Beating Blood Clots - New Concepts in Anticoagulation

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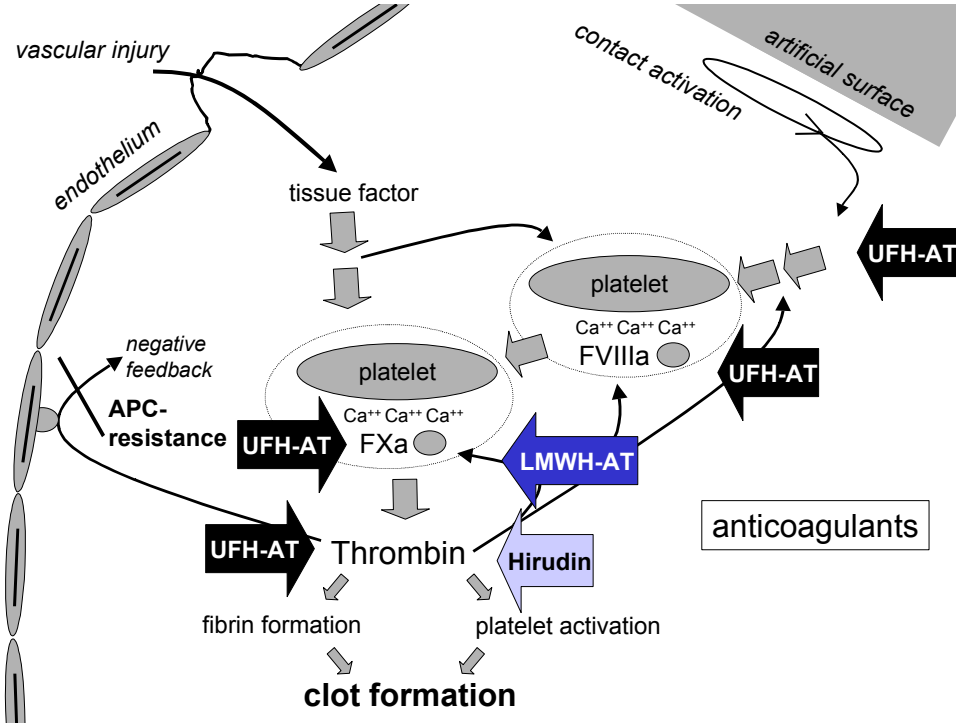
Recent progress in clarifying the molecular bases of haemostasis as delicate interaction between cells and plasma proteins has highlighted new targets for antiplatelet or anticoagulant compounds. Selective antagonists of specific platelet glycoprotein receptors (Willebrand factor- , collagen-, ADP- or thrombin- receptors) are investigated in vitro and in vivo as antiplatelet agents. Inhibitors of tissue-factor-induced clotting activation, as well as selective inhibitors of thrombin and factor Xa are being investigated as anticoagulants.



As a consequence various therapeutic interventions in patients are possible in the coagulation system. The development of heparin has finally received the synthetic production of pentasaccharide. The major effect of heparins in vivo is dependent on the complex formation with the endogeneous coagulation inhibitor antithrombin. Another class of new coagulation inhibitors like Hirudin acts independently of endogeneous proteins, thus directly inhibiting the target enzymes. Different strengths of affinity have been shown depending on bivalent or monovalent binding of thrombin inhibitors.

Direct Thrombininhibitors

Bivalent Inhibitors

Additional binding site

High specificity

Hirudin

Active site Inhibitors

monovalent Active site binding:

Low specificity

Melagatran

Advances in antiplatelet and antithrombotic therapy increased not only the practicability of administration but also efficacy and safety. On the other hand the variety of compounds administered induced a more complex situation with respect to quality management of patient care. Anticoagulants have to be selected considering the individual risk of thromboembolic events and on the other hand the probability of side effects.