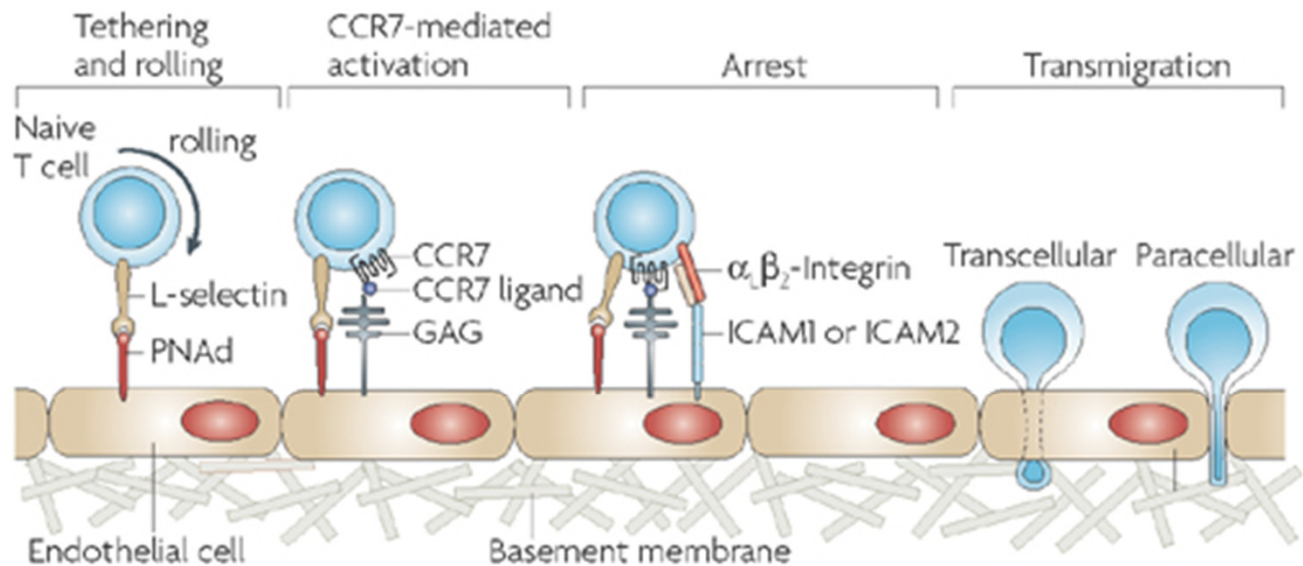


Podoplanin maintains high endothelial venule integrity by interacting with platelet CLEC-2

Brett H. Herzog, Jianxin Fu et al.

Podoplanin

- Transmembrane O-glycoprotein Podoplanin (gp38 and T1 α)
- Type 1 alveolar cells, kidney podocytes, lymphatic endothelial cells, (metastatic) tumour cells
- Thrombus stabilisation

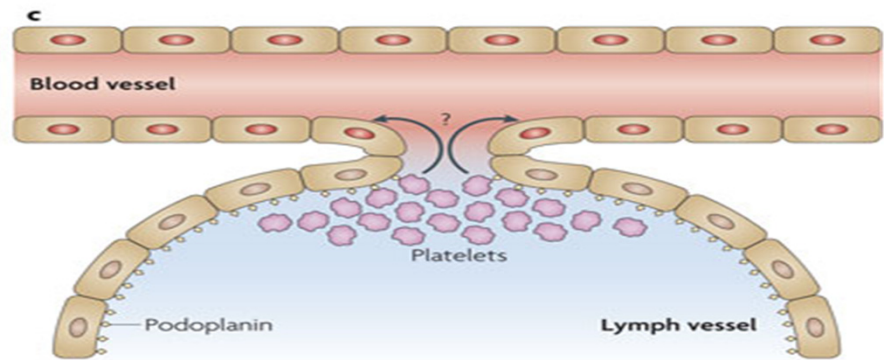
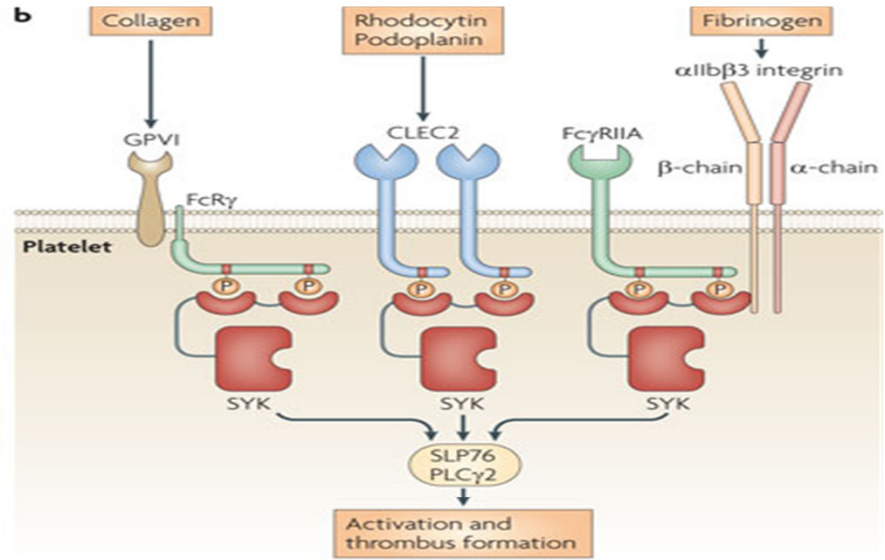


- **NOT** expressed by vascular endothelial cells
high endothelial venules (HEVs)
- Lymphocyte transmigration in LN through HEVs
- Loss of Podoplanin -> bleeding in LN
- Blocking of lymphocyte homing -> bleeding stops

CLEC-2

- PDPN expressed by fibroblastic reticular cells (FRCs) surrounding HEVs
- PDPN activates C-type lectin-like receptor 2 (CLEC-2) on platelets, myeloid cells and dendritic cells
- Lack of VE-cadherin, due to unreleased Sphingosine-1-phosphate (S1P)
-> reduced HEV integrity

CLEC-2



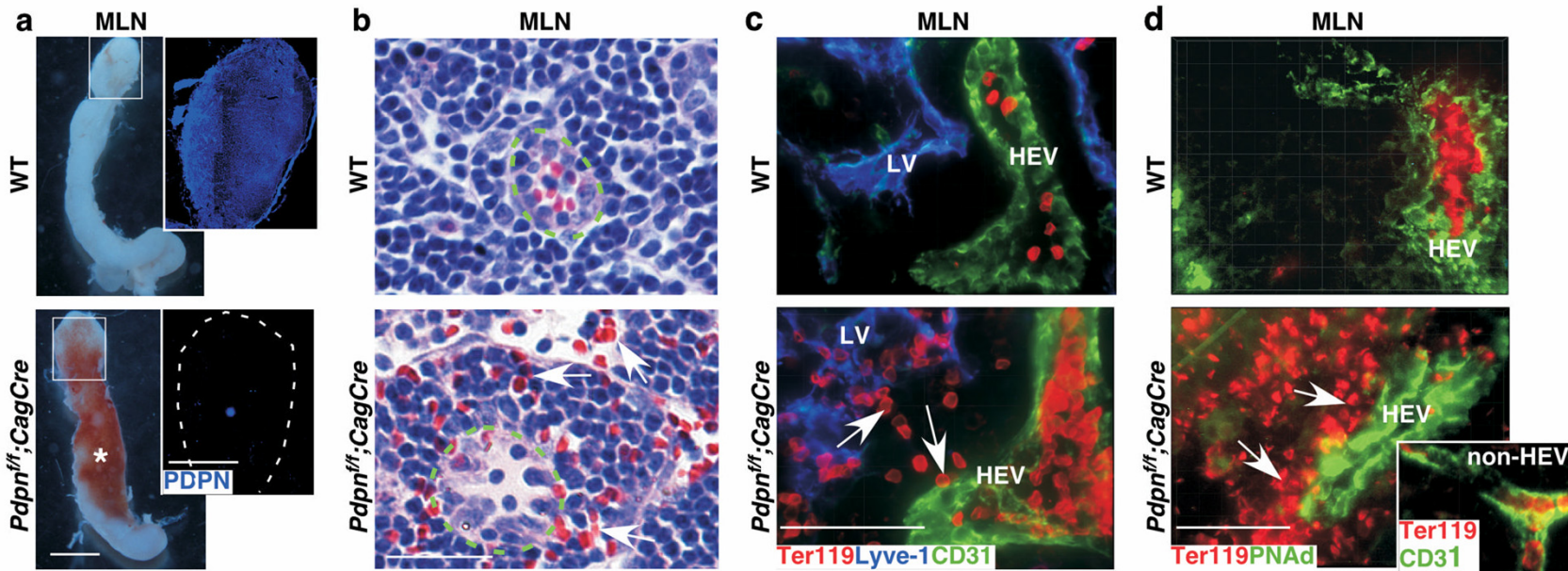
Methods

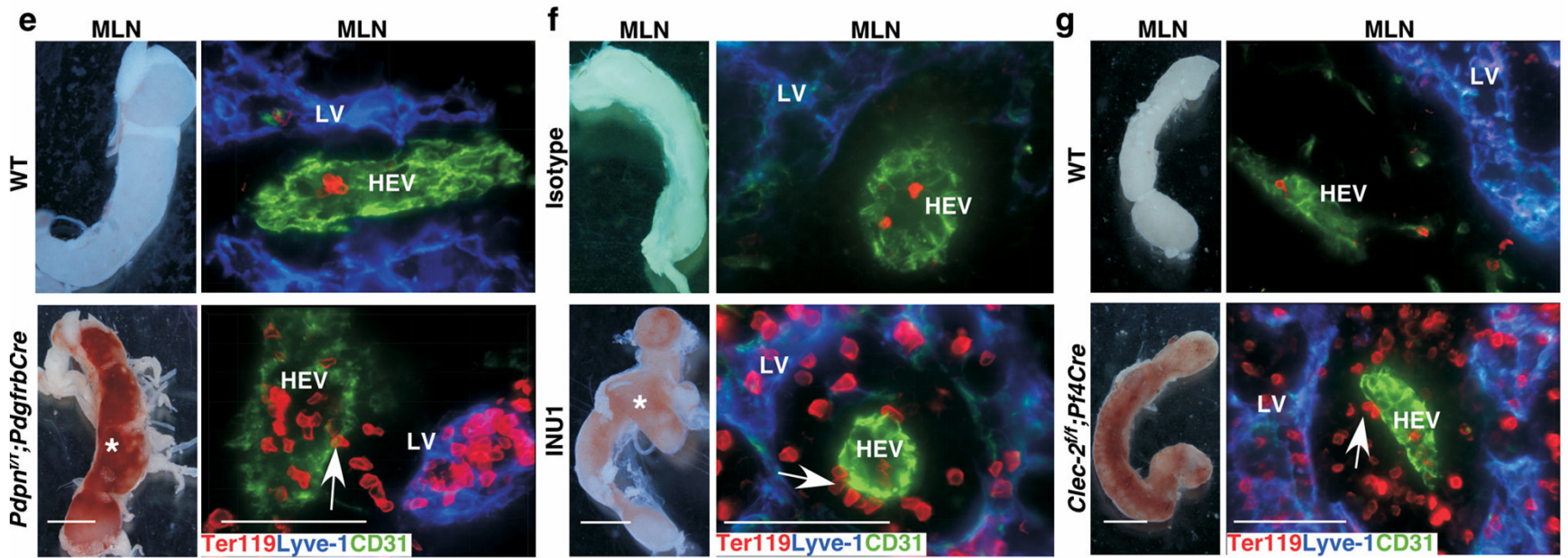
Mice lacking PDPN

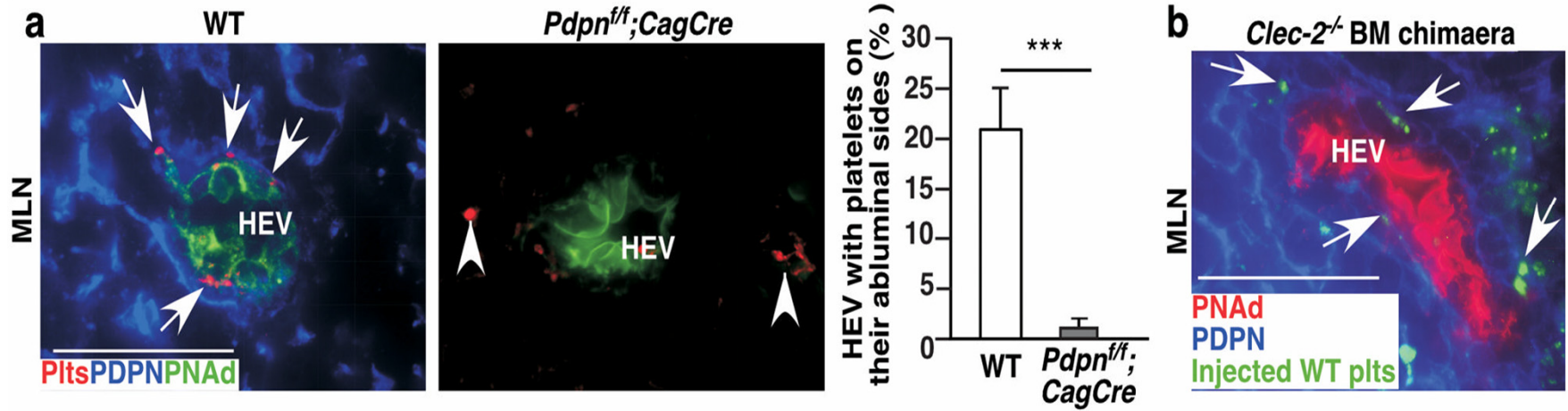
- Tamoxifen application since first postnatal day (P1)
- P15: 90% decrease of PDPN
(mucosal and peripheral LN)
- P30: total loss of PDPN

Methods

- **Pdnp^{f/f}; CagCre Mice:** tamoxifen induced deletion of Podoplanin
- **Pdnpf/f;PdgfrbCre mice:** loss of PDPN only in Fibroblastic reticular cells (FRCs)
- **Pdnpf/f;Tie2Cre mice:** loss of PDPN only in lymphatic endothelial cells (LECs) -> no bleeding
- **Clec-2^{-/-} BM chimaera:** show importance of adult CLEC-2 in LN
- **Clec-2f/f;Pf4Cre:** loss of CLEC-2 in platelets

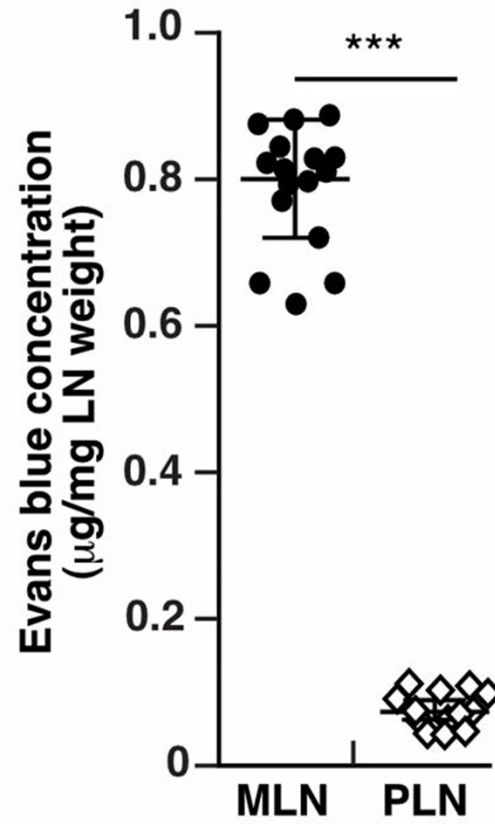


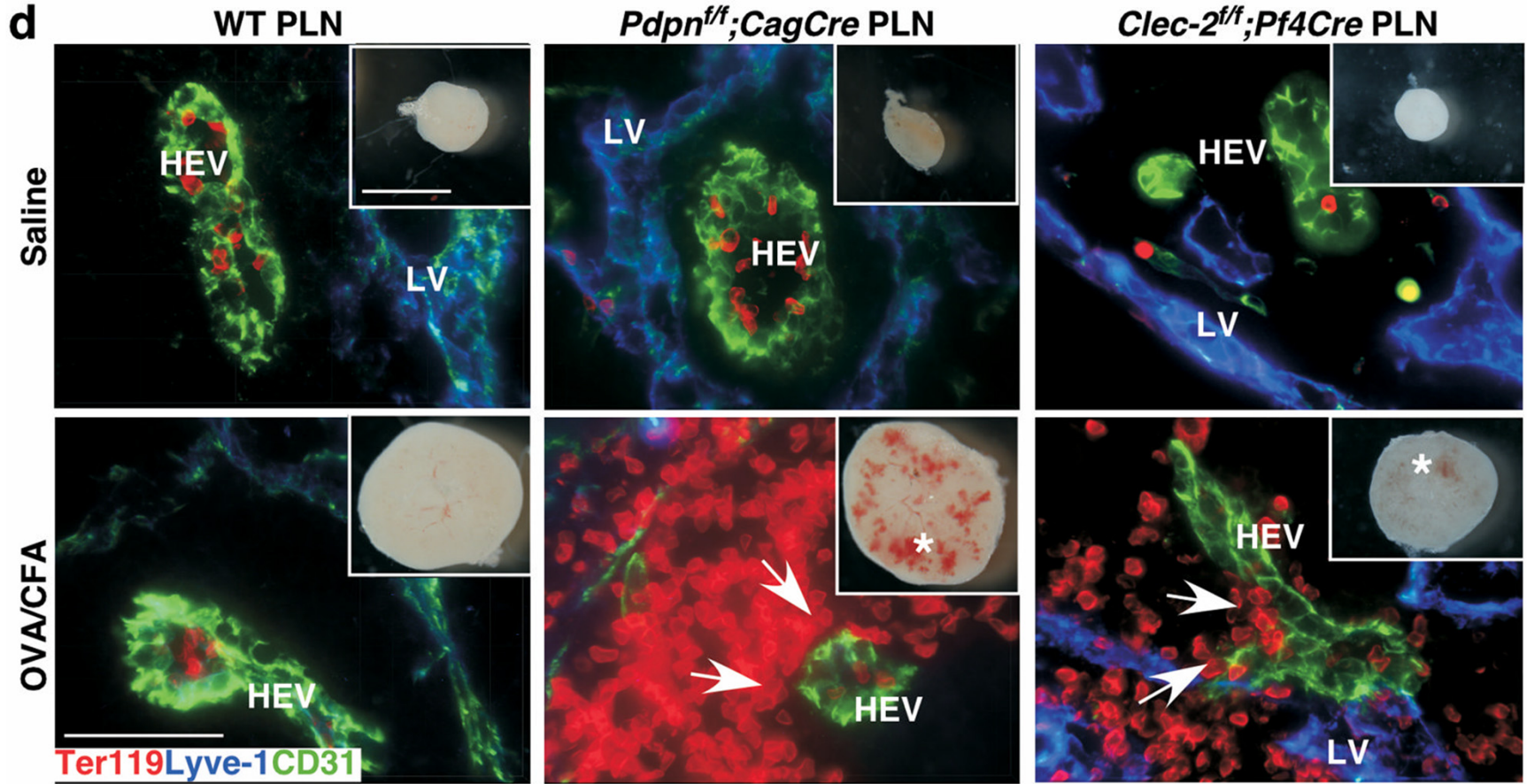


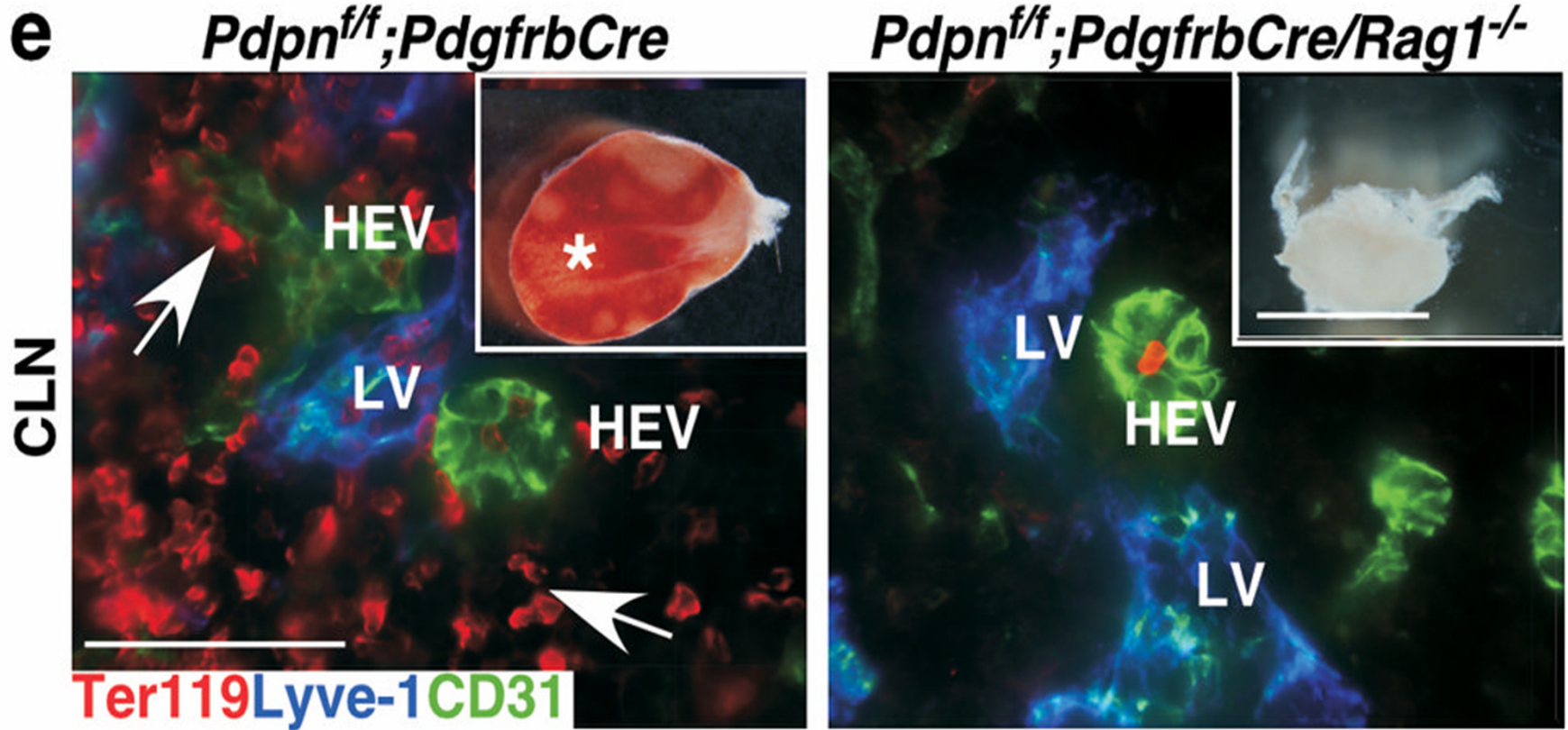


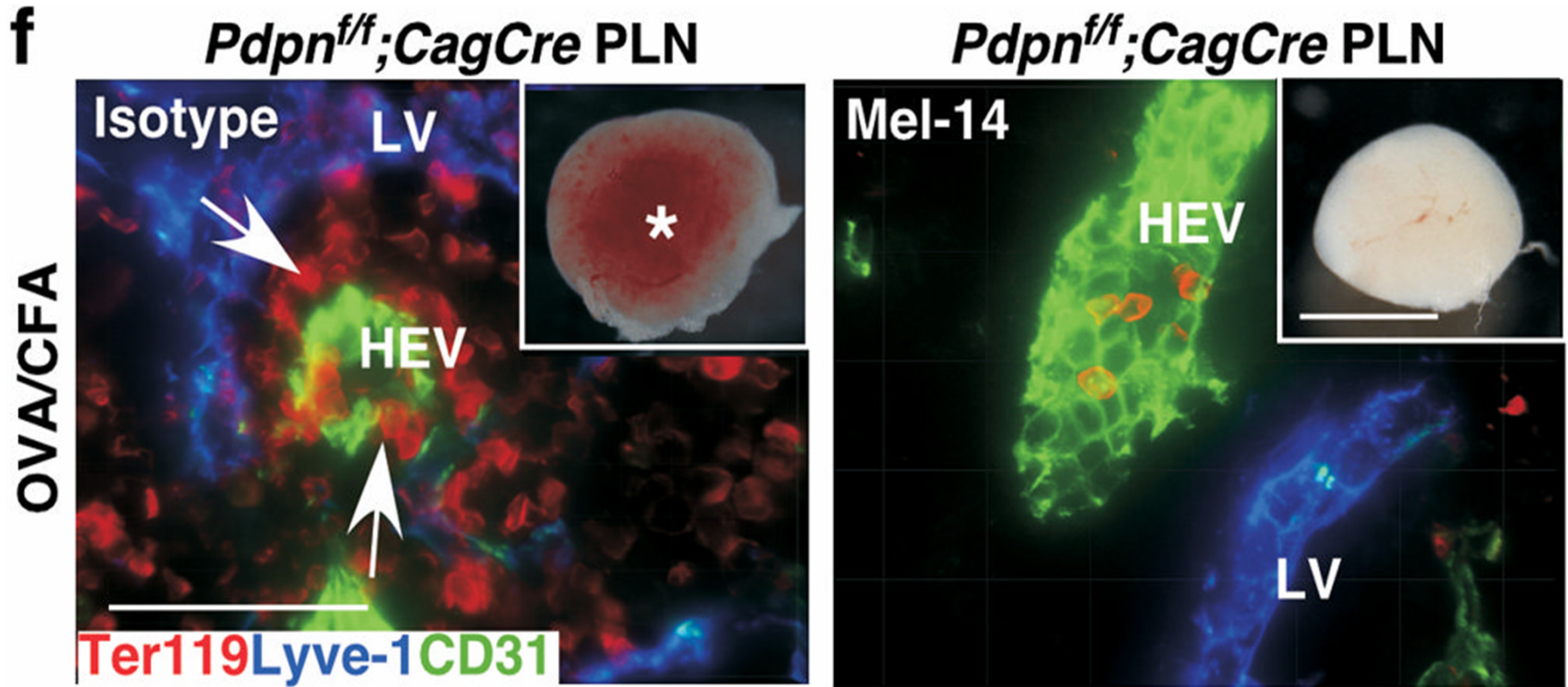


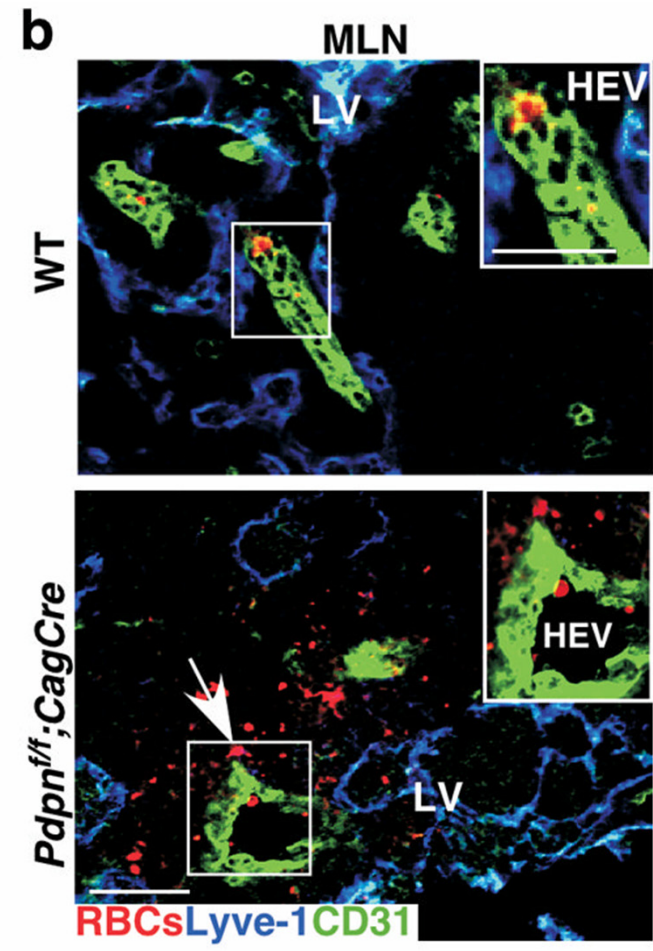
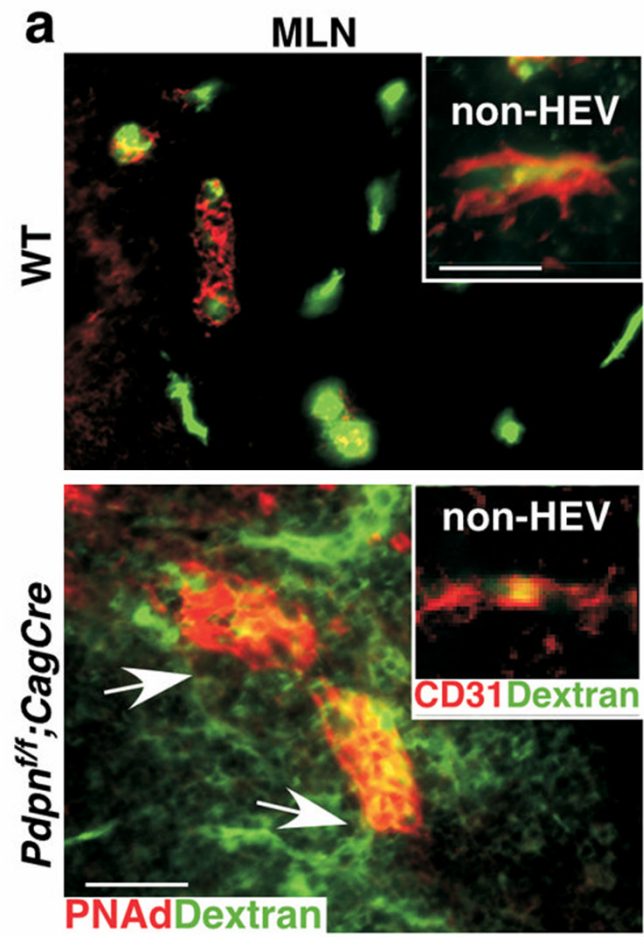
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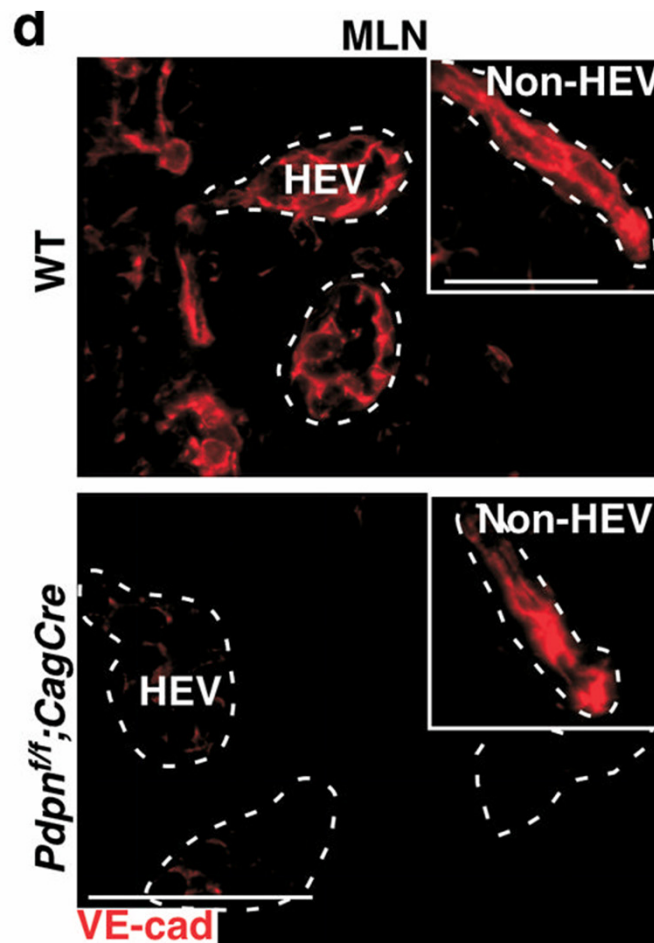
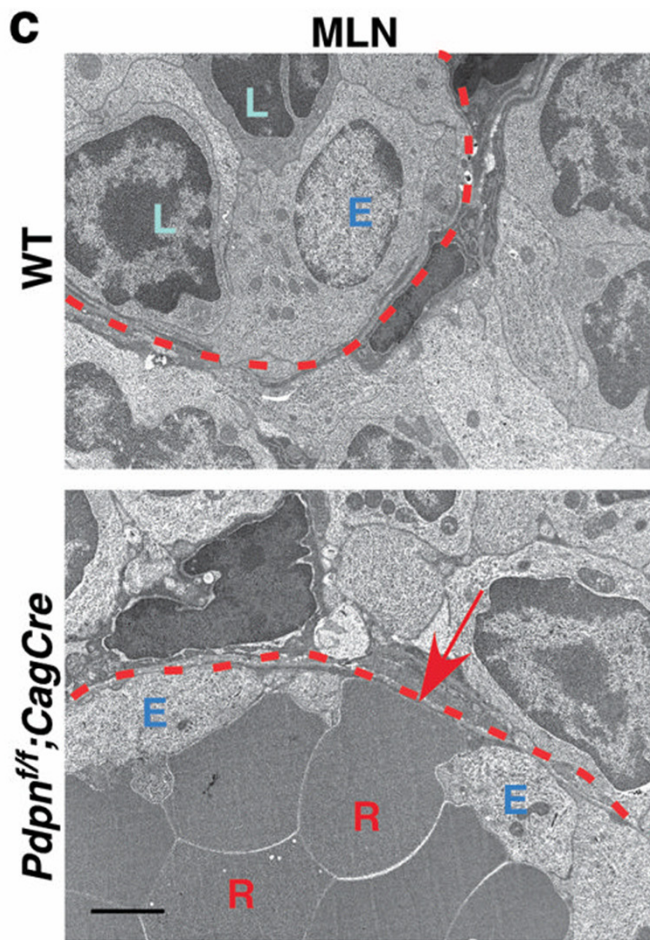


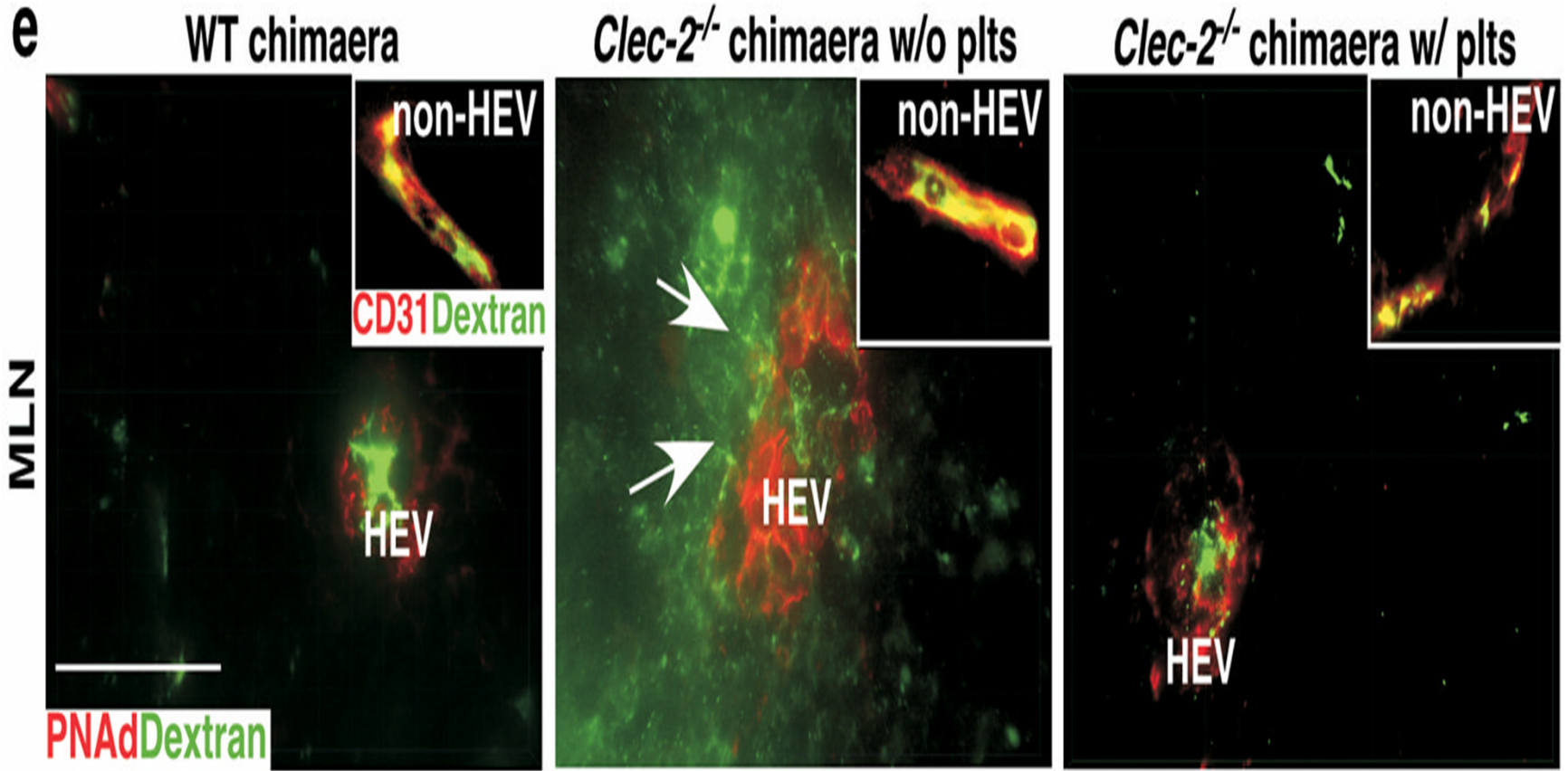


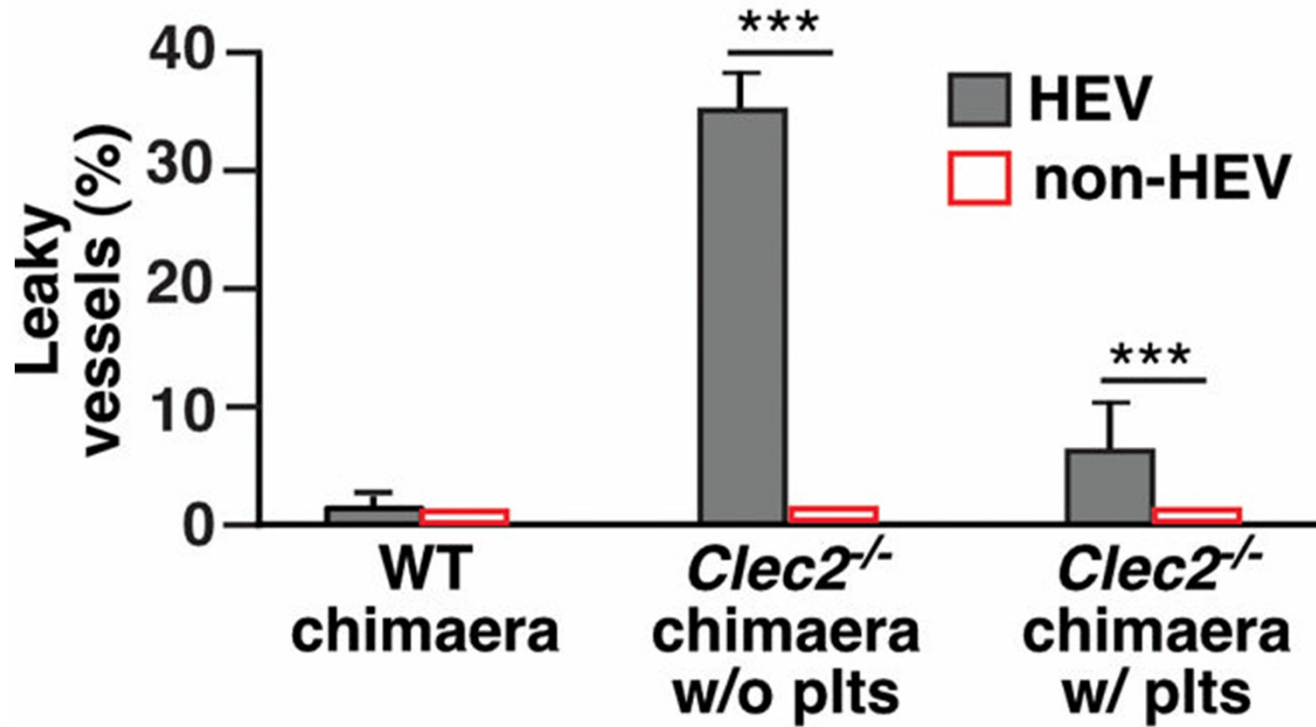


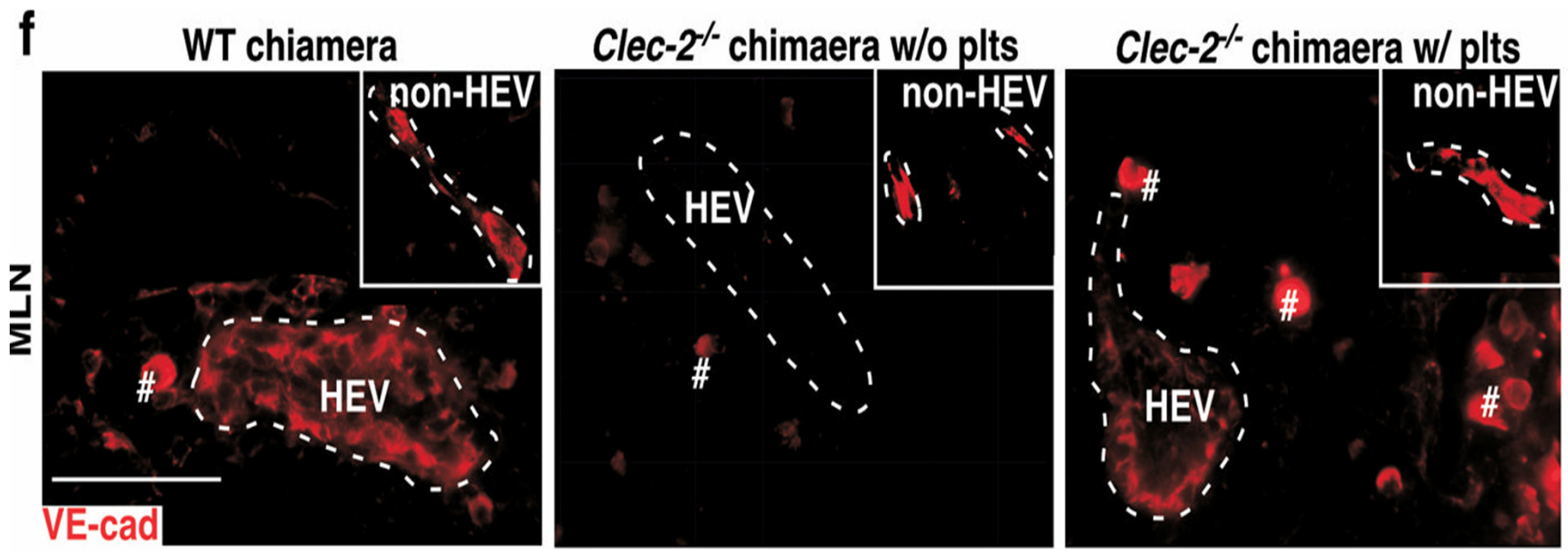


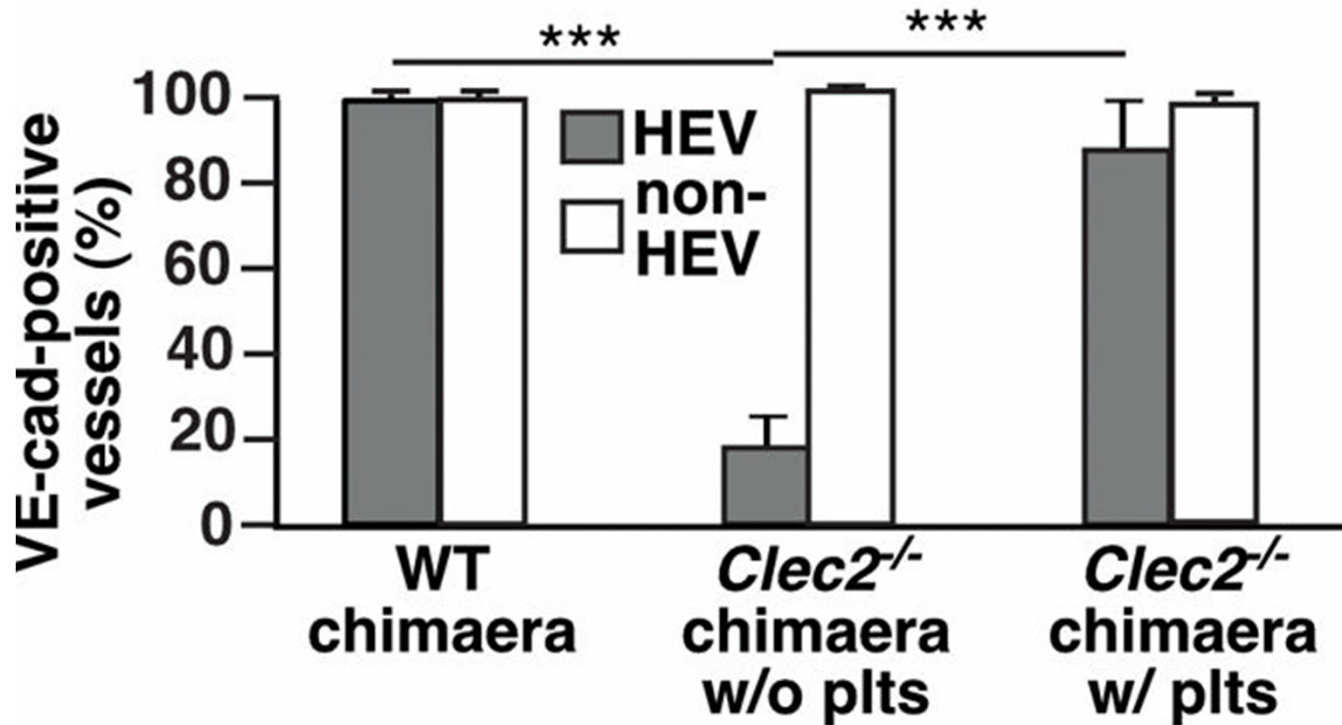






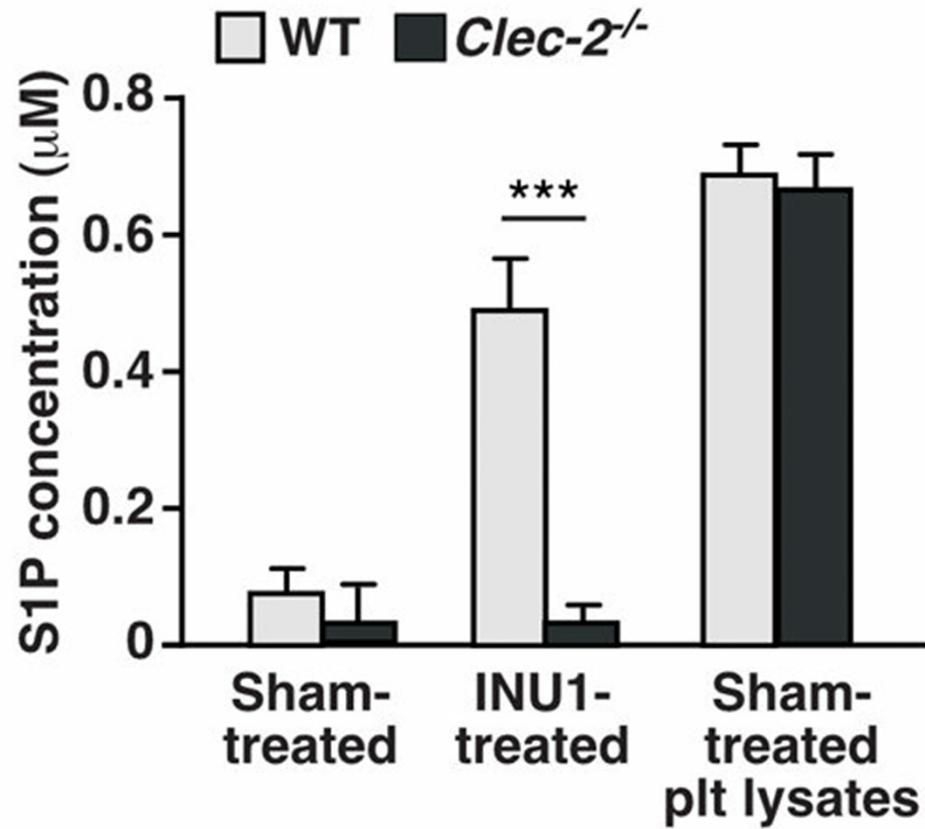




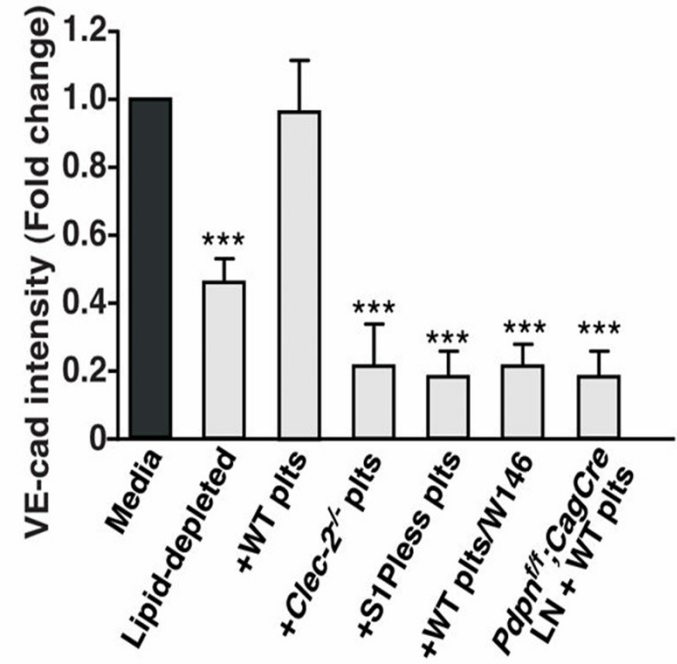
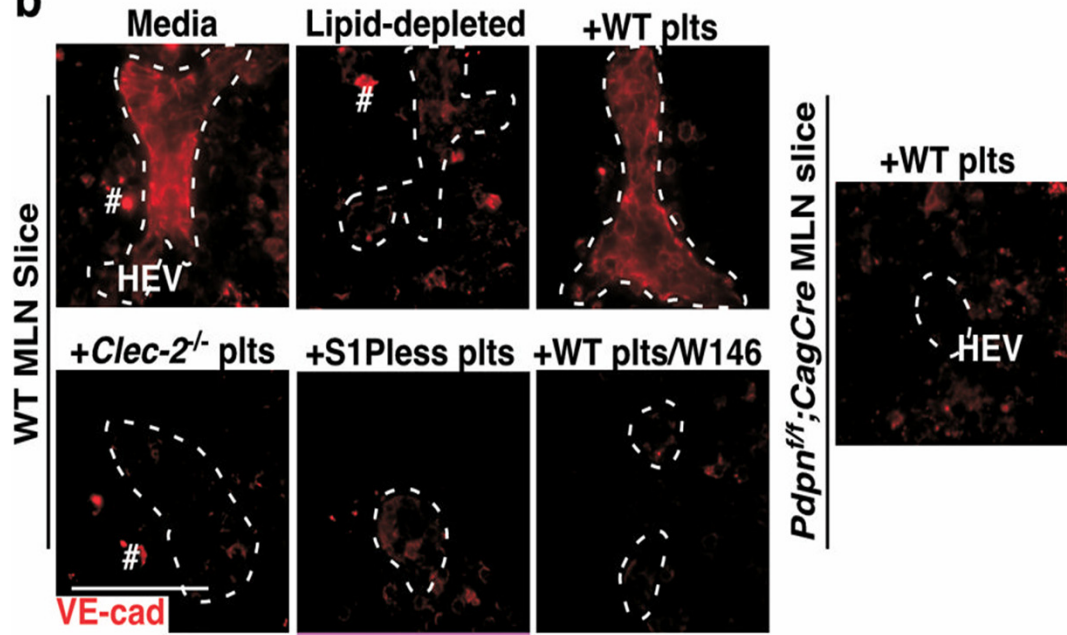




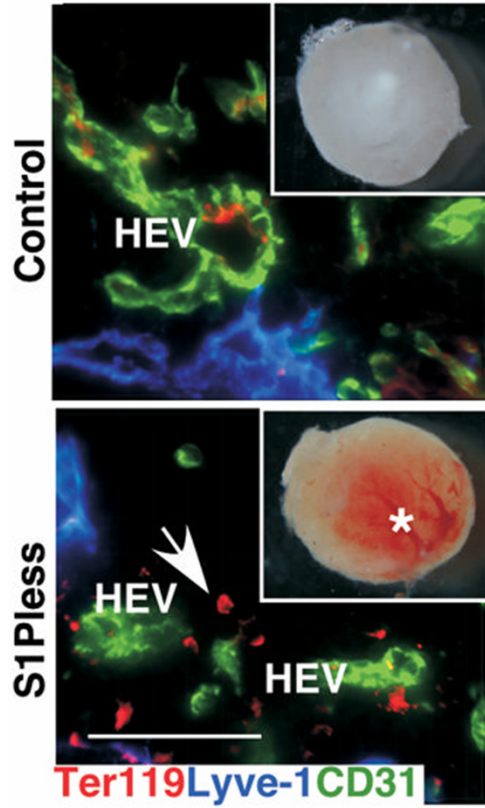
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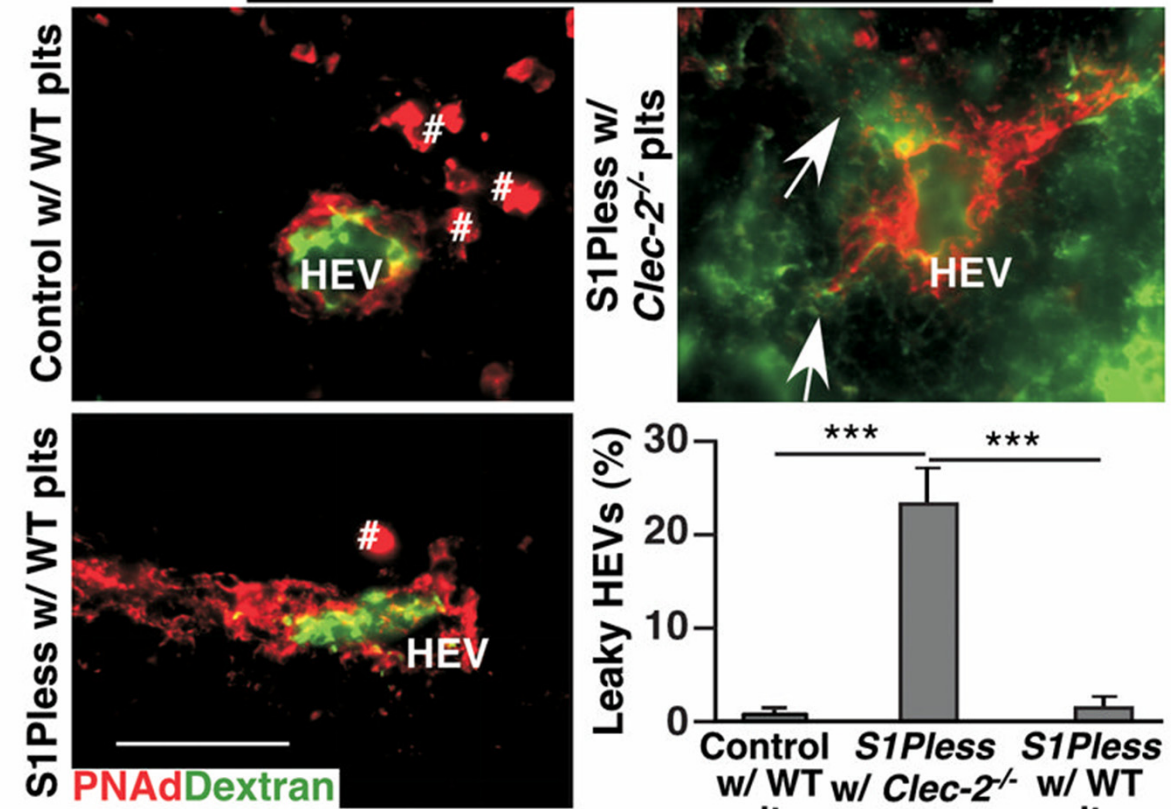
b



c PLN - OVA/CFA



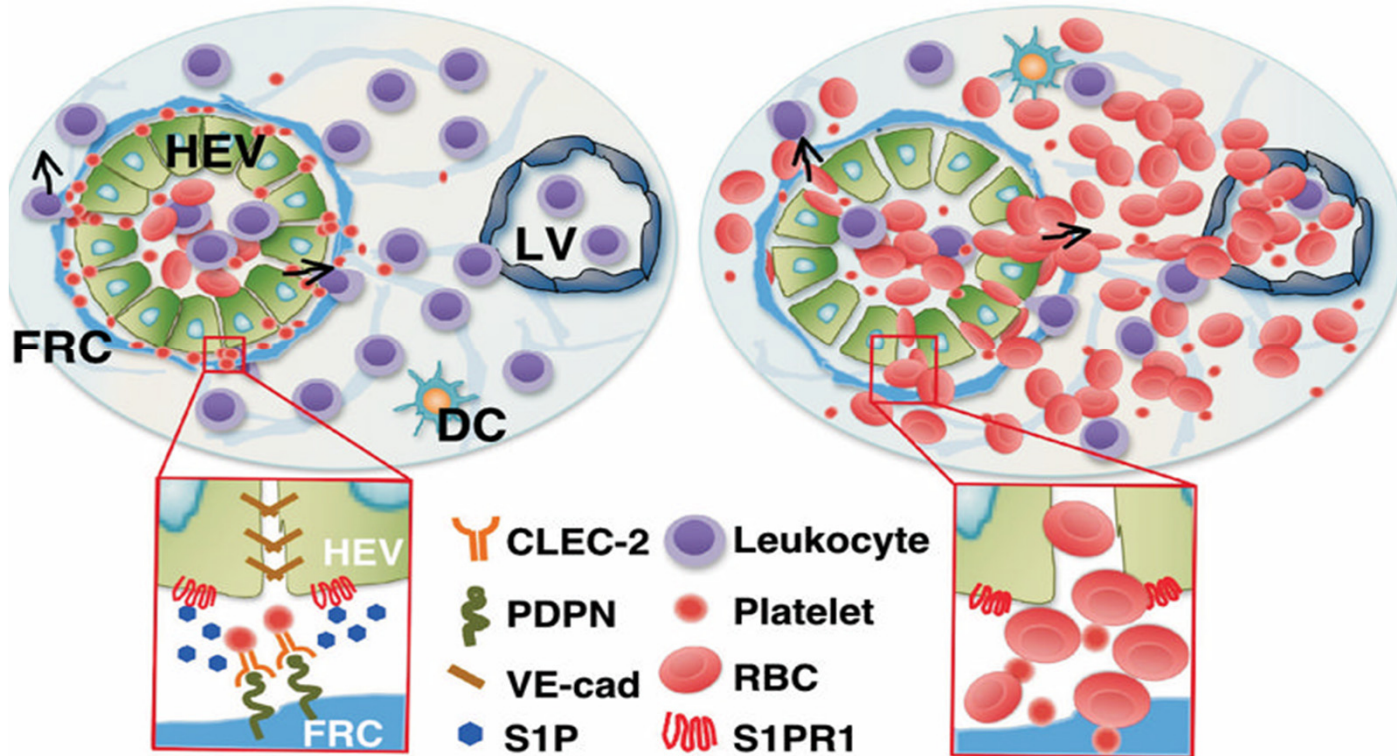
d PLN - OVA/CFA



e

WT

Loss of PDPN-CLEC-2 function



Discussion

- Importance of FRC PDPN on VE-cadherin expression
- Role in vascular integrity of HEVs
- Possible target in preventing inflammation-induced hemorrhage

Thank you for your attention!