BIOGRAPHICAL SKETCH

Gael GENET, PHD

eRA COMMONS USER NAME: GGENET

POSITION TITLE: Research Assistant Professor, University of Virginia

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE / POSITION	Completion Date	FIELD OF STUDY
Paul Sabatier University, Toulouse, France.	Bachelor degree	07/2007	Biological Science
Paul Sabatier University, Toulouse, France. National Institute of science and medical research.	M.Sc	07/2009	Cellular Biology, Physiology
Paul Sabatier University, Toulouse, France. National Institute of science and medical research	PhD	07/2013	Cardiovascular Research
Yale University, School of Medicine, New Haven, CT, USA	AHA Postdoctoral Fellow	2013-2019	Vascular Biology

A. Personal Statement.

During my graduate studies at the French National institute of Health and Medical Research (INSERM), I successfully utilized cutting edge approaches in cell and molecular biology to characterize the role of ephrin-B1 protein in cardiac physiology and physiopathology. These works have led me to acquire a broad and solid background in the understanding of cellular mechanisms controlling cell morphology, differentiation and signaling. At Yale Cardiovascular Research Center as an AHA postdoctoral fellow, my research focused on understanding the role of guidance signaling pathways and their interaction with VEGF signaling systems in vascular development and diseases. I also conducted research on the function of TGF-ß and BMP signaling in development of arterio-venous malformation in hereditary hemorrhagic telangiectasia (HHT) animal model. Since I started to develop my scientific independence as Research Assistant Professor at the University of Virginia, my research consists in unraveling the role of endothelial cell cycle control in arterial venous development and malformations.

B. Positons and Honors.

Positons and Employement

2004-2007 Bachelor Student, Paul Sabatier University, Toulouse, France
2007-2009 Masters Student, Paul Sabatier University, INSERM UMR 1048, Toulouse, France

2009-2013 PhD Student, Paul Sabatier University, INSERM UMR 1048, Toulouse, France
2013-2019 Postdoctoral Fellow, Yale University, School of Medicine, USA
2019-present Research Assistant Professor, Dept. Cell Biology, University of Virginia

Other Experience and Professional Memberships

2015-Present Member, American Heart Association
2015-Present Member, North American Vascular Biology Organization
2009-2013 Member, French society of cardiology
2009-2013 Teaching, Cell Biology course, Paul Sabatier University and Pierre Fabre, Toulouse, France

Honors

2010 First price, young investigator in fundamental research, French society of cardiology
2012 First price, PhD project, oral presentation, Paul Sabatier University
2013 First contact initiative grant, European society of cardiology
2017 Travel Award, North America Vascular Biology Organization (NAVBO)
2018 American Heart Association (AHA) Postdoctoral Fellowship
2018 Best poster presentation Award, North America Vascular Biology Organization (NAVBO)
2022 American Heart Association (AHA) Career Development Award

C. Contribution to Science

1. We have shown that in blood vessels, specialized endothelial cells called tip cells located at the extremities of growing capillary sprouts mediate guided vascular patterning. Tip cells exhibit characteristic features, including extension of filopodia that explore the tip cell environment, lack of a lumen and a slow proliferation rate. We have shown that axonal guidance molecules Slit2/Robo1&2 regulate the endothelial cell migration and capillaries growth. Robo1&2 interact with VEGFR2 and ENDOPHILIN-A2 to polarize the tip cell migration.

a. **Genet G**, Boyé K, Mathivet T, Ola R, Zhang F, Dubrac A, Li J, Genet N, Benedetti L, Pibouin-Fragner L, Thomas JL, Eichmann A. Endophilin-A2 mediated VEGFR2 endocytosis promotes endothelial cell migration. **Nat Commun.** 2019 May 28;10(1):2350. doi: 10.1038/s41467-019-10359-x

b. Zhang F, Zarkada G, Han J, Li J, Dubrac A, Ola R, **Genet G**, Boye K, Michon P, Kunzel S, Camporez Joao Paulo, Sing AK, Fong GH, Simons M, Tso P, Fermandez-Hernando C, Shulman G, Sessa W, Eichmann A. Lacteal Junction zippering protects against diet-induced obesity. **Science**. 2018 Aug 10;361(6402):599-603.

c. Zhang F, Prahst C, Mathivet T, Pibouin-Fragner L, Zhang J, **Genet G**, Tong R, Dubrac A, Eichmann A. The Robo4 cytoplasmic domain is dispensable for vascular permeability and neovascularization. **Nat Commun**. 2016 Nov 24;7:13517.

d. Dubrac A, **Genet G**, Ola R, Zhang F, Pibouin-Fragner L, Han J., Zhang J., Thomas JL, Chedotal A, Schwartz MA, Eichmann A. Targeting NCK-mediated endothelial cell front-rear polarity inhibits neo-vascularization. **Circulation**. 2016 Jan 26;133(4):409-21.

e. Rama N, Dubrac A, Mathivet T, Ní Chárthaigh RA, **Genet G**, Cristofaro B, Pibouin-Fragner L, Ma L, Eichmann A and Chédotal A. Slit2 signaling through Robo1 and Robo2 is required for retinal neovascularization. **Nat Med.** 2015 May;21(5):483-91.

2. Our Work demonstrated that the endothelial specific inhibition of TGF-ß/BMP signaling lead to arteriovenous malformation mimicking vascular malformations of Hereditary Hemorrhagic Telangiectasia.

a. **G Genet**, C Marziano, KK Hirschi. Vascular endothelial cell specification in health and disease. **Angiogenesis**, 2021 May;24(2):213-236. doi: 10.1007/s10456-021-09785-7.

b. Ola R, Kunzel S, Zhang F, **Genet G**, Chakraborty R, Pibouin-Fragner L, Martin K, Sessa W, Dubrac A, Eichmann A. SMAD4 prevents flow induced arterial-venous malformation by inhibiting Casein Kinase 2. **Circulation**. 2018 Nov 20;138(21):2379-2394.

c. Ola R, Dubrac A, Han J, Zhang F, Fang JS, Larrivée B, Lee M, Urarte AA, Kraehling JR, **Genet G**, Hirschi KK, Sessa WC, Canals FV, Graupera M, Yan M, Young LH, Oh PS, Eichmann A. PI3 kinase inhibition improves vascular malformations in mouse models of hereditary haemorrhagic telangiectasia. **Nat Commun**. 2016 Nov 29;7:13650

3. We showed that endothelial cell cycle control plays a key role in arterial-venous network formation, and distinct cell cycle states provide distinct windows of opportunity for the molecular induction of arterial vs. venous specification.

a. Chavkin NW, **Genet G**, Poulet M, Jeffery ED, Marziano C, Genet N, Vasavada H, Nelson EA, Acharya BR, Kour A, Aragon J, McDonnell SP, Huba M, Sheynkman GM, Walsh K, Hirschi KK. Endothelial cell cycle state determines propensity for arterial-venous fate. **Nat Commun**, 2022 Oct 6;13(1):5891. doi: 10.1038/s41467-022-33324-7.

b. Mehlferber MM, Jeffery ED, Saquing J, Jordan BT, Sheynkman L, Murali M, **Genet G**, Acharya BR, Hirschi KK, Sheynkman GM.mCharacterization of protein isoform diversity in human umbilical vein endothelial cells via long-read proteogenomics. **RNA Biol**. 2022 Jan;19(1):1228-1243. doi: 10.1080/15476286.2022.2141938.

c. Nafiisha Genet, **Gael Genet**, Jennifer S Fang, Nicholas W Chavkin, Hema H Vasavada, Joshua S Goldberg, Bipul R Acharya, Neha Bhatt, Kasey Baker, Stephanie McDonnell, Mahalia R Huba, Gerry Ma, Anne Eichmann, Jean Leon Thomas, Karen K Hirschi. Connexin 43-mediated Neurovascular Interactions Regulate Neurogenesis in the Adult Brain Subventricular Zone. **BioRxiv,** 2022, https://doi.org/10.1101/2022.02.28.482353.

4. Our research emphasizes the importance of the cardiac tissue cellular organization. Transition to heart failure is characterized by early alterations in heart tissue cohesion. We demonstrated a new function for ephrin-B1 protein in the cardiac tissue architecture cohesion by stabilizing the adult cardiomyocyte morphology.

a. Clément Karsenty, Céline Guilbeau-Frugier, **Gael Genet**, Marie-Hélène Seguelas, Philippe Alzieu, Olivier Cazorla, Alexandra Montagner, Yuna Blum, Caroline Dubroca, Julie Maupoint, Blandine Tramunt, Marie Cauquil, Thierry Sulpice, Sylvain Richard, Silvia Arcucci, Remy Flores-Flores, Nicolas Pataluch, Romain Montoriol, Pierre Sicard, Antoine Deney, Thierry Couffinhal, Jean-Michel Sénard, Céline Galés. Ephrin-B1 regulates the adult diastolic function through a late postnatal maturation of cardiomyocyte surface crests. **Elife**. 2023 Jan 17;12:e80904.

b. **Genet G***, Dague E*, Lachaize V, Guilbeau-Frugier C, Fauconnier J, Mias C, Payré B, Chopinet L, Alsteens D, Kasas S, Severac C, Thireau J, Heymes C, Honton B, Lacampagne A, Pathak A, Sénard JM, Galés C. Atomic force and electron microscopic-based study of sarcolemmal surface of living

cardiomyocytes unveils unexpected mitochondrial shift in heart failure. **Journal of Molecular and Cellular cardiology** 2014, 74:162-172. * co-first author.

c. Mias C, Coatrieux C, Denis C, **Genet G**, Seguelas MH, Laplace N, Rouzaud-Laborde C, Calise D, Parini A, Cussac D, Pathak A, Sénard JM, Galés C. Cardiac fibroblasts regulate sympathetic nerve sprouting and neurocardiac synapse stability. **PLoS One** 2013, 8(11):e79068.

d. Mias C, **Genet G**, Pathak A, Sénard JM, Galés C. Adult resident cardiomyocytes wake up: new axis for cardiac tissue regeneration. **Medecine et Science** 2012, 28(12):1103-9.

e. **Genet G***, Guilbeau-Frugier C*, Honton B, Dague E, Schneider MD, Coatrieux C, Calise D, Cardin C, Nieto C, Payré B, Dubroca C, Marck P, Heymes C, Dubrac A, Arvanitis D, Despas F, Altié MF, Seguelas MH, Delisle MB, Davy A, Sénard JM, Pathak A, Galés C. Ephrin-B1 is a novel specific component of the lateral membrane of the cardiomyocyte and is essential for the stability of cardiac tissue architecture cohesion. **Circulation Research** *2012*, 110(5):688-700. * co-first author.