The role of GP IIb-IIIa in modulation of adhesion reactions. J.C. Mattison (1), R.K. Ester (2), W. Peterson (1), J. LaFevre (1) and W. Rice (3). Department of Pathology, William Beaumont Hospital, Royal Oak, MI, U.S.A. (1), Medical Technology Program, Michigan State University, East Lansing, MI, U.S.A. (2) and Biomedical Engineering Laboratory, Rice University, Houston, TX, U.S.A. (3)

We have previously reported that patients with Glanzmann's thrombasthenia (GT) fail to adhere to a carbon-fortam surface and undergo contact-induced shape change in a non-flow system. The ability of ADP to reverse this adhesion defect suggested that it may be secondary to defective dense granule release rather than a direct requirement for GP IIb-IIIa. To further assess the role of GP IIb-IIIa in adhesion, we examined the effect of two mouse monoclonal antibodies to the GP IIb-IIIa complex, AP2 (IgG, kappa) from T. Kunick, Milwaukee Blood Center and MAb36 (IgM, lambda) from D. Peterson, Rice University. AP2 (1:20 dil) and MAb36 (1:200 dil) both completely abolished aggregation by ADP, collagen and epinephrine and prevented clot retraction. In a transmission EM (TEM) whole mount assay of adhesion and contact-induced shape change, both antibodies inhibited platelet attachment to the substrate and impaired spreading in those few platelets that did attach. This antibody-induced adhesion defect was reversed by the addition of 2x10^-6 M ADP just prior to exposure of platelets to the activating surface. In parallel studies, antibody treated platelets demonstrated a dose-related inhibition of ATP release as measured in a lumaggregometer with total absence of release at antibody dilutions that abolished aggregation. Binding of leupeptin to collagen and epinephrine induced shape change was not observed in antibody treated platelets induced to spread by ADP stimulation. These studies suggest that GP IIb-IIIa is strongly involved in the internalization of CF by platelets in non-flow systems, as suggested by the altered adhesion seen in GT platelets, adhesion and adhesion-induced shape change can be supported by ADP stimulation in the absence of fibrinogen binding to GP IIb-IIIa.

Recent real-time studies that collagen fibrils (CF) are internalized by platelets in citrated plasma have shown that the GP IIb-IIIa complex is strongly involved in the internalization of CF by platelets. Studies in this process by binding to the GP IIb-IIIa complex.

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Contact activated platelets bind von Willebrand factor to GP IIb-IIIa. D.M. Estry (1), J.C. Mattison (2) and J. Chediak (3). Medical Technology Program, Michigan State University, East Lansing, MI, U.S.A. (1), Department of Clinical Pathology, William Beaumont Hospital, Royal Oak, MI, U.S.A. (2) and Michael Reese Medical Center, Chicago, IL, U.S.A. (3).

Using a rabbit polyclonal anti-von Willebrand factor (vWF) antibody, normal human adherent platelets extensively bind vWF in a diffuse pattern as detected by immunogold electron microscopy. This pattern differed significantly from the dense column pattern observed for direct fibrinogen-gold labelling in contact activated platelets. In order to determine if contact activated platelets bind vWF to GP IIb-IIIa or GPIb, the extent and pattern of bound vWF in platelets from patients with Glanzmann's thrombasthenia (GT) and Bernard Soulier Syndrome (BS) was determined. Virtually no bound vWF was detected by immunogold labeling in GT platelets previously characterized as being deficient in GP IIb-IIIa. On the other hand, BS platelets, lacking GPIb, demonstrated extensive labeling of vWF in a pattern identical to that seen in normal platelets. This data is consistent with vWF binding to GPIb-IIIa in contact induced adhesion and spreading.

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