

Supplementary Table 1. Lessons from Knock-out and Knock-in Mice

Ligand/Receptor/Pathway

Gene	Survival	Phenotype				Ref.
		Vasculogenesis	Angiogenesis	Vessel maturation	Other	
<i>Vegf-A</i>	E10.5	Abnormal differentiation of blood island	Impaired angiogenesis	Impaired lumen formation Impaired special vessel organization		.2
<i>Vegf-B</i>	Alive				Atrial conduction abnormality	.4
<i>Vegf120/188</i> <i>Vegf120/164</i>	Alive Alive			Impaired arterial development		
<i>Vegf164/188</i>	Death postnatally		Impaired myocardial angiogenesis	Ischemic cardiomyopathy		
<i>Pgf</i>	Alive		Impaired pathological angiogenesis			
<i>VegfR-1</i>	E8.5	Disorganized EC				
<i>VegfR-2</i>	E8.5-9.5	Absent yolk sac blood island Reduced hematopoietic precursors				
<i>VegfR-3</i>	E9.5			Enlarged vessel lumens Cardiovascular failure		0
<i>Nrp1</i>	Alive	Impaired neural vascularization Disorder yolk sac vascular network		Agensis and transposition of the great vessels Persistent <i>truncus arteriosus</i>		1,12

Gene	Survival	Phenotype				Ref.
		Vasculogenesis	Angiogenesis	Vessel maturation	Other	
		Impaired vascular sprouting at the central nervous system and pericardium				
<i>Nrp1/2</i>	E8.5	Avascular yolk sac				3
<i>Nrp2</i>	Alive			Reduction of small lymphatic vessels and capillaries		4
<i>Jagged1</i>	E10			defects in remodeling of the embryonic and yolk sac vasculature		5
<i>Notch1/4</i>				Defect of angiogenic vascular remodeling		6
<i>EphB2 / 3</i>	E11.5	Defects in the remodeling of embryonic vascular network		Defects in the remodeling of embryonic vascular network		7
<i>Ephrin-B2</i>	E9.5		Defects in angiogenesis by both arteries and veins in the capillary network of the head and yolk sac	Defect of myocardial trabeculation		7-19
<i>Pdgf-A</i>	E10 or postnatal death				Loss of alveolar myofibroblasts Reduced number of oligodendrocytes Dysmyelination	0,21

Gene	Survival	Phenotype				Ref.
		Vasculogenesis	Angiogenesis	Vessel maturation	Other	
					ion	
<i>Pdgf-B</i>	E17.5-18.5			Lack of pericyte Microvascular aneurysms		2,23
<i>Pdgf-Rα</i>	Death at birth				Abnormal neural crest development Abnormal somite pattern	4
<i>Pdgf-Rβ</i>	Death at birth				Hemorrhage, thrombocytopenia, anemia	5
<i>Edg-1</i>	E12.5-14.5			Deficiency of vascular smooth muscle cells/pericyte		6
<i>Edg-3</i>	Alive					7
<i>Galpha13</i>	Intra-uterin death		Impaired ability of endothelial cell to develop into organized vascular system	Impaired fibroblast movement		8
<i>Ang1</i>	E10.5			Dilated vessel Impaired vessel branching		9
<i>Ang2</i>	Alive	Incomplete development of the superficial vascular bed of the retina	Absence of the intermediate and deep vascular bed of the retina		Lymphatic defect	0,31

<i>Tie-1</i>	E13.5-14.5 Death immediately after birth			Leaky vessels, Edema Leaky vessels, Small heart	unexpanded alveoli	2,33
<i>Tie-2</i>	E10.5			Dilated vessels Impaired vessel branching		3
<i>Tgf-β1</i>	Alive or E10.5	Deficient extraembryonic hematopoiesis		Poor EC differentiation and hematopoiesis		4
<i>Tgf-βRII</i>	E10.5	Defects in yolk sac hematopoiesis and vasculogenesis				5
<i>Alk1</i>	E11.5			Severe arteriovenous malformation		6,37
<i>Alk5</i>	E10.5-11.5			Severe defects in vascular development	Absence of circulating red blood cell	8
<i>Endoglin (Tgf-βRIII)</i>	E11.5			Poor vascular SMC development Arrested EC remodeling		9
<i>Smad2</i>	Perigastrulation lethality				Defective in extraembryonic and mesoderm induction/formation Abnormalities in anterior-posterior axis formation	0-42
<i>Smad3</i>	1-10 months after birth				Accelerate wound healing	3-45

<i>Smad5</i>	E9-11.5		Defect of angiogenesis	Mesenchymal apoptosis	gut heart and craniofacial defect	6,47
<i>Fgf-2</i>	Alive			Delayed skin wound healing	Abnormal cortical neurogenesis	8,49
<i>Syk/Slp-76 pathway</i>	Alive				Failure to separate emerging lymphatic vessels from blood vessels	0

Molecules governing cell-cell interaction

Gene	Survival	Phenotype				ef.
		Vasculogenesis	Angiogenesis	Vessel maturation	Other	
<i>Ve-cadherin</i>	E9.5			Impaired vascular remodeling and maturation		1,52
<i>Cx37/40</i>	Perinatal death			Vessel dilatation and congestion especially in skin, testis, gastrointestinal tissue and lung		3
<i>Cx40</i>	Alive				Lower atrial and ventricular conduction velocity	4
<i>Cx43</i>	Death at birth			Right ventricular outflow tract obstruction		5
<i>Cd31</i>	Alive					6

Gene	Survival	Phenotype				ef.
		Vasculogenesis	Angiogenesis	Vessel maturation	Other	
<i>Cd148</i>	E11.5			Enlarged primitive vessels defective in vascular remodeling and branching with impaired pericyte investment adjacent to endothelial structure		7

Molecules cell-matrix interaction

Gene	Survival	Phenotype				ef.
		Vasculogenesis	Angiogenesis	Vessel maturation	Other	
$\alpha\beta_3$	Alive				Defects in platelet aggregation and clot retraction, prolonged bleeding times, and cutaneous and gastrointestinal bleeding	8
$\alpha\beta_5$	Alive					9
β_8 <i>integrins</i>	midgestation			Distended and leaky capillary vessels and aberrant brain capillary pattern		0
<i>Mmp-2</i>	Alive					1
<i>Mmp-3</i>	Alive					2
<i>Pai-1</i>	Alive					3,64
<i>Tsp-1</i>	Alive				Impaired pulmonary homeostasis	5

Gene	Survival	Phenotype				ef.
		Vasculogenesis	Angiogenesis	Vessel maturation	Other	
<i>Tsp-2</i>	Alive			Increased vascular density	Abnormal bleeding time	6
<i>uPa</i>	Alive					7
<i>Collagen XVIII</i>	Alive				Eye abnormality	8

Transcription Factors

Gene	Survival	Phenotype				ef.
		Vasculogenesis	Angiogenesis	Vessel maturation	Other	
<i>Hey2</i> (<i>glidlock</i>)	Immediately after birth			Cardiac hypertrophy		9
<i>Bmx</i>	Alive					0
<i>Hif1α</i>	E11	Complete lack of cephalic vascularization		Cardiovascular malformation	Neural tube defect Reduction in the number of somites and abnormal neural fold formation	1,72
<i>Id1/3</i>	E10.5			Vascular malformation in the forebrain Absence of branching and sprouting of vessels into the neuroectoderm		3
<i>c-Myc</i>	E10.5	Profound defect of vasculogenesis			Defect of primitive erythropoiesis	4
<i>Prox1</i>	Alive				Budding and sprouting arrest and lymphatics defect	5