

Discrepant results of samples taken from different tissues of a single individual

E.M. Dauber^{a,*}, G. Dorner^a, M. Mitterbauer^b, S. Wenda^a,
I. Faé^a, B. Glock^c, W.R. Mayr^a

^aDepartment of Blood Group Serology and Transfusion Medicine, Division of Blood Group Serology, University of Vienna, Medical School, Austria

^bDepartment of Internal Medicine, Division of Hematology and Hemostaseology, University of Vienna, Medical School, Austria

^cAustrian Red Cross, Blood Donation Centre for Vienna, Lower Austria and Burgenland, Laboratory for Molecular Biology, Vienna, Austria

Abstract. Samples taken from different tissues of five bone marrow transplanted patients at least 5 years after successful bone marrow transplantation were investigated by STR-typing in order to find out whether or not donor cells can also be found in tissues other than blood. Donor alleles were detected in blood, buccal swabs and fingernails, but not in hair samples. © 2003 Elsevier B.V. All rights reserved.

Keywords: Blood stem cell; Bone marrow transplantation; Buccal cell; Chimerism; Hair

1. Introduction

In a prior study, different tissues were investigated by STR-analysis in a pair of chimeric twins, who are dizygotic twins sharing blood stem cells, which have been exchanged during pregnancy. These hematopoietic cells can migrate through intrauterine blood vessel anastomoses of confluent placentas into the other fetus and persist for a lifetime producing blood cells with the genetic pattern of the other twin. Therefore a mixture of their DNA profiles was expected in the blood of both twins, but was also observed to a minor extent in their buccal cells and even in the fingernails of one twin, which was not expected. Only their hair roots exhibited their true genetic pattern [1]. As congenital twin chimerism is a very rare phenomenon, a further study has been extended to bone marrow transplanted patients. After successful engraftment, they represent artificial blood chimeras: their hematopoietic tissue and their blood cells derive from the bone marrow donor, who is usually HLA identical, but genetically different in many other loci. In order to find out, whether or not donor cells can also be found in tissues other than blood, samples of different origin have been analysed.

2. Materials and methods

At least 5 years after successful bone marrow transplantation, samples from blood, buccal cells, fingernails and eyebrows were collected from five patients. DNA samples or

* Corresponding author. Klinische Abteilung für Blutgruppenserologie, Währinger Gürtel 18-20, A-1090 Vienna, Austria. Tel.: +43-1-40400-5320; fax: +43-1-40400-5321.

E-mail address: eva.maria.dauber@univie.ac.at (E.M. Dauber).

frozen lymphocytes of the patients and the donors (three siblings, two unrelated donors) prior to transplantation were analysed too. DNA was extracted from all samples with the Qiagen DNA Mini Kit (Qiagen) or the Chelex method or had already been extracted from blood prior to transplantation with the salting out method. In two out of five hair samples an alternative extraction method, which was expected to yield more DNA [2], was kindly carried out by Prof. Dr. P.M. Schneider, Institute of Legal Medicine, University of Mainz, Germany. PCR of the highly polymorphic STR-loci SE33 (fluorescein-labelled reverse primer) and D12S391 (Vic-labelled forward primer) [3,4] was carried out on a 9700 thermal cycler, further analysis on an ABI Prism 310 Genetic Analyser (Applied Biosystems). The method of quantification of the two cell populations was based on peak areas [5].

3. Results and discussion

In all patients a difference between donor and recipient was found at least in one of the two loci. After transplantation, the STR alleles found in the blood samples of all patients were identical with the donor. In all buccal swab samples a mixture of recipient and donor was observed. The median of donor cells found was 32.1% of the total cell population, ranging within 16.6% and 76.3%. In the fingernails the median of donor cells was 24%, ranging between 11.4% and 53.3%. The alleles found in the hair samples of all recipients corresponded to their blood sample prior to transplantation and represented their true genotype.

These results confirm the findings in the pair of chimeric twins [1]: donor cells originating from hematopoietic tissue can migrate into other tissues, where they are found in DNA-analysis. Blood stem cells have the ability to transdifferentiate to cells other than blood. Analogous results have been found recently using in-situ hybridization of a Y-chromosomal marker in female recipients transplanted with a male donor [6].

The findings of this study have to be considered in DNA analysis of samples, which are routinely taken for forensic and clinical genetic investigations: mixed DNA profiles can originate from a single individual. DNA profiles obtained from different tissues of the same individual and DNA profiles obtained from samples taken at different times from the same individual can be different. Only the DNA profile obtained from hair samples exhibited the true genotype of the individual.

References

- [1] E.M. Dauber, I. Faé, S. Stadlbacher, B. Glock, D.W.M. Schwartz, W.R. Mayr, STR-typing in a pair of chimeric twins, *Int. Congr. Ser.* 1239 (2003) 569–571.
- [2] A. Hellmann, U. Rohleder, H. Schmitter, M. Wittig, STR typing in human telogen hairs—a new approach, *Int. J. Legal Med.* 114 (2001) 269–273.
- [3] P. Wiegand, B. Budowle, S. Rand, B. Brinkmann, Forensic validation of the STR systems SE33 and TC11, *Int. J. Legal Med.* 105 (1993) 315–320.
- [4] M.V. Lareu, C. Pestoni, M. Schürenkamp, S. Rand, B. Brinkmann, A. Carracedo, A highly variable STR at the D12S391 locus, *Int. J. Legal Med.* 109 (1996) 134–138.
- [5] C. Thiede, M. Florek, M. Bornhäuser, M. Ritter, B. Mohr, C. Brendel, G. Ehninger, A. Neubauer, Rapid quantification of mixed chimerism using multiplex amplification of short tandem repeat markers and fluorescence detection: bone marrow transplant 23 (1999) 1055–1060.
- [6] S.D. Tran, S.R. Pillemer, A. Dutra, A.J. Barrett, M.J. Brownstein, S. Key, E. Pak, R.A. Leakan, A. Kingman, K.M. Yamada, B.J. Baum, E. Mezey, Differentiation of human bone marrow-derived cells into buccal epithelial cells in vivo: a molecular analytical study, *Lancet* 361 (2003) 1084–1088.