PLASMA HIGH-MOLECULAR-WEIGHT AND LOW-MOLECULAR-WEIGHT KININOGENS: THEIR STRUCTURES AND PHYSIOLOGICAL FUNCTIONS. S. Iwanaga, H. Kato, Y.-N. Han, N. Hashimoto, T. Sugo, and S. Fujii. Institute for Protein Research, Osaka University, Osaka.

Bovine plasma contains two kininogens. One of them, HMW kininogen, has recently been characterized as a new coagulation factor, which is required for the activation of Hageman factor-mediated pathway. To elucidate the structural differences between HMW and LMW kininogens, these were fragmented with plasma kallikrein and snake venom kininogenase, and the resulting products were chemically identified. The kallikrein simultaneously released bradykinin and fragment 1-2 from HMW kininogen. Fragment 1-2 was a histidine-rich glycopeptide consisting of 110 amino acid residues, and its whole sequence and the location of the sugar moieties were established. The venom kininogenase liberated only bradykinin from LMW kininogen. Kinin (and fragment 1-2)-free proteins consisted of heavy and light chains. These chains constituted, respectively, the NH₂- and COOH-terminal portions of both parent molecules and were held by a single disulfide bridge. The detailed studies on these chains indicated that the NH₂-terminal portions of HMW and LMW kininogens are very similar for each other, whereas their COOH-terminal portions differ significantly. Concerning the results that HMW kininogen overcomes impaired coagulation and fibrinolysis of the kininogen deficient plasmas, and the kinin-free HMW protein has a weak corrective activity, it seems that the histidine-rich region found only in HMW kininogen may be closely related to the functions of the kininogen.

INVITED SYMPOSIUM VIII

Antithrombin III: Assay Techniques and Application in Disease States.

SYMPOSIUM ON ANTITHROMBIN III: INTRODUCTORY REMARKS. S. S. Shapiro, Cardeza Foundation, Jefferson Medical College, Philadelphia, Pennsylvania, U.S.A.

Interest in Antithrombin III has increased greatly since Abildgaard's isolation of this protein and his demonstration that it is identical with the heparin cofactor. It is now clear that Antithrombin III plays a central role as an inhibitor of many serine proteases, including activated coagulation factors, kallikrein and plasmin. Heparin enhances the neutralizing activity of Antithrombin III towards each of these enzymes, from several-fold to more than 1,000-fold. Although Antithrombin III represents only a small fraction of the total protease neutralizing capacity of human blood, variation in the level of this protein seems to correlate with some clinical thromboembolic or "hypercoagulable" states. Variations in Antithrombin III levels occur regularly in several disease states, including disseminated intravascular coagulation. Heterozygosity for Antithrombin III is associated, in adult life, with a distinct tendency to thrombosis.

This symposium will be concerned with methods of measuring Antithrombin III and the correlation of its levels with disease states, the mechanism of action of this inhibitor and the role of heparin in its enhancement, and the thromboembolic tendency seen in hereditary Antithrombin III deficiency.