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MIXED POSTERS V

Coagulation

AMINO ACID SEQUENCE STUDIES ON THE γ -CHAIN OF HUMAN FIBRINOGEN. H. Bouma, III, B.A. Cottrell, S.J. Friezner, T. Takagi and R.F. Doolittle. Department of Chemistry, University of California, San Diego, La Jolla, California U.S.A.

The γ -chain of human fibrinogen contains 400 ± 10 residues, eight of which are methionines. As such, we have isolated and characterized nine cyanogen bromide peptides. The alignment of these fragments was attained by the isolation of key overlap peptides derived from the tryptic digestion of citraconylated γ -chains and succinylated and aminoethylated γ -chains. In the latter case we synthesized a radioactive aminoethylating agent which was especially useful in isolating all the cysteine-containing peptides. The amino acid sequence of most of these fragments has been accomplished by a variety of procedures. In general, our results are in harmony with those recently reported by Henschen *et al.* (Hoppe-Seyler's Z. Physiol. Chem., 357, 605, 1976), although some differences exist.

The most interesting structural features revealed by the sequence data include significant homologies with the α - and β -chains, especially with regard to the arrangement of certain key cysteine residues. Thus, the sequence at residues γ 135-139 is Cys-Gln-Glu-Pro-Cys, in striking parallel with the sequence at residues γ 19-23, which is Cys-Pro-Thr-Thr-Cys. The occurrence of similar pentapeptide skeins in the α - and β -chains, in each case separated by about the same number of residues, has both structural and evolutionary connotations.

8-HOUR RADIOIMMUNOASSAY FOR FIBRINOPEPTIDE A (FPA). V. Hofmann and P.W. Straub. Thrombos. Lab. Dept. of Medicine, Inselspital, Univ. of Berne, Switzerland.

To allow emergency measurements of FPA in patients, a RIA method was developed in which both the extraction of FPA from plasma and the incubation time of the antigen-antibody mixture were substantially reduced. Extraction with an equilibrium dialyzer allowed a recovery of $54.75 \pm 1.26\%$ of added FPA (20 ng) within 2½ hrs. At an incubation of 2½ hrs the limit of detection was 1.12 ng/ml, as compared to 0.54 ng/ml for 24-hr incubation. Rabbits were immunized with synthetic FPA coupled to thyroglobulin with the carbodiimide method. The tracer was produced acc. to Nossel (1971). To prevent label damage for 10 weeks, the purified radioiodinated peptide was rechromatographed using a QAE-A25 Sephadex column. In 24 normals FPA was 1.01 ± 0.45 ng/ml using 24-hr incubation. For FPA levels above 2 ng/ml the results obtained with the 2½-hr and the 24-hr incubation showed excellent agreement ($r=0.99$). 3.3-25.2 ng/ml were found in 7 patients with venous thromboembolism, a sharp drop to 1.6-5.1 ng/ml being observed 10 minutes after 50 mg of heparin i.v. 2.3-32 ng/ml were found in 15 patients with various disorders (4 malignancy, 4 aortic aneurysm, 2 nephropathy, 2 anginal attack, 1 septicemia, 1 lung abscess, 1 CVI). Values of 3.6-80 ng/ml were found after infusion of a prothrombin complex concentrate in 5 patients with hemophilia B. The method is valuable for the emergency coagulation work-up of patients.