

A8 Collagen-platelet interactions: recognition and signalling

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Circulating platelets scan the vascular endothelium for fibrous collagens I and III exposed in the vasculature by damage or disease. A multi-site process involving collagen receptors integrin $\alpha 2\beta 1$ and Glycoprotein (Gp) VI allows platelets to adhere to the subendothelium, become activated, aggregate, and promote coagulation. These receptors co-operate to prevent loss of blood where the vessel is breached, but may precipitate lethal occlusion in coronary vessel disease.

The collagen sequence GFOGER is a recognition motif for $\alpha 2\beta 1$. This and related sequences in collagens I, III and IV support high affinity cellular adhesion through the $\alpha 2$ I-domain. A synthetic triple-helical peptide containing the sequence GFOGER has been co-crystallised with the $\alpha 2$ I-domain, and can be used to antagonise $\alpha 2\beta 1$, the signalling properties of which remain to be established. A triple-helical collagen-related peptide (CRP) comprising 10 repeating GPO motifs binds GpVI, for which hydroxyproline is essential. Shorter GPO-containing peptides will bind GpVI, but platelet signalling occurs only if these peptides are crosslinked, to provide quaternary structure.

GPO triplets, although representing about 10% of the primary sequence of collagens, appear too widely dispersed to support platelet activation by collagen monomers. This model supports the idea that GPO triplets in adjacent collagen monomers within a collagen fibre all contribute to the activatory properties of triple-helical collagens.