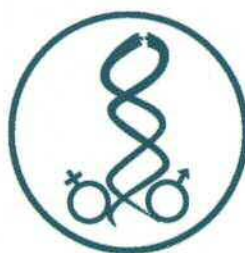


International Journal of Molecular Medicine

ISSN 1107-3756
eISSN 1791-244X

VOLUME 40, SUPPLEMENT 1, 2017



Proceedings of the Abstracts of
The 22nd World Congress on Advances in Oncology,
and
20th International Symposium on Molecular Medicine
5-7 October, 2017, Metropolitan Hotel, Athens, Greece

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 $\beta 1$ -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 $\alpha \text{IIb}\beta 3$ integrin acquire the capacity to adhere to cell transfectants expressing human endoglin, whereas platelets from Glanzmann's thrombasthenia patients lacking the $\alpha \text{IIb}\beta 3$ 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 et 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.