This complication can be caused by disparity for the products of minor Histocompatibility (minor H) systems.
Previously, we reported on the presence of cytotoxic T lymphocytes (CTLs) in a patient suffering from severe chronic GvHD. Those CTLs, which were demonstrated from two months after bone marrow grafting onwards, were directed against patient's own pre-transplant lymphocytes. Analysis of the in vitro cytotoxic activity of the patient's post-transplant lymphocytes demonstrated the presence of a minor H antigen of which the recognition was HLA restricted (Goulmy et al. 1982).
This observation prompted us to continue our search for minor H antigens and their role in bone marrow transplantation. We investigated post-transplant lymphocytes from a series (n=19) of recipients of HLA identical bone marrow grafts for the presence of anti-host cytotoxic activity. Such CTL activity could be detected post bone marrow transplant in five patients suffering from GvHD, but was absent in patients without GvHD (for review see: Goulmy 1985). Further analysis of the cytotoxic activity patterns of the post-transplant lymhocytes of the latter five patients, revealed five different CTL populations each directed against different minor H antigens. Four of the five minor H antignes were recognized in an HLA restricted fashion (Goulmy 1985). Expansion of the five CTL populations provided us with large amounts of cellular typing reagents specific for these minor H antigens.
In order to obtain information about the relevance of minor H antigens in the pathogenesis of GvHD, we performed an retrospective typing analysis for these five different minor H antigens, on a series of HLA identical bone marrow donor/recipient combinations (n=47).

The results of this analysis (see table) demonstrate that incompatibilities for one (or more) minor H antigens between HLA identical donor and recipient were found in the group of patients suffering from GvHD. Consequently, when more than one bone marrow donor is available, cellular typing for minor H antigens may be helpful in avoiding one of the risk factors for GvHD.

Table. Cellular typing of human minor H antigens with minor H antigen specific CTLs.

Donor/recipient pairs	Typing for 5 minor H antigens	
	identical	non-identical
recipients without GvHD	13	1
recipients with acute GvHD	16	3
recipients with chronic GvHD	6	8

p= 0.0045

References.

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