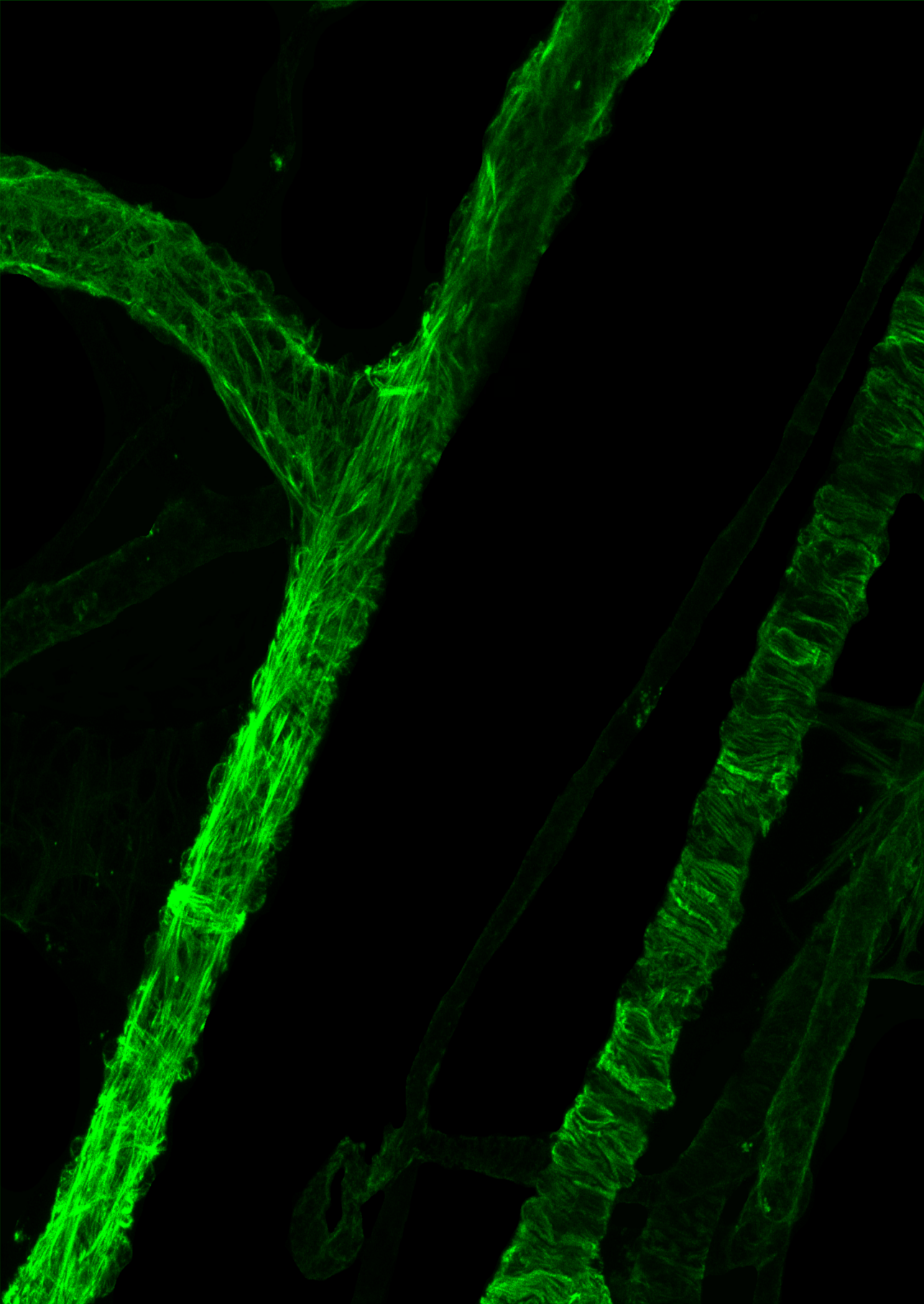

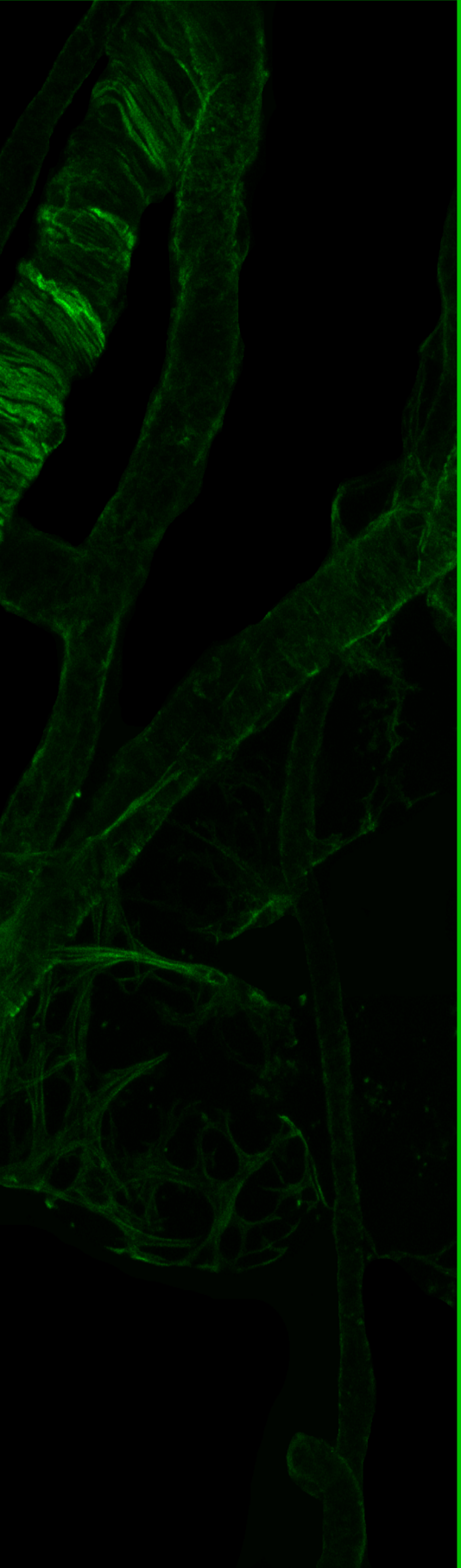

ABBREVIATIONS

A	
ACT	Activin
ActR-IB (ALK4)	Activin A receptor type IB
ActR-IIA	Activin A receptor type IIA
ActR-IIB	Activin A receptor type IIB
ACVR1 (ALK2)	Activin A receptor type 1
ACVRL1 (ALK1)	Activin A receptor type 1L
AGM	Aorta-gonal-mesonephros
Akt	Protein kinase B signaling pathway
AMHR-II	Anti-Mullerian hormone receptor type II
Ang1	Angiopoietin 1
APLNR /APJ	Apelin receptor
aSMA	a-smooth muscle actin
AVM	Arterio-venous malformation
B	
Bio	Bone morphogenetic protein
BMP	Bone morphogenetic protein receptor type 1A
BMPR-IA (ALK3)	Bone morphogenetic protein receptor type 1B
BMPR-IB (ALK6)	Bone morphogenetic protein receptor type 2
BMPR-II	Bromodeoxyuridine
BrdU	Bovine serum albumin polyvinylalchohol essential lipids
BPEL	Bovine serum albumin
BSA	
C	
Cdc42	Cell division cycle 42
Cdh5–CreER	Tamoxifen-inducible Cadherin 5 Cre recombinase
cDNA	complementary DNA
CD31 (PECAM-1)	Platelet/endothelial cell adhesion molecule 1
CD105	Endoglin
ChIP-Seq	Chromatin immunoprecipitation with sequencing
CM	Cardiomyocytes
Co-Smad	Common mediator Smad
Cre-recombinase	Tyrosine recombinase enzyme
C57BL/6 (black 6)	C57 inbred mouse strain
D	
DAPI	4’,6-diamidine-2-phenylindole-dihydrochloride
DMEM	Dulbecco’s Modified Eagle Medium
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
E	
E	Embryonic day
EB	Emrbyoid bodies
ECM	Extracellular matrix
ECs	Endothelial cells
Efnb2	Ephrin B2
eGFP	Enhanced green fluorescent protein
EMT	Epithelial-mesenchymal transition
ENG (CD105)	Endoglin
eNOS (NOS-3)	Endothelial nitric oxide synthase-3
EphB4	EPH receptor B4
Erk	Extracellular-signal-regulated kinase
ESCs	Embryonic stem cells
ESPC	Endothelial stem/progenitor cells
F	
F	Forward primer
FIAU	1-(2-deoxy-2-fluoro-,-D-arabinofuranosyl)-5- iodouracil
FISH	Florescence in situ hybridization
Flk-1 (Kdr, Vegfr2)	Fetal liver kinase-1, kinase insert domain receptor
FP	Fluorescent protein

G	
GAPDH	Glyceraldehyde 3-phosphate dehydrogenase, G3PDH
GDF	Growth and differentiation factor
GI	Gastrointestinal
GS-box	Glycine-serine rich domain
GSK3	Glycogen synthase kinase 3
GTPases	Guanosine triphosphates hydrolase enzymes
H	
h	Human
HA	Homology arms
HAoEC	Human aortic endothelial cells
HE	Hemogenic endothelium
HEY2	HES-related repressor protein 2
HHT	Hereditary hemorrhagic telangiectasia
HPC	Hematopoietic cell
HR	Homologous recombination
HSCs	Hematopoietic stem cells
HSPC	Hematopoietic stem/progenitor cells
HSV-TK	Herpes simplex virus thymidine kinase
HUVEC	Human umbilical venous endothelial cells
I	
ID1	Inhibitor of differentiation 1
INH	Inhibin
iPSCs	Induced pluripotent stem cells
I-Smad	Inhibitory Smad protein
2i	MEK inhibitor and GSK3 inhibitor
J	
Jag1	Jagged 1
JNK	c-Jun N-terminal kinase, signaling pathway
K	
KDR/VEGFR2	Kinase insert domain receptor
Ki67	Marker of proliferation ki67
L	
Lefty	Left-right determination factor
LIF	Leukemia inhibitory factor
L1-Cre	L1 driven Cre-recombinase
M	
MAPK	Mitogen activated protein kinase, signaling pathway
MEF	Mouse embryonic fibroblasts
MH1	Mad-homology 1 domain
MH2	Mad-homology 2 domain
MIS	Mullerian inhibiting substance
MKK	Mitogen-activated protein kinase kinase
mRNA	messenger RNA
mTOR	Mammalian target of rapamycin
MVD	Microvessel density
N	
NADPH	Nicotinamide adenine dinucleotide phosphate
NeoR	Neomycin resistance gene
NF-kB	Nuclear factor kappa B
NO	Nitric oxide
Nodal	Nodal growth differentiation factor
NOTCH4	Neurogenic locus notch homolog protein 4
O	
Ola /129	Ola/129 mouse strain

P	
PAH	Pulmonary arterial hypertension
PBS	Phosphate buffered saline
PBST	PBS-Tween
PCR	Polymerase chain reaction
PD	PD0325901, inhibitor of the MEK/ERK pathway
PDGF	Platelet-derived growth factor
PDGF-B	Platelet-derived growth factor B polypeptide
PDGFR-a	Platelet-derived growth factor receptor, alpha
PDGFR-b	Platelet-derived growth factor receptor, beta
Pdgfrb-iCreER	Tamoxifen-inducible Pdgfrb Cre recombinase
PECAM-1	Platelet-Endothelial Cell Adhesion Molecule-1
PGK	Phosphoglycerate kinase promoter
PI3K	Phosphoinosistide 3-kinase, signaling pathway
PreScission	PreScission Protease
PSCs	Pluripotent stem cells
P^+	Phosphorylated
Q	
Q-PCR	Quantitative polymerase chain reaction
R	
Rac1	Ras-related C3 botulinum toxin substrate 1
Ras	Ras sarcoma, small GTPases, signaling pathway
R	reverse primer
RhoA	Small GTPases, signaling pathway
RT-qPCR	Real-time quantitative PCR
RNA	Ribonucleic acid
ROSA26-CreER	ROSA26 locus driven Cre-recombinase
ROS	Reactive oxygen species
R-Smad	Receptor-Smad protein
RT-PCR	Reverse transcriptase polymerase chain reaction
RVH	Right ventricular hypertrophy
S	
SB	SB431542, inhibitor of ALK5
SCF	Stem cell factor
Scl-CreER	T-cell acute lymphocytic leukemia 1 (TAL) driven Cre
SDS	Sodium dodecyl sulfate
SEM	Standard error of the mean
Sh	Short hairpin construct
Smad	Sma mothers against decapentaplegic
SMC	Smooth muscle cells
Smurf	Smad ubiquitin regulatory factor
SM22a (TAGLN)	Transgelin 2
SSXS	Serine-serine-X-Serine motif
T	
TAK1	TGFb associated kinase 1
TAP	Tandem affinity purification
TbR-I (ALK5, TgfbR1)	TGFb type I receptor
TbR-II, TGFbR-II	Tgfb type II serine/threonine kinase receptor
TEV	TEV protease
TF	Transcription factor
TG	Targeted allele
TgfbR3, TbRIII	Tgfb receptor type III, betaglycan
TGFβ	Transforming growth factor-b
TRAF6	Tumor necrosis factor TNF receptor associated factor 6
TSP-1	Thrombospondin-1
Tyr	Tyrosine
T2A	2A peptide cleavage

V	
VCAM1	Vascular cell adhesion molecule 1
VE-cadherin (CD144)	Vascular endothelial-cadherin,
VEGF	Vascular endothelial growth factor
VEGFR	Vascular endothelial growth factor receptor
vSMC	Vascular smooth muscle cell
v/v	volume/volume
vWF	von Willebrand factor
V5	V5 tag peptide
W	
WT	wild type
w/v	weight/volume

List of publications

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Curriculum Vitae

Konstantinos Gkatzis was born on May the 14th 1987 in Athens, Hellas. At the age of 18, he moved to United Kingdom to continue his swimming career and to study Molecular and Cellular Biology at the University of Bath. In September 2009, he moved to The Netherlands and enrolled at Leiden University to study a two-year master's program in Biomedical Science with a focus on Stem Cell Biology. During his study, he performed research on human induced pluripotent stem cells at the Department of Anatomy and Embryology at Leiden University Medical Center as well as on mouse embryonic stem cells at the Center of Regenerative Medicine in Dresden (Germany). This was followed by his doctoral scientific research project on "*in vitro* and *in vivo* models for studying endothelial cell development and hereditary hemorrhagic telangiectasia". This project was performed in a combined program between the Department of Anatomy and Embryology at Leiden University Medical Center (Prof. Christine Mummery) and the Center for Interdisciplinary Research in Biology at College de France (Dr. Franck Lebrin). The results of this work are presented in this thesis. At the end of 2016 he will move to Lisbon (Portugal) to continue working on endothelial cell development and disease at Instituto de Medicina Molecular.