Role of Glycoprotein IIb:IIIa in the Adhesion of Platelets to Collagen Under Flow Conditions

To the Editor:

In their interesting report, Moroi et al.1 studied the adhesion of platelets to a collagen-coated surface and they described, among others, the influence of anti-glycoprotein (GP) IIb:IIIa antibodies and RGD-containing peptides. Their observation was that these compounds inhibited the adhesion of platelets to collagen and their conclusion was that GPIIb:IIIa plays an important role in the adhesion of platelets with collagen types I and III. These observations are diametrically opposed to our experiments in which we have found that those compounds stimulate the adhesion to collagen.2 The increased platelet adhesion we found was due to an inhibition of the aggregate formation, platelets are not incorporated in the aggregates and an increased number of platelets is available for platelet adhesion. The reason for the discrepancy between our results and the results of Moroi et al is the used anticoagulant. We have used in our experiments blood anticoagulated with low-molecular-weight heparin (LMWH) whereas Moroi et al used citrated blood. The differences between both anticoagulants are striking, as shown in Table 1.

The influence of the anticoagulant on platelet-collagen interaction can be easily explained. Platelet adhesion to collagen is sensitive to the presence of Mg$^{2+}$-ions. The adhesive properties of VLA-2 (GPIa:IIa), the major collagen receptor on the platelet membrane, are dependent on Mg$^{2+}$. In the presence of physiologic concentrations of Mg$^{2+}$, platelet adhesion to collagen depends on VLA-2, GPIb- von Willebrand interaction, and probably GPVI, and there is no support by other platelet membrane GPs. In the absence of cations, when VLA-2 loses its activity, other receptors like GPIb:IIIa and GPIV may become involved in the adhesion of platelets to collagen.

In conclusion, under physiological cation concentrations platelet adhesion to collagen type I and III is not dependent on GPIIb:IIIa. However, there may be an alternative adhesive mechanism based among others on GPIIb:IIIa which functions when no Mg$^{2+}$ is present.

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REFERENCES


Lack of Evidence of HHV-8 DNA in Blood Cells From Heart Transplant Recipients

To the Editor:

The human herpesvirus type 8 (HHV-8), previously named as Kaposi’s sarcoma-associated herpesvirus (KSHV),1 has been suggested to play a major role in the etiology and the pathogenesis of acquired immunodeficiency syndrome (AIDS)-associated and iatrogenic Kaposi’s sarcoma (KS). In addition, evidence for HHV-8 involvement in primary effusion lymphomas has been recently provided.2 Although a role for HHV-8 in the pathogenesis of the above neoplasms is presently accepted by most investigators, controversial results have been obtained in molecular epidemiology studies with regard to the distribution of the virus in the healthy population. Two recent reports have shown detection of HHV-8 DNA sequences in semen from the vast majority of healthy adults3 and in peripheral blood mononuclear cells (PBMC) from ~10% of healthy subjects,4 suggesting that HHV-8 is a fairly common virus latently infecting humans. Thus, the involvement of HHV-8 in KS lesions3 and in non-KS skin lesions from immunosuppressed transplant recipients5 raises the possibility that the virus can reactivate in the presence of various immunosuppression conditions. By contrast, other investigators have failed to identify HHV-8 DNA in non-KS skin lesions from immunosuppressed transplant patients6 and in PBMC from a healthy adult population.7,8

We looked for the presence of HHV-8 DNA in 54 buffy-coat samples from 28 KS-negative immunosuppressed heart transplant recipients and 134 control buffy-coat samples from healthy blood donors. Periodical shell-vial culturing of oropharyngeal washing showed reactivation of cytomegalovirus (CMV), and/or herpes simplex virus 1 (HSV-1) in 18 of the 28 (64.3%) transplant patients during immunosuppressive treatment. DNA fromuffy-coat cells was prepared by a ‘‘salting out’’ procedure and polymerase chain reaction (PCR) suitability of the samples was assessed by amplification of a human β-globin gene region. One microgram of each DNA sample was tested for the presence of HHV-8 DNA sequences by nested PCR amplification.9 HHV-8 PCR was performed on 1 to 4 serial samples per transplant patient, of whom at least one was drawn at the time when CMV and/or HSV-1 reactivation was demonstrated. Reconstruction experiments with titrated cloned HHV-8 templates showed that the nested amplification procedure used was able to detect five copies of target DNA sequence. However, HHV-8 DNA was found neither in the blood donors nor in the transplant patients, including those with concomitant reactivation of CMV and/or HSV-1.

Our failure to detect HHV-8 DNA sequences in buffy-coat cells from the healthy blood donors and the transplant patients examined does not support that HHV-8 is a common infectious agent typically

Table 1. Platelet Adhesion to Collagen

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Without dRGDW</th>
<th>With dRGDW</th>
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<tr>
<td>LMWH-blood</td>
<td>29.8 ± 6.2</td>
<td>39.7 ± 2.3</td>
</tr>
<tr>
<td>Citrated-blood</td>
<td>26.0 ± 2.7</td>
<td>1.6 ± 0.2</td>
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Collagen type III was perfused with whole blood at a shear rate of 1,600 s$^{-1}$ for 5 minutes with or without 50 μmol/L dRGDW. Results are expressed as percent surface coverage with platelets (mean ± SD, n = 4).

Abbreviation: dRGDW, D-arginyl-glycyl-L-aspartyl-L-tryptophan.
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