0789

RECENT ADVANCES IN THE STUDY OF THE MECHANISM OF FIBRIN POLYMERIZATION. Stephanie A. Olexa, Thrombosis Research Center, Temple University Health Sciences Center, Philadelphia, Pa. 19140

Fibrinogen is converted to fibrin monomer by thrombin, which cleaves the fibrinopeptides A and B. The resulting fibrin monomers spontaneously polymerize to form a fibrin network, which is later stabilized with covalent cross-linking bonds. Although the action of thrombin and Factor XIIIa have been fairly well defined, the mechanism of fibrin polymerization is not yet understood. Electron microscopy and light scattering studies have provided information on the arrangement of molecules within the fiber. Monomers appear to align with a half-staggered overlap, resulting in a fiber with a width equal to twice that of fibrinogen. Detailed studies on the location and interaction of polymerization sites have been done primarily by using fibrinogen and fibrin degradation products. The studies indicate that polymerization is due to the interaction of complementary binding sites which are located on the Fragment D and the NH_2-terminal domains in the fibrinogen molecule. One of these sites, located in the sequence 373-410 of the gamma chain, is available on fibrinogen in the Fragment D domain. This site is complementary to the site revealed by the loss of fibrinopeptide A, which is probably located in the sequence contiguous to FPA. A second polymerization site in the NH_2- terminal domain of fibrin may be located in the sequence following fibrinopeptide B. The recriprocal site may also be located on the Fragment D region. The polymerization of fibrin appears to be due to a complex interaction between molecules with both the primary sequence and the three-dimensional conformation having vital roles.

0790

COMPLEX FORMATION OF PLATELET GLYCOPROTEINS IIB AND IIIA WITH FIBRINOGEN. R. Nachman and L. Leung. Cornell University Medical College, New York, N.Y.

Platelet membrane glycoproteins IIb and IIIa were isolated and purified from human platelet membranes using lentil lectin affinity chromatography and electrophoretic elution from SDS-poly-acrylamide gels. Two dimensional immunoelectrophoresis of a mixture of the purified proteins against monospecific antisera showed antigenic uniqueness of the separate polypeptides. Computerized analysis of autoradiographs of two dimensional tryptic ^{125}I peptide maps revealed that the two glycoproteins had completely different structures. Thus human platelet membrane glycoproteins IIb and IIIa are separate molecular entities. Monospecific anti-GPIIb and anti-GPIIIa were utilized in an enzyme linked immunosorbent assay system to demonstrate complex formation of the platelet glycoproteins with purified human fibrinogen. The formation of this GPIIb-GPIIIa fibrinogen complex is calcium dependent, fibrinogen specific, saturable, and inhibited by specific amino sugars and amino acids. These observations suggest that the GPIIb-GPIIIa macromolecular complex on the platelet surface acts under the proper physiologic circumstances as the fibrinogen binding site required for normal platelet aggregation.