QUESTION 41 VWF
During normal haemostasis, von Willebrand factor (vWF) plays a role in platelet adhesion/aggregation. During this process, which of the following is the primary binding site of vWF to platelets?
A. Collagen receptor.
B. Platelet glycoprotein Ib-IX-V.
C. Adenosine diphosphate receptor.
D. Platelet glycoprotein IIb-IIIa.
E. Ristocetin.

**Function:**
- Acts as a bridging molecule for normal platelet adhesion and aggregation
- Acts as a carrier for factor VIII in the circulation – increases half life of factor VIII by 5X

**Synthesized**
- In endothelial cells and megakaryocytes
- vWF production in endothelial cells is increased by both estrogen and thyroid hormone

**Functions**
- Primary hemostasis by forming an adhesive bridge between the platelets and vascular subendothelial structures
- Acts as carrier protein for factor VIII which has a greatly shorted half life unless it is bound to VWF.

**Binding to platelets**
- Binding of VWF to platelets and subendothelial components is critical for normal platelet adhesion and for platelet aggregation
- Requires initial activation or alteration in the structure of VWF so that the binding sites in the A1 domain can engage the *platelet receptor GP Ib-IX-C complex* on the platelet surface

“Activation may occur as VWF binds to subendothelial structures exposed after endothelial damage, possible immobilizing and exposing multiple VWF A1 domains toward the vessel lumen where platelets are present

2\textsuperscript{nd} platelet receptor for VWF – GP IIb/IIIa
- does not bind VWF unless the platelets are activated
- undergoes conformational change and becomes accessible on the platelet surface
- this interaction appears to contribute to the final, irreversible binding of platelets to the subendothelium after VWF has bound to GP Ib

**Binding to subendothelium**
- VWF binds to multiple types of collagen but type VI appears to be especially important
- Binding to collagen induce a conformational change within the factor VIII binding motif of VWF that lowers the affinity for factor VIII → releasing factor VIII locally to aid in formation of fibrin clot

**Ristocetin**
- Has a binding site of the A domain of the VWF propeptide
- Ristocetin induced platelet aggregation (RIPA)
- Measures the affinity with which VWF binds to the platelet receptor GPIb by limiting concentration of ristocetin in the assay
- Used to look for the type 2B variant of VWF which has mutations in the binding site for GP IB such that type 2B VWF binds to GP Ib more readily than normal

Answer : B