
BIOGRAPHICAL SKETCH

NAME: Fantin, Alessandro

POSITION TITLE: Associate Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
University of Milano-Bicocca, Milan, Italy.	B.Sc.	10/2000	04/2004	Biotechnology, specialization in Medical Biotechnology
University of Milano-Bicocca, Milan, Italy.	M.Sc.	10/2004	12/2006	Industrial Biotechnology, specialization in Pharmacogenomics
University College London, London, United Kingdom.	Ph.D.	12/2007	08/2011	Cell and Developmental Biology

A. Personal Statement

I started my scientific career by conducting my MSc project followed by postgraduate research on brain ischemia at Mario Negri Institute in Milan, Italy, where I demonstrated that inhibiting the lectin pathway of the complement system results in a wide therapeutic window for stroke treatment (*Annals of Neurology*, 2009). My focus on neurovascular patterning continued with my PhD and postdoctoral experience in Prof Ruhrberg's lab at University College London, United Kingdom (see **C. Contribution to Science** – points 1, 2 and 3).

After 11 years in UK, I then joined University of Milan (Dept of Biosciences) in 2018 to start my own lab (fantinlab.unimi.it) and study cellular and molecular mechanisms that regulate vascular morphogenesis and function in health and disease thanks to funding from both private foundations and governmental schemes (see **C. Contribution to Science** – point 4). Our latest high profile publications describe the generation of a novel transcriptomic tool, the BulkECexplorer, that allows to interrogate gene expression in different organ endothelial cells and predict active versus leaky genes (*Nature Cardiovascular Research* 2024), the identification of SEMA6A as a driver of GnRH neuron-dependent puberty onset by tuning median eminence vascular permeability (*Nature Communications* 2023) and the establishment of *in vitro* vascularized tissue constructs that allow the use of human cells in 3D microfluidic devices as an alternative to *in vivo* animal models (*Science Advances* 2023).

Finally, I published several book chapters and protocol papers (see **C. Contribution to Science** – point 5), to make methods accessible to a wide audience interested in studying vascular biology. These achievements (PubMed articles=47; Scopus h-index=25, citations=2787) helped me gain recognition in the field of vascular biology, as evidenced by invitations to international meetings, peer-review for international journals and by contributions to influential reviews on vascular biology as corresponding author (*Mechanisms of Development* 2015; *Frontiers in Cell and Developmental Biology* 2021; *Biomolecules* 2021).

- Brash JT, Diez-Pinel G, Colletto G, Castellan RFP, **Fantin A***, Ruhrberg C. The BulkECexplorer compiles endothelial bulk transcriptomes to predict functional versus leaky transcription. *Nat Cardiovascular Research*. 2024. ***co-corresponding author**
- Domingues A, **Fantin A**. Neuropilin 1 regulation of vascular permeability signaling. *Biomolecules*. 2021, 11(5), 666.

- c) Lettieri A, Oleari R, van den Munkhof MH, van Battum EY, Verhagen MG, Tacconi C, Spreafico M, Paganoni AJJ, Azzarelli R, Andre' V, Amoroso F, Palazzolo L, Eberini I, Dunkel L, Howard SR, **Fantin A***, Pasterkamp RJ, Cariboni A. SEMA6A drives GnRH neuron-dependent puberty onset by tuning median eminence vascular permeability. *Nat Commun*. 2023 Dec 7;14(1):8097.
***co-corresponding author**
- d) Whisler J, Shahreza S, Schlegelmilch K, Ege N, Javanmardi Y, Malandrino A, Agrawal A, **Fantin A**, Serwinski B, Azizgolshani H, Park C, Shone V, Demuren OO, Del Rosario A, Butty VL, Holroyd N, Domart MC, Hooper S, Szita N, Boyer LA, Walker-Samuel S, Djordjevic B, Sheridan GK, Collinson L, Calvo F, Ruhrberg C, Sahai E, Kamm R, Moeendarbary E. Emergent mechanical control of vascular morphogenesis. *Sci Adv*. 2023 Aug 11;9(32):eadg9781.

B. Positions and Honors

Positions and Employment

2003 - 2004	B.Sc. student internship, University of Milano-Bicocca, Monza. Advisor: Prof. Gabriella Nicolini.
2005 - 2006	M.Sc. student internship, Mario Negri Institute for Pharmacological Research, Milan. Advisor: Dr. Maria Grazia De Simoni.
2006 - 2007	Postgraduate fellow, Mario Negri Institute for Pharmacological Research, Milan. Advisor: Dr. Maria Grazia De Simoni.
2007 - 2011	Ph.D. student, University College London, London. Advisor: Prof. Christiana Ruhrberg.
2011 - 2018	Postdoctoral research associate, University College London, London. Advisor: Prof. Christiana Ruhrberg.
2018 - 2021	Assistant Professor, University of Milan, Milan.
2019 - 2020	Visiting scientist, European Institute of Oncology (IEO), Milan. Advisor: Prof. Saverio Minucci.
2021 -	Associate Professor, University of Milan, Milan.

Other Experience and Professional Memberships

2009 -	Member, British Society of Developmental Biology (BSDB).
2010 -	Member, North America Vascular Biology Organization (NAVBO).
2013 - 2013	EMBL Advanced Course on Development of Transgenic Animal Models Using Zinc Finger Nucleases, EMBL Heidelberg, Germany.
2014 -	Member, European Vascular Biology Organization (EVBO).
2018 -	Member, Italian Society of Cardiovascular Research (SIRC).
2018 - 2018	University of Cambridge Training - Introduction to RNA-seq data analysis, University of Cambridge, Cambridge, UK.
2020 -	Active Member, American Association for Cancer Research (AACR).

Honors

2009	Travel Grant, BSDB/Company of Biologists, United Kingdom.
2009	Prize for best poster , London Vascular Biology Forum, United Kingdom.
2010	Travel Award, North American Vascular Biology Organisation (NAVBO), United States of America.
2011	Travel Grant, BSDB/Company of Biologists, United Kingdom.
2012	Postdoctoral Travel Grant, London Vascular Biology Forum, United Kingdom.
2012	Prize for best poster , London Vascular Biology Forum, United Kingdom.
2013	Prize for best poster , London Vascular Biology Forum, United Kingdom.
2013	Travel Grant, Boehringer Ingelheim Fonds, Germany.

2013	Best poster prize, Innovations in Cardiovascular Science Symposium, University College London, United Kingdom.
2014	Travel Award, European Vascular Biology Organisation (EVBO).
2014	Travel Grant, BSDB/Company of Biologists, United Kingdom.
2014	Travel Award, North American Vascular Biology Organisation (NAVBO), United States of America.
2017	Travel Award, European Vascular Biology Organisation (EVBO).
2017	Travel Grant, BSDB/Company of Biologists, United Kingdom.
2018	Travel Award, North American Vascular Biology Organisation (NAVBO), United States of America.
2019	Distinguished International Young Investigator award , Lund Stem Cell Center, Sweden.
2019	Research Excellence Award , UCL Institute of Ophthalmology, United Kingdom.
2019	Hermann Rein Award , runner up prize, German Society of Microcirculation and Vascular Biology (GfMVB), Germany.
2019	Valsalva prize , Italian Society of Cardiovascular Research (SIRC), Italy.

Research support

2018-2021	British Heart Foundation project grant, United Kingdom (Co-Applicant): <i>A novel progenitor for blood vessel growth</i> (£260,465.00; 3 years).
2019-2022	Cariplo Foundation grant "Ricerca biomedica condotta da giovani ricercatori", Italy (PI): <i>Defining the molecular and cellular mechanisms by which tissue macrophages promote angiogenesis in neovascular diseases</i> (€209,550.00; 3 years).
2020-2025	AIRC Foundation for Cancer Research, Italy (PI): <i>Defining novel roles for myeloid cells in cancer angiogenesis</i> (€500,000.00; 5 years).
2022-2025	PON "RICERCA E INNOVAZIONE 2014-2020": <i>Establish novel organ-on-a-chip technologies to unravel vascular dynamics in health and disease</i> (salary for a senior Postdoctoral research associate; 3 years).
2023-2025	Joint Call for Applications Fondazione Cariplo e Fondazione Telethon 2022, Italy (partner): <i>MAU2: the (T)dark side of Cornelia de Lange syndrome</i> (€46,000.00; 2 years).
2023-2026	Ricerca finalizzata 2022, Italian Ministry of Health, Italy (partner): <i>Unveiling the microbial impact on intestinal fibrosis: new insights for the pathogenesis and treatment of Crohn's disease-associated complications</i> (€67,500.00; 3 years).
2023-2025	PRIN 2022, Italian Ministry of University and Research, Italy (partner): <i>Exploiting organ-on-a-chip technology to unravel the dynamic adaptation of microvasculature to biomechanical environmental cues</i> (€81,080.00; 2 years).
2023-2025	PRIN 2022 PNRR, Italian Ministry of University and Research, Italy (PI): <i>Novel roles for CXCR4 signaling in hematovascular development</i> (€103,008.00; 2 years).

C. Contribution to Science

1. During my British Heart Foundation-funded PhD in Professor Ruhrberg's lab at University College London, I demonstrated that macrophages/microglia act as bridge cells to promote vessel fusion during angiogenesis and was covered by a News & Views article in *Nature*, was commended as a "must read" by the Faculty of 1000 and has attracted more than 500 citations. More recently, I collaborated with the lab of Professor Jim Bainbridge at the UCL Institute of Ophthalmology to study how microglia/macrophages promote pathological angiogenesis in models of eye disease (*Arteriosclerosis, Thrombosis, and Vascular Biology*, 2016, as first author).

- a. **Fantin A**, Vieira JM, Gestri G, Denti L, Schwarz Q, Prykhodzhiy S, Peri F, Wilson SW, Ruhrberg C. Tissue macrophages act as cellular chaperones for vascular anastomosis downstream of VEGF-mediated endothelial tip cell induction. *Blood*. 2010 Aug 5;116(5):829-40. PMID: 20404134.
 - b. Liyanage S, **Fantin A***, Villacampa P, Lange C, Denti L, Cristante E, Smith A, Ali R, Luhmann U, Bainbridge J, Ruhrberg C. Myeloid-Derived Vascular Endothelial Growth Factor and Hypoxia-Inducible Factor Are Dispensable for Ocular Neovascularization—Brief Report. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2016 January; 36(1):19-24. PMID: 26603154. ***co-first author**
2. During my postdoctoral experience in Professor Christiana Ruhrberg's lab, UCL, I focused on the vascular endothelial growth factor A (VEGF) receptor neuropilin 1 (NRP1) in both developmental angiogenesis and in models of neovascular eye disease. In particular, I successfully researched mechanisms of NRP1 signaling in angiogenesis, arteriogenesis and vascular permeability and showed that the cytoplasmic domain of NRP1 is required for VEGF-induced arteriogenesis (published in *Developmental Cell*, 2013) and hyper-permeability (*Journal of Experimental Medicine*, 2017, in which I am first and corresponding author), but not angiogenesis (published in *Development*, 2011, as first author with a Faculty of 1000 recommendation). Importantly, these studies suggest that targeting NRP1 or its cytoplasmic interactors may be a useful therapeutic strategy in neovascular disease to reduce VEGF-induced oedema without compromising vessel growth. Moreover, I demonstrated for the first time a VEGF-independent functional role for NRP1 in angiogenesis via CDC42 and the kinase ABL1 (*Blood*, 2013; *Development*, 2014; *Journal of Experimental Medicine*, 2014, and *Cell Reports*, 2015, all as first author), suggesting that ABL kinase inhibition provides a novel opportunity for anti-angiogenic therapy to complement VEGF or VEGFR2 blockade in eye disease or solid tumor growth. These studies also resulted in a successful patent application for the use of ABL inhibitors to treat neovascular eye disease.
- a. **Fantin A***, Lampropoulou A, Senatore V, Brash J, Prahst C, Lange C, Liyanage S, Raimondi C, Bainbridge J, Augustin H, Ruhrberg C. VEGF165-induced vascular permeability requires NRP1 for ABL-mediated SRC family kinase activation. *Journal of Experimental Medicine*. 2017 April 03; 214(4):1049-1064. PMID: 28289053. ***co-corresponding author**
 - b. **Fantin A**, Lampropoulou A, Gestri G, Raimondi C, Senatore V, Zachary I, Ruhrberg C. NRP1 Regulates CDC42 Activation to Promote Filopodia Formation in Endothelial Tip Cells. *Cell Reports*. 2015 June; 11(10):1577-1590. PMID: 26051942.
 - c. Raimondi C, **Fantin A***, Lampropoulou A, Denti L, Chikh A, Ruhrberg C. Imatinib inhibits VEGF-independent angiogenesis by targeting neuropilin 1-dependent ABL1 activation in endothelial cells. *J Exp Med*. 2014 Jun 2;211(6):1167-83. PMID: 24863063. ***co-first author**
 - d. **Fantin A**, Vieira JM, Plein A, Denti L, Fruttiger M, Pollard JW, Ruhrberg C. NRP1 acts cell autonomously in endothelium to promote tip cell function during sprouting angiogenesis. *Blood*. 2013 Mar 21;121(12):2352-62. PMID: 23315162.
3. While in Prof Ruhrberg's lab, I demonstrated that erythro-myeloid progenitors (EMPs) not only contribute erythrocytes, megakaryocytes and tissue macrophages to the developing embryo, but also provide a hitherto unrecognized source of endothelial cells for blood vessel growth (*Nature* 2018, first author; News & Views article in *Nature*).
- a. Plein A, **Fantin A***, Denti L, Pollard J, Ruhrberg C. Erythro-myeloid progenitors contribute endothelial cells to blood vessels. *Nature*. 2018; 562(7726):223-228. PMID: 30258231. ***co-first author**
4. Since my appointment as a group leader at University of Milan, I have shown that the tyrosine kinase receptor KIT is expressed by EMPs and required for their expansion during fetal liver hematopoiesis (*Front Cell Dev Biol*, 2021; both first and corresponding author), including the generation of a new scRNAseq dataset of the fetal liver (*J Dev Biol* 2023; last author) that was made freely browsable on

the lab website (<http://www.fantinlab.unimi.it/links.html#menu1-2f>). Moreover, KIT is expressed by blood vessel endothelial cells but is dispensable for physiological angiogenesis in the mouse embryo. Interestingly, we unveiled that KIT is particularly enriched in a subset of microvascular endothelial cells in the lung and maintained until adulthood (*Angiogenesis*, 2022; as corresponding author).

- a. Ceccacci E, Villa E, Santoro F, Minucci S, Ruhrberg C, **Fantin A**. A Refined Single Cell Landscape of Haematopoiesis in the Mouse Foetal Liver. *J Dev Biol*. 2023, 11(2), 15.
 - b. Tacconi C, Plein A, Colletto C, Villa E, Denti L, Barone C, Javanmardi Y, Moeendarbary E, Azzoni E, **Fantin A***, Ruhrberg C. KIT is dispensable for physiological organ vascularisation in the embryo. *Angiogenesis*. 2022 Apr 13. PMID: 35416527. ***co-corresponding author**
 - c. **Fantin A***, Tacconi C, Villa E, Ceccacci E, Denti L, Ruhrberg C. KIT Is Required for Fetal Liver Hematopoiesis. *Front Cell Dev Biol*. 2021 Jul 29;9:648630. PMID: 34395414. ***co-corresponding author**
5. I published several book chapters and protocol papers (e.g. *Nature Protocols*, 2013, as first author) on the mouse embryonic hindbrain, pioneered by the Ruhrberg lab, and the postnatal retina, to make these methods, now widely used for studying the molecular and cellular mechanisms of angiogenesis, accessible to a wide audience. More recently, I presented a protocol to measure the vascular leakage induced by intradermal administration of permeability promoting agents into the murine skin (*J Vis Exp* 2018, corresponding author), which is useful to study vascular permeability.
- a. **Fantin A**. Quantifying and Characterizing Angiogenesis Using the Postnatal Mouse Retina. *Methods in Molecular Biology*. 2022;2441:63-73. PMID: 35099728.
 - b. **Fantin A**, Ruhrberg C. The Embryonic Mouse Hindbrain and Postnatal Retina as In Vivo Models to Study Angiogenesis. *Methods in Molecular Biology*. 2022;2475:275-287. PMID: 35451765.
 - c. Brash J, Ruhrberg C, **Fantin A**. Evaluating Vascular Hyperpermeability-inducing Agents in the Skin with the Miles Assay. *Journal of Visualized Experiments*. 2018 Jun 19;(136):57524. PMID: 29985309.
 - d. Plein A, Ruhrberg C, **Fantin A**. The Mouse Hindbrain: An In Vivo Model to Analyze Developmental Angiogenesis. *Methods in Molecular Biology* 2015;1214:29-40. PMID: 25468597.
 - e. **Fantin A**, Vieira J, Plein A, Maden C, Ruhrberg C. The embryonic mouse hindbrain as a qualitative and quantitative model for studying the molecular and cellular mechanisms of angiogenesis. *Nature Protocols*. 2013; 8(2):418-429. PMID: 23424750.

Bibliographic information (retrieved from Scopus on December 28, 2024)

Number of publications: 47

Number of citations: 2787

h-Index: 25

URL to a full list of published work:

<https://pubmed.ncbi.nlm.nih.gov/?term=Fantin%2C+Alessandro%5BAuthor%5D&sort=date>