Blood monocyte concentration is critical for enhancement of collateral artery growth

Matthias Heil, Tibor Ziegelhoeffer, Frederic Pipp, Sawa Kostin, Sandra Martin, Matthias Clauss, and Wolfgang Schaper

Department for Experimental Cardiology, Max Planck Institute for Physiological and Clinical Research, 61231 Bad Nauheim, Germany

ABSTRACT

0.1152/ajpheart. 01098.2001. Arteriogenesis has been associated with the presence of monocytes/macrophages within the collateral vessel wall. We tested the hypothesis that arteriogenesis is functionally linked to the concentration of circulating blood monocytes. Monocyte concentrations in peripheral blood were manipulated by single injections of the antimetabolite 5-fluorouracil (5-FU), resulting in a marked rebound effect in New Zealand White rabbits. Collateral artery growth was assessed by the use of a model of acute femoral artery ligation. Seven days after ligation, collateral conductance and the number of visible collateral arteries were increased in the rebound group. This increase was accompanied by an increased monocyte accumulation as demonstrated by immunohistology in the thigh 3 days after surgery. In a second animal model (129S2/SvHsd mice), 5-FU treatment caused a remarkable decrease in blood monocyte numbers at day 4, followed by a rebound effect at day 12. Foot blood flow, assessed by laser-Doppler imaging before and at various time points after surgery, increased from day 7 through day 21 in mice from the rebound group. In contrast, ligation during the phase of monocyte depletion resulted in a reduction of blood flow reconstitution. This inhibition could be reversed by an injection of isolated monocytes. In conclusion, we have demonstrated a functional link between the monocyte concentration in the peripheral blood and the enhancement of arteriogenesis.

collateral circulation; monocytes; hindlimb; angiogenesis; leukocytes