

Fibrin and Activated Platelets Cooperatively Guide Stem Cells to a Vascular Injury and Promote Differentiation Towards an Endothelial Cell Phenotype

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Objective—Bone marrow-derived progenitor cells play a role in vascular regeneration. However, their homing to areas of vascular injury is poorly understood. One of the earliest responses to an injury is the activation of coagulation and platelets. In this study we assessed the role of hemostatic components in the recruitment of CD34⁺ cells to sites of injury.

Methods and Results—Using an ex vivo injury model, representing endothelial cell (EC) injury or vessel denudation, we studied homing of CD34⁺ under flow. Platelet aggregates facilitated initial tethering and rolling of CD34⁺ cells through interaction of P-selectin expressed by platelets and P-selectin glycoprotein ligand-1 (PSGL-1), expressed by CD34⁺ cells. Ligation of PSGL-1 activated adhesion molecules on CD34⁺ cells, ultimately leading to firm adhesion of CD34⁺ cells to tissue factor-expressing ECs or to fibrin-containing thrombi formed on subendothelium. We also demonstrate that fibrin-containing thrombi can support migration of CD34⁺ cells to the site of injury and subsequent differentiation toward a mature EC phenotype. Additionally, intravenously injected CD34⁺ cells homed in vivo to denuded arteries in the presence of endogenous leukocytes.

Conclusions—We provide evidence that hemostatic factors, associated with vascular injury, provide a regulatory microenvironment for re-endothelialization mediated by circulating progenitor cells. (*Arterioscler Thromb Vasc Biol.* 2006;26:1653-1659.)

Key Words: platelets ■ coagulation ■ fibrinogen/fibrin ■ aggregation ■ other vascular biology