Witold W. Kilarski, PhD

Personal Details

Citation metrics:	**H-index**; *citations*: Web of Science : **19**; 1597; Scopus: **19**; 1696; Google Scholar: **22**; 2295
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Employment History

06/2017 – 07/2020	Research Assistant Professor at the Pritzker School of Molecular Engineering (PME), **University of Chicago, USA**
07/2014 - 06/2017	Postdoctoral Research Fellow (Senior Scientist) at the laboratory of Melody Swartz, Institute for Molecular Engineering (IME), **University of Chicago, USA**
02/2008 - 07/2014	Postdoctoral position at the Laboratory of Lymphatic and Cancer Bioengineering, led by Melody Swartz, Ph.D., at the **École Polytechnique Fédérale**, **Lausanne, Switzerland**
11/2005 - 12/2007	Postdoctoral position at the Molecular Angiogenesis Laboratory led by Andreas Bikfalvi M.D., Ph.D. (INSERM U01029), at the **Université de Bordeaux, France**
06/2005 - 11/2005	Postdoctoral position in the lab of Pär Gerwins, M.D., Ph.D., **Uppsala University, Sweden**

PhD

22 April 2005	Ph.D. (public defense on 8th of April) Thesis: "Mechanism of tissue vascularization" defended at the Faculty of Medicine in the Vascular Biology Unit, **Rudbeck Laboratory**, **Uppsala University**. Supervised by Pär Gerwins, M.D., Ph.D. and Lena Claesson-Welsh, Ph.D.
1999-2005	Doctoral studies at the Uppsala University, Sweden

MSc

21 June 1999	M. Sc. in Biology with specialization in Molecular Biology (graded with distinction) Thesis: "*Thermodynamics of zinc binding to Inter-α-Inhibitor and its heavy chains.*"
1994-1999	Master's studies at the Institute of Molecular Biology**, Jagiellonian University in Krakow, Poland**

Earlier Lab Experience

2002	Project on xenograft bone marrow transplantation between a chicken and a mouse host in Prof. MZ Ratajczak lab, Stem Cell Biology Institute at the **University of Louisville** (two months)
1998-1999	Research assistant in the lab of Prof. T Kordula at the Institute of Molecular Biology at the **Jagiellonian University** (1 year). Establishing cloning, PCR, and other molecular biology tools.
1998	Six-month research project in the lab of Erik Fries at the Department of Medical Biochemistry and Microbiology, **Uppsala University** with the aim to solve a paradoxical problem of defining thermodynamic properties of zinc ions binding to a serum protein (inter-α-inhibitor) that is unstable in millimolar zinc concentrations.

Research Interests

Anti-thrombotic properties of lymphatic endothelium

Lymph never clots as long as it stays within lymphatic or blood vessels; it is a truism recognized since the first description of lymphatics by Rudbeck. However, the mechanism behind the lymphatic abilities to counteract lymph thrombosis has never been studied despite that its dysregulation might contribute to lymphedema or even venous embolism. My recent results showed that anti-thrombotic properties are critical for the preservation of lymphatic drainage, and that similar to blood vessels, lymphatic endothelium forms a unique surface capable of maintaining a clottable plasma in its liquid state. The anti-thrombotic features of the lymphatics, their dysregulation in the disease, and derived therapeutic opportunities are the subject of my recent unpublished work and the core of my planned research.

Subcutaneous allograft of humoral (e.g., pancreatic islets) tissue

Fault tolerance of lymphatic vessels makes them a relatively safe target for proxy therapeutic intervention, where modification of lymphatics is barely a means to influence other, more sensitive systems, such as blood vessels or immunity. For example, hyperplastic lymphatic capillaries generated before subcutaneous grafting increase the micro density of blood vessels and might mitigate fibrosis by buffering tissue tension. Contrary, blocking anti-thrombotic properties of lymphatic collectors with, e.g., lymphatic-specific photodynamic therapy (PDT), leads to intralymphatic thrombosis that prevents antigen drainage and allows immunosuppression-free allografting within the generated immune-privileged zone. The subcutaneous graft can additionally benefit from the off-target effects of VEGF-C on blood vessels. For instance, stimulation of the pro-lymphangiogenic pathway with VEGF-C might delay the ingrowth of pro-fibrotic granulation tissue, while the inhibition of the re-growth of lymphatic collectors after PDT could protect the subcutaneous allograft from immune-recognition. The spatial and temporal combination of these seemingly contradicting approaches can enhance the vascularization of **subcutaneously grafted humoral tissues** while protecting the ectopic implants from host immunorecognition.

Lipedema – a non-inflammatory disease of the extracellular matrix

Lipedema is an idiopathic disease where adipocyte overgrowth is located mainly along the thighs and buttocks. In the absence of experimental results, the explanation of this condition is primarily speculative, with an abnormality in lymphatics, sex hormones, or inflammatory events functioning as the most probable hypothesis. My hypothesis, however, points to case reports that show the absence of major inflammatory manifestations in the fat and a lack of functional abnormality in blood and lymphatic vessels as well as the peripheral psychomotor nerves. Instead, my hypothesis postulates that the prime cause of the disease is caused by low stiffness and high compliance of the skin, which in turn is a result of abnormal cross-linking and deposition of structural proteins. This view should be verified with an experimental approach, where the number and quality of cross-links within the extracellular matrix scaffold proteins will be correlated with the structural organization of the tissue. Notably, the design of the experiments should unequivocally support or exclude my hypothesis, narrowing the need for further experimentation.

Infective filaria as a tumor vaccine

The intrinsic properties of **lymphatic filaria** infective larvae, i.e., the preferential homing to lymph nodes and symbiosis with intracellular Wolbachia bacteriae, are features that could be employed in formulations of alternative vaccines. Orthogonal coupling of protein to the cuticle creates a biological carrier capable of delivering non-filarial antigens precisely into the core of the immune system. Once there, attenuated worms become a prolonged source of custom antigen that is released bound to the larvae particles. A parallel co-release of intracellular Wolbachia bacteria acts as a natural type 1 immunostimulatory adjuvant.

Research publications

First ([א]) or last ([Ω]) author, corresponding author [✉], equal contribution [ס]

Five Most Important Research Publications

V. [א,Ω] Inherent biomechanical traits enable infective filariae to disseminate through collecting lymphatic vessels Kilarski WW[✉], Pisano, Bain, Martin, Babayan and Swartz MA[✉]. (2019) **Nat Commun**

Our intravital imaging provides the first glimpse into the migratory phase of the filaria parasite infection. We found that parasitic nematodes do not need complex parasite-specific mechanisms of dissemination because simple morphological adjustments to the length and diameter should be sufficient for infective larvae to reach specific destinations in the body. Such a simple mechanism can exist because the set of skills needed to cross the granular materials, such as mud, sand, or soil, also predispose nematodes for migration in a structurally similar collagenous environment of the skin.

IV. [Ω] Local induction of lymphangiogenesis with engineered fibrin-binding VEGF-C promotes wound healing by increasing immune cell trafficking and matrix remodeling. Güç, et al., Kilarski WW[ס,✉] & Swartz MA[ס,✉]. (2017) **Biomaterials**

In this publication, we challenged the simplistic view of the pro-lymphangiogenic effect of VEGF-C, usually tested at the abnormally high doses at which it stimulates angiogenesis and dysfunctional hyperplasia of lymphatic collectors. Instead, we designed a targeted strategy for drug delivery but also developed a set of methods to test the physiologically relevant parameters of lymphatics. We showed that a specific, pro-lymphangiogenic therapy promoted wound healing without collateral activation of the blood vessel.

III. [א] Optimization and regeneration kinetics of lymphatic-specific photodynamic therapy in the dermis. Kilarski WW[✉] et al. (2014) **Angiogenesis**

This is the first publication detailing the methodology for specific targeting and occlusion of lymphatic collecting vessels. Here, I also planned and performed most of the experiments and wrote the majority of the publication. A continuation of this project provided material for two research publications, including one describing the mechanism and application of anti-hemostatic properties of lymphatic vessels (final manuscript).

II. Growth factors engineered for super-affinity to the extracellular matrix enhance tissue healing. Martino et al. (2014) **Science**

A method of in vivo immunofluorescence that allows long-term imaging of physiological processes at the cellular level in the context of defined components of the extracellular matrix. This technique was initially described in PLOS ONE and JOVE; we used it in other projects published in Nature Cell Biol, Biomaterials, and Nat Commun. In this paper, I designed variants of this method for the quantitative imaging of vascular leakage and ex vivo staining of the unfixed skin. Here, we showed that the engineered, matrix-bound form of VEGF-A is pro-angiogenic with little toxicity as compared to its free form; This is because it binds initially to the extracellular matrix from which it is gradually released.

I. [א] Biomechanical regulation of blood vessel growth during tissue vascularization. Kilarski WW[✉] et al. (2009) **Nat Med**.

Here I proposed a new mechanism of post-developmental (e.g., wound healing) blood vessel growth. Except for cornea surgery, I planned and performed all of the experiments and wrote most of the manuscript and rebuttals.

Reviewed Research Publications

First author (ᴷ)–17; Last author (Ω)–**6;** Corresponding author (✉)-**15**; Equal contribution (ꝏ)-**3**; Key publications are **bolded**

43. Lymphatic coagulation and neutrophil extracellular traps in lung-draining lymph nodes of COVID-19 decedents. Margo MacDonald et al., Witold W Kilarski, and Melody A Swartz (2022). **Blood Adv**

42. **Lymphatics regulation of the inflammatory clotting creates the natural on-off switch for the immune ignorance that allows subcutaneous allografting.** Malgorzata Wachowska & Witold W Kilarski[ᴷ] (2021) **bioRxiv**

41. Lymphatic endothelial cells educate naive CD8+ T cells under steady-state conditions to promote a memory-like phenotype. Vokali, Yu , Hirosue , Rincon-Restrepo, Duraes, Scherer, Corthésy-Henrioud , WW Kilarski , Mondino, Zehn , Hugues and MA Swartz. (2020) **Nat Commun,** 5-year **IF - 13.610**

40.[Ω,✉]**Adjuvant-free immunization with infective filarial larvae as lymphatic homing antigen carriers.** Card, Wilson, Hirosue, Rincon,de Titta, Güç, Martin, Bain, Swartz MA & Kilarski WW (2020) **Sci Rep,** 5-year **IF - 4.576**

39. [ᴷ,✉]**Inherent biomechanical traits enable infective filariae to disseminate through collecting lymphatic vessels** Kilarski WW[✉], Pisano, Bain, Martin, Babayan, and Swartz MA[✉]. (2019) **Nat Commun,** 5-year **IF - 13.610**

38. Characterization of the B16-F10 melanoma model locally transplanted on the ear pinnae of C57BL/6 mice. Potez, et al., Kilarski WW, Hlushchuk, Laissue, and Djonov V. (2018) **PLOS ONE,** 5-year **IF - 3.1**

37. [ᴷ,✉]Dorsal ear skin window for intravital imaging and functional analysis of lymphangiogenesis. Kilarski WW[✉], Güç, Swartz MA (2018) **Methods Mol Biol.** ***Lymphangiogenesis*** 261-277 (Book chapter)

36.[ᴷ]Methods for mapping the extracellular and membrane proteome in the avian embryo. Kilarski WW, Herbert and Bikfalvi A (2018) **Methods Mol Biol.** ***Surfectome*** 31-56. (Book chapter)

35. Inhibition of lymphangiogenesis impairs antitumor effects of photodynamic therapy and checkpoint inhibitors in mice. Muchowicz, et al., Kilarski WW, Boon, Klaus, Golab J (2017) **Eur J Cancer,** 5-year **IF - 7.121**

34.[Ω,✉]**Local induction of lymphangiogenesis with engineered fibrin-binding VEGF-C promotes healing by increasing immune trafficking and matrix remodeling**. Güç, et al., Swartz MA[ꝏ,✉] & Kilarski WW[ꝏ,✉] (2017) **Biomaterials**, 5-year **IF - 9.656**

33. Transcellular transport pathways in lymphatic endothelial cells regulate changes in lymph formation by fluid stress. Triacca, Güç E, Kilarski WW, Pisano, and Swartz MA (2017) **Circ Res, IF – 14.467**

32. Perivascular macrophages limit permeability. He, Mack, Güç, Warren, Kilarski WW, Baer, Freshman, McDonald AI, Ziyad, Swartz, De Palma, Iruela-Arispe LM (2016) **Arterioscler Thromb Vasc Biol, IF – 5.98**

31. Investigation of cell death mechanisms in human lymphatic endothelial cells undergoing photodynamic therapy. Wachowska, et al., Kilarski WW, Golab J (2016) **Photodiagnosis Photodyn Ther, IF – 3.39**

30. Combined CSL and p53 downregulation promote cancer-associated fibroblast activation. Procopio, et al., Kilarski WW, Swartz, Brisken, Lefort & Dotto GP (2015) **Nature Cell Biol,** 5-year **IF – 20.96**

29. ADAM17 promotes motility, invasion, and sprouting of lymphatic endothelial cells. Mężyk-Kopeć, Wyroba, Stalińska, Próchnicki, Kilarski WW, Swartz MA, Bereta J (2015) **PLOS ONE,** 5-year **IF - 3.1**

28. Overcoming inefficient secretion of recombinant VEGF-C in baculovirus expression vector system by simple purification of the protein from cell lysate. Klaus, Kulesza, Bzowska, Wyroba, Kilarski WW and Bereta J (2015) **Protein Expr Purif**, **IF 1.64**

27. Photoactivation of lysosomal sunitinib after angiostatic treatment causes vascular occlusion and enhances tumor inhibition. Nowak-Sliwinska, Weiss, Beijnum, Tse, Wong, Kilarski WW, et al. & Griffioen AW (2015) **Cell Death Dis, IF 7.57**

26.[Ω,✉]**Long-term intravital immunofluorescence imaging of tissue matrix components with epifluorescence and two-photon microscopy.** Güç, Fankhauser M, Lund, Swartz AM and Kilarski WW[✉] (2014) **J Vis Exp**

25. **Growth factors engineered for super-affinity to the extracellular matrix enhance tissue healing.** Martino, Briquez, Güç, Tortelli, Kilarski WW, et al., Swartz MA and Hubbell JA (2014) **Science, IF – 41.846**

24. VEGFR-3 neutralization inhibits ovarian lymphangiogenesis, follicle maturation, and murine pregnancy. Rutkowski, Ihm, Quazolla, Kilarski WW, Greenwood, Trono, Hubbell JA and Swartz MA (2013) **Am J Pathol,** 5-year **IF 4.227**

23.[¤,✉] **Optimization and regeneration kinetics of lymphatic-specific photodynamic therapy in the mouse dermis.** Kilarski WW[✉], Muchowicz, Wachowska, Mężyk-Kopeć, Gołąb J, Swartz MA & Nowak-Śliwińska[✉](2014) **Angiogenesis, IF – 9.78**

22.[¤] Mapping the extracellular and membrane proteome associated with the vasculature of the embryo. Soulet[$], Kilarski WW[$], Roux-Dalvai[$], Herbert[$], et al. & Bikfalvi A (2013) **Mol Cell Proteomics, IF – 4.87**

21.[¤,✉] **Intravital immunofluorescence for visualizing the microcirculatory and immune microenvironments in the mouse ear dermis.** Kilarski WW[✉], Güç, Teo, Oliver, Lund, Swartz MA[✉] (2013) **PLOS ONE,** 5-year **IF - 3.1**

20. The experimental renal cell carcinoma model in the chick embryo. Fergelot, Bernhardt, Soulet, Kilarski WW, et al. & Bikfalvi A (2013) **Angiogenesis, IF – 9.78**

19.[¤,✉] **An *in vivo* neovascularization assay for screening regulators of angiogenesis and assessing their effects on pre-existing vessels.** Kilarski WW[✉], Petersson, Fuchs, Zielinski, Gerwins P[✉] (2012) **Angiogenesis, IF – 9.78**

18. First quantitative imaging of organic fluorine within angiogenic tissues by particle-induced gamma-ray emission (PIGE). Lavielle, Gionnet, Ortega, Deves, Kilarski V, Wehbe, Bikfalvi, Deleris G (2011) **Pharmaceutics, IF – 6.07**

17 .[¤] Gene signatures in wound tissue as evidenced by molecular profiling in the chick embryo model. Soulet[$], Kilarski WW[$], Antczak[$], Herbert, Bicknell, Falciani, Bikfalvi A (2010) **BMC Genomics,** 5-year **IF – 3.8**

16. A combined metabolomic and transcriptomic approach to investigate metabolism during development in the chick chorioallantoic membrane. Cavill R, Sidhu, Kilarski W, et al., Bikfalvi A & Keun HC (2010) **J Proteome Res,** 5-year **IF – 4.184**

15. **Transmural flow modulates cell and fluid transport functions of lymphatic endothelium.** Miteva, Rutkowski, Dixon, Kilarski W, Shields JD, Swartz MA (2010) **Circ Res, IF – 14.467**

14. [¤] **Biomechanical regulation of blood vessel growth during tissue vascularization.** Kilarski WW[✉], Samolov, Petersson, Kvanta and Gerwins P[✉] (2009) **Nature Medicine,** 5-year **IF - 36.23**

13. [¤,] An *ex vivo* model for functional studies of myofibroblasts. *Kilarski WW*, Jura, Gerwins P (2005) **Lab Invest,** 5-year **IF - 4.411**

12. Efficient human interferon-alpha gene transfer to neuroendocrine tumor cells with long-term and stable expression. Liu, Kilarski WW, Gerwins, Öberg and Zhou Y (2005) **Neuroendocrinology,** 5-year **IF - 4.877**

11. [¤] **Inactivation of Src family kinases inhibits angiogenesis in vivo. Implications for a mechanism involving organization of the actin cytoskeleton**. *Kilarski WW*, Jura, Gerwins P (2003) **Exp Cell Res, IF - 3.38**

10. Differential effects of Oncostatin M and leukemia inhibitory factor expression in astrocytoma cells. Kasza, Rogowski, *Kilarski W*, Sobota, Bernas, Dobrucki, Travis J, Koj, Bugno, Kordula T (2001) **Biochem J**. 5-year **IF - 4.146**

9. Binding of Zn^{+2} to the plasma inter-α-inhibitor. Blom, Thuveson, *Kilarski W*, Fries E (1999) **Clin Chim Acta,** 5-year **IF – 2.781**

Reviews in JCR journals

8.[¤,Ω,✉] **Physiological perspective on therapies of lymphatic vessels.** Kilarski WW[✉] (2018) Special ed. **Adv Wound Care,** 5-year **IF - 3.523**

7. The dual role of tumor lymphatic vessels in the dissemination of metastases and immune response development. Stachura, Wachowska, Kilarski WW, Güç, Gołąb J, Muchowicz J (2016) **Oncoimmunology,** 5-year **IF – 6.255**

6. [Ω,✉] Mechanisms of angiogenesis: perspectives from antiangiogenic tumor therapies. Rice, Gerwins, Kilarski WW[✉] (2012) **Curr Angiogenesis**

5. ¥,✉**New mechanism of vessel growth-hope for new treatment strategies.** Kilarski WW✉&Gerwins✉ (2009) **Discov Med, IF - 2.174**
4. ¥Experimental approaches to study in vivo angiogenesis. Kilarski WW & Bikfalvi A (2007) **Bull Cancer, IF 0.912**
3. ¥Recent developments in tumor angiogenesis. Kilarski WW & Bikfalvi A (2007) **Curr Pharm Biotechnol,** 5-year **IF – 2,121**

Non-JCR publications

2. ¥,✉Intravital immunofluorescence for visualizing the microcirculatory and immune microenvironments in the mouse ear dermis. Kilarski WW✉, Güç, Swartz MA (2013) **Leica Sci Lab**
1. Ω,✉Blood vessel growth by matrix contraction (Looping angiogenesis Angiogenèse d'un troisième type contrôlée par les forces contractile). Greenwood & Kilarski WW✉ (2010) **Med Sci** (Paris)

Publications in Preparation

4. ¥***Intravascular lymph thrombosis blocks tissue drainage and prolongs acceptance of subcutaneous allografts***. Kilarski WW✉, Wachowska, Muchowicz, Hirosue and Swartz MA (Final manuscript)
3. ¥*Epimorphic regeneration after limited lymphatic vessels injury*. Kilarski WW✉, Wachowska, Muchowicz & Swartz MA
2. ¥*Differential regulation of lymph flow and leukocyte trafficking by inflammation*. Kilarski WW✉ & Swartz MA✉
1. ¥*Interaction of metastasis and leukocytes with tumor scaffold determines the type and speed of metastatic spread*. Kilarski WW✉, Lund & Swartz MA✉

Awards and Highlights

2017 Cover image of the April edition Circulation Research (the highlight of the article published in the same issue)
2016 Cover image of the November edition of Arteriosclerosis, Thrombosis and Vascular Biology journal
2014 Cover image of the academic book: Immunology: Basic problems and current status
2014 Cover image of the special issue of the Cancer Immunology Research
2014 Cover image of the special issue of the Angiogenesis J: Lymphangiogenesis in Inflammation
2013 Cover image for **GRC Science** advertisement
2013 Cover image of the review Tracking metastasis and tricking cancer (**Nature**) featuring our intravital technique
2012 Cover image of the website **American Society for Photobiology**
2012 Andrew Moisoff Young Investigator Award for the best talk at the **GRC on Lymphatics**
2011 Winning image in Nikon Small World Contest
2009 **Poster award**: **Angiogenesis Gordon Research Conference**, Salve Regina University
2009 **Nature Medicine** News and Views: Benest and Augustin. Tension in the vasculature; **Science Editorial's choice,** Gilbert Chin: Tissue-Engineering Principals; Research Highlight in **Nature Biotechnology** Wound Healing by force; Yasuko Iwakiri and Andrius Kazlauskas highlights in Faculty of 1000
2002 On-cover highlights in Annual Journal of Uppsala University (Horizons) on the perspectives of angiogenesis studies
2001 **Experimental Cell Research** highlighting of the article published in the same issue
1998 **European Union TEMPUS** Fellowship support for six months project at the Uppsala University

Patents

2018 Patent-pending for a method of immunization against custom macromolecule coupled to nematode carrier. **WW Kilarski**

Other Professional Activities

- Ad hoc reviewer for journals: Adv Wound Care, Sci Rep, Angiogenesis, Cell Mol Bioeng, Biotechnol Lett, Oncogene, J Invest Dermatol, JOVE, Cancers, Parasitology Open, ACS Cent Sci, Dove Med Press, PLOS ONE
- Ad hoc reviewer for grant foundations: The National Fund for Scientific Research for Flanders (FWO), The National Science Centre, in Polish Narodowe Centrum Nauki.
- Member of Nature Research Microbiology Community
- Member of North American Vascular Biology Organization (NAVBO)
- Member of Lipedema Foundation (LF)
- Member of Lymphatic Education & Research Network

Skills

Training on Advance fluorescence imaging techniques and 2Photon microscope.

Imaging techniques:

- Intravital model on mouse ear skin.
- Whole-mount staining and immunofluorescence imaging.
- Two-photon-imaging.

Experimental methods:

- In vitro methods of cell isolation, differentiation, and function.
- Ex vivo enzymatic assays, standard molecular biology techniques.
- Transcriptomics, proteomics, and peptide mass fingerprinting techniques.
- Generation of iPSCs and methods for their redifferentiation in vitro and in vivo.
- Glia development in chicken by embryo electroporation.

Experimental animal models:

- Mouse models of skin wound healing, tail lymphedema, lymphangiography, and angiography, a technique for subcutaneous transplantation of oxygen-sensitive tissues (muscle, islets, etc.), a method for cornea transplantation.
- Göttingen Minipigs which are intensively used in diabetes research, but became an advantageous model in regulatory pharmacology and toxicology. They are also recognized as a useful animal model for translational neuroscience (e.g. Parkinson Disease, depression).
- Chick embryo chorioallantoic membrane (CAM) as a valuable model for angiogenesis and metastasis, but also an experimental system for analysis of transplant immune responses. Due to its extensive vascularization, lack of adaptive immunity, and fast, non-traumatic access to the virtually two-dimensional vascular bed of chorioallantoic plexus (a homologue to the human placenta) it is broadly used in xenografting, neurosurgery, and the blood-brain barrier research.

Computer skills:

- Computer 3D Image editing software: Imaris, FIJI;
- 2D image and graphic design: Photoshop, Illustrator, In Design;
- Office and statistics software;
- Basic programming tools;

- In Windows, OS X and Linux environment.

Languages: Polish (native), English (advanced), French (basic), German (basic), Russian (basic)

Grants Received

2012-15 **Polish-Swiss Research Program** Novel therapeutic strategies to target tumor lymphangiogenesis, in partnership with Warsaw Medical and Jagiellonian Universities. Grant Number: PSPB-057/2010, value: 1 million CHF for three years. I wrote most of Swiss and edited Polish part of the grant, quaternary and annual grant reporting. The grant application was scored as the second out of approximately two hundred applications.

2006 **Foundation Lefoulon-Delalande-Institute de France**. Personal grant for a project: Comparative profiling of endothelium proteome in normal and granulation tissue vasculature. Value: 25 000 € for one year.

1998 European Union TEMPUS stipend for six months personal support in Erik Fries lab at the Uppsala University Biomedical Centre, Sweden. Value: 3800 € for 5 months.

Teaching and Tutoring

2016 Co-tutoring (H. Paymen) and training (T. Mercer) Ph.D. students at the University of Chicago on animal models and immunohistochemistry techniques.

2010-14 Co-mentoring Ph.D. student Esra Güç, which included the teaching of basic animal models and imaging methods, academic planning and direct help with experiments but also troubleshooting of newly developed techniques. Finally, I took part in writing manuscripts and rebuttals of reviewers' comments.

2013 Scientific planning and guidance for M. Wachowska, a Ph.D. student from Medical University of Warsaw (a one-month project)

2013-14 Organizing and conducting two, one week each, Imaging courses for researchers and staff. **(1) Intravital imaging of immune-cells interaction with lymphatic vessels**; for E. Wagena, Research Assistant (Prof. Peter Friedl, Nijmegen), L. Johnson, Ph.D. (Prof. David. Jackson, Oxford) and **(2) Intravital imaging of tumor cell migration and interaction with non-fibrillar matrices**, for M. Potez, Ph.D. student (Prof. Valentin Djonov, Bern). These courses were also attended by members of Melody Swartz lab Ph.D. students M. Fankhauser, E. Guc, V. Triacca, and S. Raghunathan. This program included the basics of fluorescence imaging and a theoretical and practical introduction to intravital tissue labeling and long-time imaging. These courses were entirely self-developed. Each class involved 30 hours of tutoring.

2012 Plan and guidance of two Ph.D. students from Warsaw Medical University: A. Muchowicz and M. Wachowska (two-month project). The research was conducted in our lab at the EPFL.

2009-13 Teaching and mentoring of two undergrads: F. Bochner, V. Greenwood, three Ph.D. student S. Raghunathan, M. Fankhauser, V. Triacca and one post-doc: Tine Karlsen.

2006-08 Instructing and mentoring graduate students I. Sacewicz and M. Studer.

2001-05 Undergraduate teaching. Assistance in teaching in courses for a medical student at the Uppsala University. Teaching based on scripts. Tuition for two undergrads and two graduate students: N. Jura and L. Petersson.

1999 Undergraduate education. Teaching assistant on the main study course for biotechnology students at Jagiellonian University: "Biochemistry–practical course." Detection and characterization of mono- and polysaccharides. Isolation, purification, and separation of nucleic acids. Class time: 60 hours and, included a theoretical introduction, practical experimentation, and final examination of students. Teaching based on scripts and books). Examination test was self-developed. Leading Professor: Joanna Bereta.

Conferences and invited presentations

Selected Oral Presentations

2018 *Normalized revascularization permits a subcutaneous grafting of pancreatic islets into an induced immune-privileged site.* **Vascular Biology 2018**, Newport, RI, USA. Poster judge at the Immunity session

2018 *Study of the migratory phase of filaria infection as an example application of tissue whole-mount imaging techniques*. **GRS on Lymphatics,** Il Ciocco, Italy

2017 *Local induction of lymphangiogenesis with engineered fibrin-binding VEGF-C promotes wound healing by increasing immune cell trafficking and matrix remodeling*. **Lymphatic forum**, Chicago, USA

2016 *Engaging lymphatic control of lymph fluidity to block antigen drainage and prolong acceptance of subcutaneous allografts*. **EMBL Australia Group Leader Interview**, Melbourne, Australia

2015 *Lymphatic control of lymph fluidity to block the tissue drainage and extend acceptance of subcutaneous allografts*. **Lymphatic Forum**, Chicago, USA

2015 *Exploiting morpho-physiological features of collecting lymphatics to control antigen-specific immunity*. Faculty talk at the **Institute of Anatomy, University of Bern**, Switzerland

2013 *Imaging matrix heterogeneity, metastasis, and immune surveillance in mouse melanoma.* Faculty talk at the **Rudbeck Laboratories, Uppsala University**, Sweden

2013 *Live imaging of metastatic cell interactions with tumor matrix*. **5th Conference on Imaging of Tumor Matrix Heterogeneity Tumor-Host Interaction and Angiogenesis**, Ascona, Switzerland

2013 *Live imaging of metastatic cell interactions with components of the tumor matrix.* **7th Winter Conference of the ESMI** on **Imaging Hallmarks of Cancer** in Les Houches, France

2012 *Looping angiogenesis, can solid tumors recruit neo-vessels by non-sprouting vessel growth?* Faculty talk at the **Breakthrough TR Breast Cancer Research Centre**, London, UK

2012 *Live imaging of metastatic cell interactions with components of the tumor matrix*. **Tumor Ecosystem in Cancer Metastasis**, Niece, France

2012 *Intravital immunofluorescence within dermis microenvironment*. **GRC on Lymphatic**, Ventura, USA

2011 *Selective photodynamic occlusion of lymphatic vessels*. **GRC on Angiogenesis**, Salve Regina, Newport, RI, USA

Selected Poster Presentations

2018 Local occlusion of lymphatics permits immunosuppression-free transplantation of pancreatic islets into a subcutaneous immune-privileged zone. **Frontiers in Islet Biology and Diabetes**, Keystone, USA

2016 *Lymphatic control of lymph fluidity to block the tissue drainage and prolong acceptance of subcutaneous allografts.* **GRC on Lymphatic**, Ventura, USA

2014 *Induced intravascular lymph coagulation blocks tissue drainage and extends the acceptance of subcutaneous grafts.* **18th International Vascular Biology Meeting**, Kyoto, Japan

2011 *Lymphatic invasion of tumor cells and migration of cytotoxic leukocytes depends on matrix remodeling by tumor-associated fibroblasts.* **AACR's Tumor Microenvironment,** Orlando, USA

2009 *Mechanical tension mediates and directs the growth of vascularized tissue; a novel view on non-developmental angiogenesis.* **GRC on Angiogenesis**, Newport, USA

2006 *In vivo biotinylation of the chicken organ-specific, granulation tissue, and tumor endothelium.* **6th ESH Euro Conference on Angiogenesis**, Cannes, France

2002 *A novel assay for study angiogenesis and lymphangiogenesis*. **Keystone Symposium on Angiogenesis in Cancer and Other Diseases**, Banff, Canada

Personal Statement

I must begin with a surprising observation that emerged only recently. While I was glimpsing through Nature's career columns, a title of one subchapter, '*Get stuck after one failure*,' triggered a revelation. I realized that I actually never failed in or abandoned any project. In fact, the history of my research, imprinted primarily in my first and last author publications, can illustrate the most notorious of my character traits, the compulsive perseverance in pursuit after the real nature of a thing.

Trained as a molecular biologist, I graduated from the Cracow Jagiellonian University. I started my Ph. D. training in the Vascular Biology group at the Uppsala University under the mentorship of Lena Claesson-Welsh, an esteemed expert in signal transduction and vessel physiology, and her senior scientist Par Gerwins. My doctoral studies culminated with the discovery of a non-developmental, inflammatory-driven mechanism of growth of blood vessels. During my first postdoctoral training at the University of Bordeaux in the laboratory of Andreas Bikfalvi, an eminent angiogenesis researcher, I initiated metabolomic and proteomic projects aiming at the comparison of pathological and organ-specific changes of blood vasculature. Later, at the École Polytechnique Fédérale de Lausanne, in the group of Melody Swartz, a renowned leader in lymphatic and cancer mechanobiology. There I became interested in the imaging of various pathological processes that take place at the interfaces of extracellular matrices and the lumen of blood and lymphatic vessels.

My first author publications are the milestones of my career that usually brought to an end a long and uncertain struggle with paradigms or ambiguous hypotheses rooted in various biological fields of research. The time-consuming persistence in overcoming obstacles often paid back, such as when Nature Medicine published my hypothesis backed by doctoral study-long research showing that tension-driven looping angiogenesis, that is, the biomechanical relocation and stretching of vessels dominates blood restoration in post-developmental inflammatory settings. Soon after, in Andreas Bikfalvi lab, I designed a system for *in vivo* labelling of the chicken embryo vasculature, an invaluable tool for upcoming proteomic projects. Fast forward a decade for two publications that sum up a large endeavor that unfolded from a single experiment aiming to verify a lymphatic preference by mouse filaria nematode. The results published in Nature Communications provide the first glimpse into an almost mystical and rarely studied phase of parasitic nematode infection, the early asymptomatic spread of filaria worms. I showed that parasitic nematodes, in general, did not need to develop complex mechanisms of navigation throughout a vertebrate host because their specific dissemination can be achieved with inherent skills that evolved for crossing the granular materials, such as mud, sand, or soil.

However, the development of the intravital imaging platform, a cost-effective alternative to multiphoton imaging, turns out to be the most prolific of all my projects. Published in PLOS ONE, this immunofluorescence method allows for tracking metastasis or leukocytes, quantifying vascular or lymphatic leakage, localizing stores of extracellular chemokines or growth factors, or imaging post-developmental processes of lymphangio- and angiogenesis. Also, in contrast to multiphoton imaging, it provides means to prevent phototoxic bleaching of fluorophores, and by this, allows continued imaging of the same skin locations tissue for days. The most significant advantage of this method is the ability to image all kinds of physiological processes in the context of real tissue boundaries delineated by basement membranes, structures that cannot be visualized in a multiphoton microscope. Due to the versatility of this system, the ensuing collaborations spanned through a variety of biological fields. They resulted in publications in journals, such as Science, Circulation Research, Nature Cell Biology, Biomaterials, and Nature Communications.

Yet, my most recent, unpublished discoveries carry the highest potential to profoundly influence numerous biomedical disciplines. I have found that similar to blood vessels, which are known to form the only surface capable of keeping blood in a fluid state, lymphatics serve the same function for the lymph. Despite the absence of the literature describing the anti-haemostatic properties of lymphatics I quickly realized the consequences of their loss; from the prevention of infection spread to promotion of vascular embolism and arrest of lymphocytes in viral infection such as COVID-19; from the spread of metastasis to induction of idiopathic post-mastectomy lymphedema in women to the prevention of anti-graft immunity in hormone-producing grafts.

My current goal is to translate to clinique a method that was considered a Holy Grain in the field of Type-1-Diabetes, that is, sustained transplantation of pancreatic islets under the skin of subcutaneous grafting of pancreatic islets. This technique holds promise for low-cost treatment of diabetic patients with self-isolated pluripotent-stem cells, and in

contrast to previous attempts, leads to physiological revascularization of islets and restoration of glucose control in diabetic individuals.

Past Research

During my postdoctoral work, I was focused on the physiology underlying the remodeling of blood and lymphatic vessels in tumors and during healing and inflammation. I demonstrated a new mode of post-developmental vessel growth and developed new in vivo assays on the chicken chorioallantoic membrane (CAM). I also initiated the research on RNA and proteome profiling of normal and pathological blood endothelium in the embryo. To open the possibility for the visualization of various extracellular matrix components (e.g., basement membranes, fibrin or tenascin) with any fluorescent imaging technique, including IVIS macroscopy, traditional epifluorescence, and confocal or multiphoton microscopy, I developed protocols for intravital staining and imaging. We have applied this imaging technique to phenomena as diverse as the early stages of filaria infection, lymphatic intravasation, measurement of vascular leakage and interactions between metastasis and dendritic cells, CAFs or T cells. More recently, I established a method for subcutaneous grafting of Langerhans islets and continue work on a new anti-hemostatic role of lymphatic collecting vessels. Interference in this activity blocks the drainage of antigens and thus generates a subcutaneous, immune-privileged site that can accept subdermal allografts without systemic immunosuppression. This research has direct translational potential and can be used to protect endocrine allografts, such as pancreatic islets, from immune response.