Immunogenetics (1996) 45: 78–79

SEQUENCE REGISTER

Mary Ellexson · Marie Lau · Paul Terasaki
William Hildebrand

Molecular characterization of *HLA-A*6803*

Received: 29 May 1996 / Revised: 23 June 1996

More than 200 *HLA* class I and class II typing laboratories participate in the International Cell Exchange (ICE). Laboratories participating in the typing of HLA class I molecules as part of the exchange are sent four unknown samples each month upon which class I typing is completed. The participating laboratories then communicate the class I type identified, the data from all participants is combined, and a report assessing class I typing consistency from laboratory to laboratory is published. Laboratories participating in the ICE have historically determined a class I type using alloantibodies: however, the realization that serologic typing cannot discriminate among all class I subtypes has led to the implementation of molecular class I *HLA* typing methods.

In the autumn of 1995, serologic typing indicated that cell 859 expressed *HLA-A32* and *-A68* [with no allelic subtypes assigned; Fig. 1 (Lau 1995)], while the consensus *HLA-A* type assigned by the various DNA-based methods was *A*3201/A*68012*. Because two of 14 DNA labs assigned an *A68* variant and four DNA labs failed to assign a type other than *A*3201* (data not shown), we cloned and sequenced the two *HLA-A* alleles from cell 859 under the hypothesis that a new *HLA-A* variant was present in cell 859 (Domena et al. 1993; Ellexson 1996). Indeed, a new *HLA-A68* allele elusive to both serologic and DNA typing techniques was identified. A similarity search found this new *HLA-A68* allele to be most homologous to *A*68012*, from which it differs at a single nucleotide (C instead of G) at position 282. In accordance with this high level of similarity to other *A68* alleles, the WHO nomenclature committee (Bodmer et al. 1995) assigned the name *A*6803* to the new *HLA-A* allele.

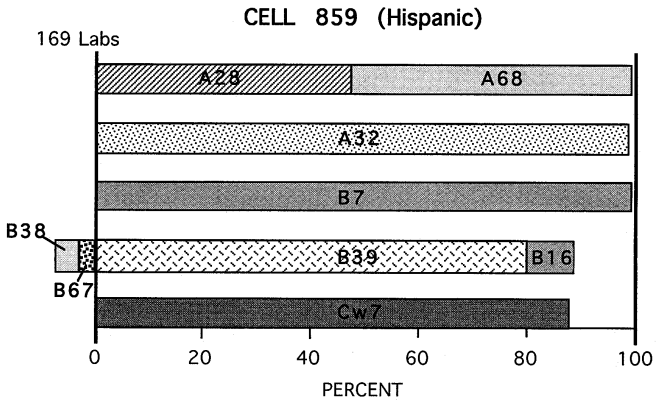

Fig. 1 Serologic typing data of cell 859 from the 215th International Cell Exchange

The single nucleotide substitution which differentiates *A*6803* from *A*68012* is a coding substitution; *A*6803* has a histidine at position 70 in the α1 domain of the class I heavy chain, while *A*68012* has a glutamine (Table 1). Because the side chain of amino acid 70 is positioned to affect the stereochemistry of specificity pockets B and C (Saper et al. 1991), the substitution of a positively charged histidine (*A*6803*) for an uncharged glutamine (all other A68s) may alter the peptides bound by these A68 molecules; no other pair of class I molecules differs only at amino acid 70 (Parham 1995), such that comparisons of peptides eluted from *A*68012* and *A*6803* will help to elucidate the effect of polymorphisms at amino acid 70.

Acknowledgements This work was supported by the Department of Defense Office of Naval Research grant N00014-95-0074.

The nucleotide sequence data reported in this paper have been submitted to the GenBank nucleotide sequence database and have been assigned the accession number U41057

M. Ellexson · W. Hildebrand (✉)
Department of Microbiology & Immunology,
University of Oklahoma Health Sciences Center, P.O. Box 26901,
Oklahoma City, OK 73190, USA

M. Lau · P. Terasaki
Department of Surgery, UCLA School of Medicine,
Tissue Typing Laboratory, 1000 Veteran Avenue,
Los Angeles, CA 90024, USA

Table 1 All amino acid differences between *A*6803* and homologous *HLA-A* alleles. The alleles compared are listed in descending order of similarity to *A*6803*, ranging from 99.9% to 99.1%, respectively. Dashes represent positions of similarity to *A*6803* and numbering indicates each nucleotide position within the designated exon

	Exon 2		*Exon 3*							*Exon 4*
Allele	12	70	5	7	15	17	24	26	66	63
*A*6803*	*V*	H	*I*	*M*	*S*	*G*	*R*	*D*	*W*	*V*
*A*68012*	–	Q	–	–	–	–	–	–	–	–
*A*68011*	–	Q	–	–	–	–	–	–	–	–
*A*6802*	*M*	Q	–	*R*	*P*	–	*H*	*Y*	–	–
*A*6901*	–	Q	*V*	*R*	–	*W*	*H*	*Y*	*L*	*A*

References

Bodmer, J. G., Marsh, S. G. E., Albert, E. D., Bodmer, W. F., Bontrop, R. E., Charron, D., Dupont, B., Erlich, H. A., Mach, B., Mayr, W. R., Parham, P., Sasazuki, T., Schreuder, G. M., Strominger, J. L., Svejgaard, A., and Terasaki, P. I. Nomenclature for factors of the HLA system, 1995. *Tissue Antigens 46:* 1–18, 1995

Domena, J. D., Little, A.-M., Madrigal, J. A., Hildebrand, W. H., Johnston-Dow, L., du Toit, E., Bias, W. B., and Parham, P. Structural heterogeneity in HLA-B70, a high frequency antigen of black populations. *Tissue Antigens 42:* 509–517, 1993

Ellexson, M., Stewart, D., Chretien, P., Zhang, L., and Hildebrand, W. H. A modified sequencing strategy for the molecular characterization of HLA-B*8201. *Tissue Antigens 47:* 438–441, 1996

Lau, M., Park, M. S., and Terasaki, P. I. *Report of the 215th Cell Exchange, October 4, 1995,* University of California Tissue Typing Laboratory, Los Angeles, 1995

Parham, P., Adams, E. J., and Arnett, K. L. The Origins of HLA-A,B,C polymorphism. *Immunol Rev 143:* 141–180, 1995

Saper, M. A., Bjorkman, P. J., and Wiley, D. C. Refined structure of the human histocompatibility antigen HLA-A2 at 2.6 Å resolution. *J Mol Biol 219:* 277–319, 1991