SUMMARY

VWF is a multimeric glycoprotein that mediates thrombus formation at sites of vascular injury by means of specific interactions with components of extracellular matrix and platelet receptors. The essential biologic properties of vWF have been elucidated in the areas of genetic regulation, biosynthesis and specific biomolecular interactions. The three-dimensional structure of selected domains has been solved, but our understanding of detailed structure-function relationships is still fragmented, partly because of the complexity and the size of the vWF molecule. The biomechanical properties of the interaction between the VWF A1 domain and the platelet receptor GPIbα are also better known, but we can still only hypothesize how this adhesive bond can oppose the fluid dynamic effects of rapidly flowing blood to initiate thrombus formation and contribute to platelet activation. Elucidating the details of VWF and GPIbα function will lead to a more satisfactory definition of the role of platelets in atherothrombosis, since hemodynamic forces greatly influence responses to vascular injury in stenosed and partially occluded arteries.

Antiplatelet agents are the cornerstone in treatment of cardiovascular diseases and other thrombotic diseases. The majority of these drugs focus on targeting either surface receptors or enzymes in the platelet in order to protect against thrombus formation following initial platelet activation. According to the previous paragraph the binding of vWF A1 domain to platelet receptor GPIbα is an attractive drug target. Here are summarized the different classes of drugs targeting vWF-GPIbα interaction and is given an account of their level of clinical development. In particular, the following compounds are discussed: monoclonal antibodies AJvW-2 and AJW200, nanobodies ALX-0081 and ALX-0681, aptamers ARC 1779, ARC 1172 and ARC 15105. A specific reference is being made for vWF A2 domain which effectively inhibits the binding of vWF to GPIbα under high shear stress.

The human gene encoding A1 domain was cloned and expressed in a bacterial system and the recombinant A1 protein was overexpressed, biotinylated and purified successfully. The recombinant A1 domain and the biotinylated product are now available in a large amount and with great purity, ready to be used in experiments for protein immobilization on nanosurfaces. Later, the interaction between A1 and A2 domain could be studied to provide evidence for the design for new and potent antithrombotic factors against the vWF-GPIbα axis.