**LEUKOCYTES, HAEMOSTASIS AND THROMBOSIS**

**1051**

**FIBRINOGEN BINDS TO HUMAN NEUTROPHILS AT A SITE DISTINCT FROM GP1IIIa, E.2, Gustafsson, M. Lukaszewicz, H.W. Schmerer, S. Newbourn and P. Girolami**

Department of Medicine, Temple University, Philadelphia, PA, USA.

Many observations suggest a potential role for neutrophils in the hemostasis and thrombosis. Arterial thrombi are characterized by the presence of large numbers of neutrophils. The parameters of platelet aggregation while investigating the binding of high molecular weight kininogen (HMWK) to neutrophils, we found that fibrinogen (Fb) could inhibit binding of [125I-HMKW as did [125I-Fb] and also already bound by neutrophils. We have therefore attempted to determine whether Fb could bind to human neutrophils. Both Zn**2+** and Ca**2+** were required for maximal binding of [125I-Fb] to neutrophils. Binding did not occur with Ca**2+** (2 mM) alone and was only 1/3 the maximal amount with Zn**2+** (50 μM) alone. At 4° the amount of [125I-Fb] bound to neutrophils reached a plateau by 15 minutes and remained at this level over the next 30 minutes. At 23° and 37° the amount of [125I-Fb] bound peaked by 4 minutes and then decreased over the next 30 minutes indicating receptor-mediated internalization. Excess Fb inhibited binding of [125I-Fb] to neutrophils while prechallenge, free Fb and fibronectin did not. Binding of [125I-Fb] was 95% reversible after 90 minutes with 0.5 Molar molar excess of either Fb or fibronectin. The apparent KD was approximately 0.45 μM, Arg-Gly-Asp-Ser (RGDS) is a tetrapeptide common to Fb, fibronectin and other cell-attachment proteins. Fb has been demonstrated to bind to the glycoprotein IIb/IIIa (GP1IIIa) complex which is the platelet membrane receptor for Fb, fibronectin and other cell-attachment proteins.

**1052**

**STRUCTURAL DIVERSITY AMONG CELLULAR ADHESION RECEPTORS: FIBRINOGEN BINDING IS A NOVEL BIOLOGICAL PROPERTY OF THE MONOCYTE DIFFERENTIATION ANTIGEN, CD11b/CD18, J. Bevan and S. Heptinstall, Department of Pathology, University of Oxford, Oxford, UK.**

Many observations suggest a potential role for neutrophils in the hemostasis and thrombosis. Arterial thrombi are characterized by the presence of large numbers of neutrophils. The parameters of platelet aggregation while investigating the binding of high molecular weight kininogen (HMWK) to neutrophils, we found that fibrinogen (Fb) could inhibit binding of [125I-HMKW as did [125I-Fb] and also already bound by neutrophils. We have therefore attempted to determine whether Fb could bind to human neutrophils. Both Zn**2+** and Ca**2+** were required for maximal binding of [125I-Fb] to neutrophils. Binding did not occur with Ca**2+** (2 mM) alone and was only 1/3 the maximal amount with Zn**2+** (50 μM) alone. At 4° the amount of [125I-Fb] bound to neutrophils reached a plateau by 15 minutes and remained at this level over the next 30 minutes. At 23° and 37° the amount of [125I-Fb] bound peaked by 4 minutes and then decreased over the next 30 minutes indicating receptor-mediated internalization. Excess Fb inhibited binding of [125I-Fb] to neutrophils while prechallenge, free Fb and fibronectin did not. Binding of [125I-Fb] was 95% reversible after 90 minutes with 0.5 Molar molar excess of either Fb or fibronectin. The apparent KD was approximately 0.45 μM, Arg-Gly-Asp-Ser (RGDS) is a tetrapeptide common to Fb, fibronectin and other cell-attachment proteins. Fb has been demonstrated to bind to the glycoprotein IIb/IIIa (GP1IIIa) complex which is the platelet membrane receptor for Fb, fibronectin and other cell-attachment proteins. Fb has been demonstrated to bind to the glycoprotein IIb/IIIa (GP1IIIa) complex which is the platelet membrane receptor for Fb, fibronectin and other cell-attachment proteins.

**PLATELET INHIBITION (2)**

**1053**

**ADMINISTRATION OF TICLOPOIDINE INDUCES ADP-INDUCED ACTIVATION BUT DOES NOT INDUCE A THROMBOGENIC STATE. F. Petojin, T. Lecompte, C. LeCrubier, M. Samama, Lab. Hématologie, Hôpital-Dieu, Paris.**

The aim of this study was to reassess the pattern of aggregation and to investigate the platelet-fibrinogen interaction, in response to various agonists, following T treatment: (a) treatment of 0.1 M b.i.d. for at least 1 week. Platelets were obtained from healthy volunteers (-8) as well as from patients with cerebral-vascular disease (-5), and washed platelets were prepared according to MUSTARD et al. (1983). (1) In the absence of experimental conditions T treatment only induced slight modification in the levels of aggregation induced by ADP (5 μM). (2) The association of human fibrinogen -Fb with platelets was not inhibited by RGDS that inhibited fibrinogen binding to monocytes. To investigate if T could bind to neutrophils, the method employed was the following: T was administered to patients with Glanzman's thrombasthenia, by our way the same as that used to normal neutrophils. These studies indicate that human neutrophils specifically bind to a site similar to HMWK and distinct from GP1IIIa.

**1054**

**HOW CAN WE INHIBIT SHT-INDUCED PLATELET AGGREGATION AND WHY SHOULD WE BOTHER? Jane Heyman and S. Heptinstall, Department of Medicine, University Hospital, Nottingham, NG7 2UH, UK.**

Platelets are induced to aggregate when 5-hydroxytryptamine (SHT) is added to citrated whole blood and the extent of aggregation depends on the concentration of the agonist. SHT is a potent agonist for platelet aggregation and is the most potent agonist for aggregation in blood from patients with peripheral vascular disease (PVD). Previous studies of platelet aggregation in platelet-rich plasma have indicated an increased platelet sensitivity to SHT in PVD, and a multicentre study of ketanserin (a 5-HT antagonists) is in progress.

SHT induces a transient reversible aggregation in human whole blood which can be prevented by SHT receptor antagonists. The inhibitory effects of 7 relatively potent antagonists (IC50 = 32, 33 and 34, respectively) and the inhibitory effects of 25 I-Fb binding to monocytes was not inhibited by RGDS. A monoclonal antibody to 5 hydroxytryptamine (5HT) is added to citrated whole blood and the extent of aggregation depends on the concentration of the agonist. SHT is a potent agonist for platelet aggregation and is the most potent agonist for aggregation in blood from patients with peripheral vascular disease (PVD). Previous studies of platelet aggregation in platelet-rich plasma have indicated an increased platelet sensitivity to SHT in PVD, and a multicentre study of ketanserin (a 5-HT antagonists) is in progress.

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