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Emerging role of endothelial endoglin in integrin-mediated cell adhesion

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Endoglin is highly expressed by endothelial cells during angiogenesis and is heavily involved in vascular development, maturation and remodeling. Mutations in the endoglin (ENG) gene are responsible for Hereditary Hemorrhagic Telangiectasia type 1 (HHT1), an autosomal dominant vascular dysplasia associated with frequent epistaxis, gastrointestinal hemorrhages, cutaneous telangiectasias and arteriovenous malformations in the lung, liver and brain. Its 3D-structure has revealed that endoglin displays an accessible RGD sequence which is a consensus recognition motif for integrins (1). Indeed, endothelial endoglin can bind leukocyte surface integrins (2). We have recently analyzed the role of endothelial endoglin as a possible counter-receptor for integrins on platelets and vascular mural cells, as well as the implications of this novel function in the pathogenesis of HHT1 (3,4). We find that adhesion between vascular endothelial cells and vascular mural cells is enhanced by the integrin activator CXCL12 and inhibited upon suppression of membrane endoglin or β1-integrin. In Eng+/- mice, a model for HHT1, endoglin haploinsufficiency induces a pericyte-dependent increase in vascular permeability (3). In addition, endoglin promotes specific platelet adhesion under static conditions and confers resistance of adherent platelets to detachment upon exposure to flow. Also, platelets adhere to confluent endothelial cells in an endoglin-mediated process. Remarkably, Chinese hamster ovary cells ectopically expressing the human αIIbβ3 integrin acquire the capacity to adhere to cell transfectants expressing human endoglin, whereas platelets from Glanzmann's thrombasthenia patients lacking the αIIbβ3 integrin are defective for endoglin-dependent adhesion to endothelial cells. Furthermore, the bleeding time, but not the prothrombin time, is significantly prolonged in Eng+/- mice compared to Eng+/+ animals (4). These results suggest a new role for endoglin in integrin-mediated adhesion of vascular mural cells and platelets to the endothelium, and may provide a better understanding on the biological processes involved in HHT1, including vessel maturation, hemostasis, and thrombo-inflammatory events.

1. Saito al., Cell Rep. 19:1917-28, 2017.
2. Rossi et al., Blood 121:403-15, 2013.
3. Rossi et al., Cell Mol Life Sci 73:1715-39, 2016.
4. Rossi et al., 12th HHT International Scientific Conference, Dubrovnik (Croatia), June 8-11, 2017.