Nomenclature of Human Platelet Alloantigens

To the Editor:

In his article, "Nomenclature of Human Platelet Alloantigens: A Problem With the HPA System?", Peter Newman discussed the scientific merit of the new human platelet antigen (HPA) nomenclature, recently introduced by the Platelet Serology Working Party.1,2 He suggested that this nomenclature is scientifically inaccurate and proposed three alternative nomenclatures; two glycoprotein (GP) based and one modification of the existing HPA nomenclature.

Originally, a GP-based nomenclature was considered, but this idea was rejected because of the possibility of antigenicity based not only on allotypic variations in the aminoacid sequence of proteins, but also on variation in the composition of polysaccharide chains attached to cell-membrane proteins or glycolipids. Furthermore, a definitive nomenclature for platelet glycoproteins has not been agreed upon. For example, GPIIIa is also known as the β3-integrin chain and as CD61-protein. However, more importantly we have conceptual difficulties with Newman's proposals.

At the most basic level, antigens are defined as molecules to which antibodies bind.3 In an immune response against an antigen, a diversity of antibodies may be produced. Each antibody may bind to a particular part of the antigen called the antigenic determinant or epitope. A particular antigen can have several epitopes, and antibodies are specific for the epitopes rather than for the antigen. When translated to platelet immunobiology, this means that HPA-1a, HPA-4a, HPA-6a, HPA-7a, and HPA-8a are not five different names for the same molecular species (the wild type GPIIIa as suggested by Newman), but titles for five different, nonidentical epitopes of GPIIIa.

An individual who differs from Newman's wild type, in being homozygous for HPA-1b, has a significant opportunity to be immunized by an HPA-1a positive blood transfusion. Immunization then occurs against the HPA-1a epitope, determined by the aminoacid leucine in position 33 of the GPIIIa peptide, in contrast to the HPA-1b/b individual who has the aminoacid proline in the same position.4 Likewise, individuals who differ from the dominant HPA-1a, -4a, -6a, -7a, and -8a allele in other GPIIIa aminoacid positions are at risk of developing platelet alloantibodies directed against other epitopes after transfusion therapy.

All the low-frequency antigenic variants of platelet membrane glycoproteins described to date have arisen as single point mutations of the wild type glycoproteins. We have some insight into how point mutations arise, but we do not understand the reasons for or the nature of the selection mechanisms by which such mutations increase in frequency in populations. However, it is a definite possibility that new point mutations may occur in already mutated glycoproteins. The proposals put forward for consideration by Newman were discussed in depth at the most recent (7th) meeting of the ISBT/ICSCH Platelet Serology Working Party on July 2, 1994 in Amsterdam, The Netherlands. Most participants felt that to support the Working Party's serologic and clinical goals, the HPA nomenclature is still adequate, and should be retained for the time being.

This nomenclature was originally conceived as a replacement for the confusing personalized nomenclature that existed before 1990, mostly based on abbreviated patient surnames with often multiple names for the same antigen and/or antigen systems. For those of us in daily clinical practice, HPA nomenclature is not confusing, but simple and easy to understand. It is based on serologic findings and does not make complete genotyping of an individual necessary, which would be the consequence of nomenclatures proposed by Newman.

However, many Working Party members agreed that it is now appropriate to develop a supplementary nomenclature based on molecular genetics as suggested by Newman. This could be used together with the HPA nomenclature, for instance by appending the new information between brackets. For example the HPA-1 system may be denoted as HPA-1 (GPIIIa-Leu33Pro) and the HPA-1 alloantigens as HPA-1a (GPIIIa-Leu33) and HPA-1b (GPIIIa-Pro33).

In conclusion, many members of the ISBT/ICSCH Working Party on Platelet Serology do not at present support an entirely new nomenclature. However, a supplementary GP-based nomenclature for the existing HPA system that is used together is supported and welcomed. A suggestion is made in Table 1. A minor change in the HPA-nomenclature was suggested during the Workshop. Serologically, a biallelic antigen system can only be defined when antibodies against both alleles are available. If this is not the case it may be more desirable to signal the new system by way of a "W" designation (from "Workshop", or "has yet to be worked out") (see also the Table 1).

<table>
<thead>
<tr>
<th>Table 1.</th>
<th>System</th>
<th>Alternative Names</th>
<th>Molecular Name</th>
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</thead>
<tbody>
<tr>
<td>HPA-1</td>
<td>Zw, P1A</td>
<td>GPIIIa-Leu33Pro</td>
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</tr>
<tr>
<td>HPA-2</td>
<td>Ko, Sib</td>
<td>GPIIIa-Thr145Met</td>
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<td>HPA-3</td>
<td>Bak, Lek</td>
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<td>HPA-4</td>
<td>Yuk, Pen</td>
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<td>HPA-5</td>
<td>Br, Zaw, Hc</td>
<td>GPIIIa-Lys505Glu</td>
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<td>HPA-6W</td>
<td>Ca, Tu</td>
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<td>HPA-7W</td>
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<td>Sr</td>
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<td>HPA-9W</td>
<td>Max</td>
<td>GPIIIa-Val837Met</td>
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REFERENCES

Nomenclature of human platelet alloantigens [letter; comment]

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