



Universiteit
Leiden
The Netherlands

Evidence for minor Histocompatibility expression in human skin.

Goulmy, E.A.J.M.; Els, C.A.C.M. van; Bueger, M.M. de; Kempenaar, J.; Ponec, M.; Rood, J.J. van

Citation

Goulmy, E. A. J. M., Els, C. A. C. M. van, Bueger, M. M. de, Kempenaar, J., Ponec, M., & Rood, J. J. van. (1989). Evidence for minor Histocompatibility expression in human skin. *Bone Marrow Transplantation*, 4-117. Retrieved from <https://hdl.handle.net/1887/2946>

Version: Not Applicable (or Unknown)

License:

Downloaded from: <https://hdl.handle.net/1887/2946>

Note: To cite this publication please use the final published version (if applicable).

Evidence for minor histocompatibility antigen expression in human skin

E. Goulmy, C. van Els, M. de Bueger, J. Kempenaar, M. Ponc and J.J. van Rood. Dept.'s of Immuno-haematology and Dermatology, University Hospital of Leiden, The Netherlands.

Introduction

The success of HLA genotypically identical marrow grafting is still hampered by Graft-versus-Host Disease (GvHD) and rejection of the graft. One of the causes of the latter complications could be attributed to minor Histocompatibility (minor H) antigen disparities between HLA genotypically identical sibs.

The aetiology of GvHD presumes that immunocompetent donor T cells are reacting against the host tissues. Although the precise nature of the composition of the effector cells mediating the host attack is still unknown, one can assume that at least also the anti-host cytotoxic T cells (CTLs) play a role. In support of the latter notion, our in vitro studies indeed demonstrate anti-host CTL activities in host post-transplant bloodsamples of patients suffering from GvHD (1). These CTL populations are directed against host specific target structures i.e. minor H antigens which are absent on the donor cells; sofar, besides the male specific antigen H-Y, five minor H antigens designated HA-1 to HA-5 have been identified (1). One of the affected organs during GvHD after bone marrow grafting is the skin. Dermal and epidermal infiltration by CD8+ cells correlated with the severity of GvHD (2); moreover keratinocytes appeared to be a target for the GvHD attack (3). Consequently, the aim of our study was to investigate the expression of human minor H antigens on keratinocytes by studying their susceptibility for lysis by our MHC restricted H-Y and minor HA antigen specific CTLs.

Materials and Methods

- Effector cells: the CTLs specific for H-Y and minor H antigens HA-1 to HA-5 are described in ref. 1.
- Target cells: human keratinocytes (K) obtained from skin biopsy from healthy volunteers were cultured and used as target cells in a for K modified 51Cr Cell-Mediated-Lympholysis assay (4). (Dr. R. Teepe is kindly acknowledged for taken the biopsis).

Results

Since the recognition of minor H antigens is MHC restricted, a prerequisite for their detection is adequate susceptibility for lysis of K by allo MHC class I directed CTLs. Up to 100% specific lysis of the HLA-A2+ve K could be obtained by addition of allo HLA-A2+ve specific CTL clones. Next, the expression of the minor H antigen H-Y on male HLA-A2+ve K was explored. The results are summarized in the table.

Table: Male keratinocytes function as target cells for H-Y specific CTLs.

Target cells	% lysis by HLA-A2 H-Y spec. CTLs	
	keratinocytes treated without IFN γ	with IFN γ
HLA-A2+ve ♀	1 \pm 4	5 \pm 3
HLA-A2+ve ♂	18 \pm 3	52 \pm 15

* mean values of 2 experiments and 3 different donors, \pm SD; N. effector cells: 150.10³/well.

As shown in the table, male HLA-A2+ve K are susceptible for lysis by HLA-A2 restricted H-Y specific CTLs; the specific recognition is clearly enhanced by IFN γ treatment of K.

With regard to the other minor H antigens HA-1 to HA-5, our recent studies revealed expression of the minor H antigen HA-3 on human K.

Conclusions

Although the male specific antigen H-Y has sofar not been demonstrated in vitro on mouse male epidermal cells (5), we report here that human K are specifically lysed by MHC class I restricted H-Y specific CTL clones. It is worth noting that concordance in tissue distribution is observed for H-Y and HA-3; i.e. both are clearly expressed on human hemopoietic progenitor cells (HPC) (6, 7) and as reported herein in human skin. These findings emphasize further the potential role of minor H antigens in bone marrow transplantation. Expression of minor H antigens on HPC may give rise (in case of disparities between donor and recipient) to graft rejection especially in case of a presensitized patient receiving T cell depleted marrow. The expression of minor H antigens in the skin may bring us closer to the possible target functions of these antigens locally in the by GvHD affected organs.

- (1) Goulmy E. Transplant Rev 1988, 2:29
- (2) Guyotat D., Mauduit G., Chouvet B. et al. Transplantation 41:340
- (3) Sale G.E., Shulman H.M., Gallucci B.B. & Thomas E.D. Am J Path 1985, 118:278
- (4) de Bueger M. et al. manuscr. in prep.
- (5) Steinmuller D. & Burlingham W.J. Transplantation 1984, 37:22
- (6) Voogt P.J., Goulmy E., Fibbe W.E., Veenhof W.F.J., Brand A. & Falkenburg J.H.F. J Clin Invest 1988, 82:906
- (7) Voogt P.J., Goulmy E., Veenhof W.F.J. et al. J Exp Med 1988, 168:2337

This work was supported by the Dutch Foundation for Medical and Health Research and the J.A. Cohen Institute for Radiopathology and Radiation Protection (IRS).