WASHINGTON, Dec. 5 -- Scientists at Scripps Clinic and Research Foundation have developed potent, short-acting peptides that may interfere with the body's ability to form blood clots, a development that could lead to new treatments for heart attack and stroke patients.

In a related project, the research team has also developed antibodies that can identify activated platelets, cells essential to the blood-clotting process, said Dr. Mark Ginsberg of the Research Institute of Scripps Clinic. This, using diagnostic imaging technologies, could allow physicians to locate the exact area of a life-threatening blood clot.

Ginsberg, addressing "Immunological and Peptide Strategies for the Detection and Therapeutic Inhibition of Platelet Thrombi," spoke at the annual meeting of the American Society of Hematology, held Dec. 5-8 in Washington, D.C, and attended by more than 4,000 hematologists.

In work so far confined to the laboratory, Ginsberg and Dr. Edward Plow, also of the Research Institute, have developed two groups of peptides that inhibit platelet functions.
In the normal blood-clotting process, blood platelets bind to fibrinogen; through an enzyme-assisted reaction, the fibrinogen is converted to fibrin, which binds the platelets into a tough mass, or clot.

However, one of the peptides developed by the Scripps Clinic investigators binds to fibrinogen, and blocks the area on the fibrinogen molecules to which platelets can attach - thus, platelets are prevented from binding together.

The second group of peptides mimics the structures in fibrinogen recognized by platelet receptors. These peptides competitively inhibit the ability of platelets to bind to fibrinogen, and thus platelet aggregation.

Should this development reach the clinical stage, a person suffering a thrombotic heart attack or stroke would receive an infusion of the peptide, which would inhibit clot formation and restore normal blood flow.

This possible therapy would have advantages over present methods of treatment, according to Ginsberg. For example, the peptides are potent and short-acting, losing their effect within minutes or hours of infusion; blood-thinners such as warfarin may take days to lose their effect.

The antibodies used to track down blood clots, useful in conjunction with imaging technology, are able to detect platelet receptors which have bound to fibrinogen molecules. The antibodies, designed to detect the change in structure of an occupied receptor, could eventually be designed to detect occupied receptor cells of many kinds, such as migratory cells. In addition, through molecular cloning techniques, Ginsberg and his colleagues have identified the site on the receptor molecule that antibodies recognize and attach to; this could lead to the development of synthetic peptides capable of fitting into the same site.

(More)
Ginsberg, a member of the immunology department since 1975, served his medical residency and internship at the University of Chicago Hospitals. He is a diplomate of the American Board of Internal Medicine and the National Board of Medical Examiners, and a founding fellow of the American Rheumatism Association. He is also a member of the American Association of Immunologists, the American Society for Clinical Investigation, the American Federation for Clinical Research and the Thrombosis Council of the American Heart Association.

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