



Universiteit
Leiden
The Netherlands

Hemodialysis vascular access failure: novel pathophysiological mechanisms and therapeutic strategies

Bezhaeva, T.

Citation

Bezhaeva, T. (2019, March 7). *Hemodialysis vascular access failure: novel pathophysiological mechanisms and therapeutic strategies*. Retrieved from <https://hdl.handle.net/1887/68702>

Version: Not Applicable (or Unknown)

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/68702>

Note: To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The following handle holds various files of this Leiden University dissertation:

<http://hdl.handle.net/1887/68702>

Author: Bezhaeva, T.

Title: Hemodialysis vascular access failure: novel pathophysiological mechanisms and therapeutic strategies

Issue Date: 2019-03-07

Curriculum Vitae

Taisiya Bezhaeva was born on 10 December 1986 in Moscow, Soviet Union (present Russian Federation). In 2003 she began her study in Moscow Medical Academy in the faculty of Pharmaceutical Sciences. In 2008 she obtained a master's degree in pharmacy and started to work in the field of drug development. During the following three years, while working as a monitor of clinical trials, she developed a strong interest in pre-clinical research aimed towards understanding the molecular mechanisms of drug action and underlying disease pathobiology. This experience resulted in her decision to obtain a second master's degree. In 2011 she was accepted into an international master program in Molecular Medicine at Charite University, Berlin, Germany.

During this two year degree, she became actively engaged in research on vascular biology and inflammation. First, Taisiya joined the laboratory of Prof. dr. med. Philipp Stawowy at the German Heart Institute, Berlin where she studied the role of PCSK9 in atherosclerosis. Later, she performed an internship in the group of "Inflammation biology" headed by Prof. dr. Sergei A. Nedospasov at the German Rheumatism Research Center (DRFZ), a Leibniz Institute, Berlin. Under the supervision of Dr. Yuri Schebzukov she successfully completed her master thesis on the transcriptional regulation of tumor necrosis factor (TNF α).

In October 2013 Taisiya received her second M.Sc. in Molecular Medicine and in December same year became a PhD candidate at the Department of Internal Medicine and Einthoven Laboratory for Vascular and Regenerative Medicine at Leiden University Medical Centre.

In following years, Taisiya focused on hemodialysis vascular access dysfunction. To untangle this major clinical problem: Taisiya designed, performed and coordinated several *in vivo* and *in vitro* studies under the supervision of Prof. dr. A.J. van Zonneveld, Prof. dr. P.H.A. Quax and Dr. J.I. Rotmans.

During her Doctoral degree, Taisiya spent eight months at the University California, Los Angeles at the Department of Bioengineering. Under the supervision of Prof. dr. Song Li she performed a research project in the field of vascular tissue engineering. The results of her research are published in peer-reviewed international scientific journals and presented in this thesis.

Her work was presented in number of national and international conferences, including an oral presentation at the Kidney Week of the American Society of Nephrology (2016). At the congress of European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) Taisiya won a price in a category Best Abstracts presented by Young Authors.

Supplementary to her research, Taisiya is involved in teaching activities, providing lectures and supervision to medical and biomedical students of the "Heart and blood vessels" and "Biomedical Translational Research in Surgery" minors.

It is her sincere desire and ambition to improve current patient care therapies through translational medical research. Taisiya remains passionate towards development of her career in academia, and currently continues her work in the vascular biology field as a postdoctoral fellow.

List of publications:

1. Rotmans JI, **Bezhaeva T**.
The battlefield at arteriovenous crossroads: invading arterial smooth muscle cells occupy the outflow tract of fistulas.
Kidney Int. 2015 Sep;88(3):431-3.
2. Wong C, **Bezhaeva T**, Rothuizen TC, Metselaar JM, de Vries MR, Verbeek FP, Vahrmeijer AL, Wezel A, van Zonneveld AJ, Rabelink TJ, Quax PH, Rotmans JI.
Liposomal prednisolone inhibits vascular inflammation and enhances venous outward remodeling in a murine arteriovenous fistula model.
Sci Rep. 2016 Jul 27;6:30439.
3. Grune J, Meyborg H, **Bezhaeva T**, Kappert K, Hillmeister P, Kintscher U, Pieske B, Stawowy P.
PCSK9 regulates the chemokine receptor CCR2 on monocytes.
Biochem Biophys Res Commun. 2017 Apr 1;485(2):312-318.
4. Shebzukhov YV, Stanislawiak S, **Bezhaeva TR**, Nedospasov SA, Kuprash DV.
Low level of Lck kinase in Th2 cells limits expression of CD4 co-receptor and S73 phosphorylation of transcription factor c-Jun.
Sci Rep. 2017 May 24;7(1):2339.
5. **Bezhaeva T**, Wong C, de Vries MR, van der Veer EP, van Alem CMA, Que I, Lalai RA, van Zonneveld AJ, Rotmans JI, Quax PHA.
Deficiency of TLR4 homologue RP105 aggravates outward remodeling in a murine model of arteriovenous fistula failure.
Sci Rep. 2017 Aug 31;7(1):10269.
6. van Alem CMA, Boonstra M, Prins J, **Bezhaeva T**, van Essen MF, Ruben JM, Vahrmeijer AL, van der Veer EP, de Fijter JW, Reinders ME, Meijer O, Metselaar JM, van Kooten C, Rotmans JI.
Local delivery of liposomal prednisolone leads to an anti-inflammatory profile in renal ischaemia-reperfusion injury in the rat.
Nephrol Dial Transplant. 2018 Jan 1;33(1):44-53.
7. **Bezhaeva T**, de Vries MR, Geelhoed WJ, van der Veer EP, Versteeg S, van Alem CMA, Voorzaat BM, Eijkelkamp N, van der Bogt KE, Agoulnik AI, van Zonneveld AJ, Quax PHA, Rotmans JI.
Relaxin receptor deficiency promotes vascular inflammation and impairs outward remodeling in arteriovenous fistulas.
FASEB J. 2018 Jun 8.

8. **Taisiya Bezhaeva**, Wouter J. Geelhoed, Dong Wang, Haoyong Yuan, Eric P. van der Veer, Carla M.A. van Alem, Febriyani F.R. Damanik, Xuefeng Qiu, Anton Jan van Zonneveld, Lorenzo Moroni, Song Li and Joris I. Rotmans. Contribution of bone marrow-derived cells to in situ engineered tissue capsules in a rat model of chronic kidney disease.
Biomaterials - In press (available online 15 December 2018).

Acknowledgement

Every single step of this thesis was done in a very collaborative and supportive environment. Here, I would like to reflect upon the people who have supported and helped me so much throughout this entire period.

My thesis advisors **Prof. Anton Jan van Zonneveld** and **Prof. Paul Quax**.

Anton Jan. A professor who can really “rock-and-roll”. Thank you for your inspiring guidance. Our Monday group meetings provided me with very insightful discussions.

Paul. You are truly a **visionary of science** and have been an exemplary mentor for me. I appreciate and value everything you have taught me. Our interesting and long-lasting chats and insightful discussions were always very motivating and inspiring.

I would like to thank my dear mentor **Dr. Joris Rotmans**.

Joris, you are everything one could look for in a good mentor and I could not have imagined having a better advisor and supervisor for my Ph.D. than you. Your invaluable feedback to all of my scientific drafts were always full of **enthusiasm** and **motivation**. Your critical analysis and excellent advice during the entire period make the completion of this thesis successful and groomed me to be sound professional. Special thanks for your personal support, in times of my scientific or personal black holes. After meetings with you there was always a light at the end of the tunnel.

My sincere thanks also go to **Prof. Song Li**, for offering me the 8-month internship opportunity in your group. It was an unforgettable time in sunny **California** for me. To work under your supervision at UCLA helped me to realize what interdisciplinary cutting edge research truly means.

Prof. Cees van Kooten, dear Cees. The immunology guru and an extremely friendly professor whose door is always open for questions. Thank you for your time, your insightful suggestions and support of my research.

Margreet. Magician of mouse surgery, great scientist, colleague and a friend. Thank you for always giving me your **honest advice**. It was a pleasure to have you by my side during all these years and I really value all the scientific and personal contribution from your side.

Carla. Wonderful and generous friend who has always been ready to **support** and help me. I admire your positive, honest and loyal outlook. I will never forget the many wonderful lunches, trips and fun activities we have done together. Black humor is a sign of high intelligence, as a recent study in the journal *Cognitive Processing* suggests. I think you get it all.

Wouter. “Als je wilt chillen, is het geen probleem.” Great colleague, who can construct almost anything ranging from a homemade fish smoker to highly-tech medical devises. It was always a lot of **fun** to plan and to perform experiments with you.

Reshma. Your willingness to give your time for my research so generously has been very much appreciated. Not to forget, your Surinamese treats definitely had a positive influence on the quality of the research I was doing.

Eric. One of the most enthusiastic, life-energizing, funny and intelligent person I know. Eric you were someone who was always ready to brainstorm on science and give me a fresh look, when I felt stuck. Special thanks to all your proofreading.

C7 senior crew: **Janine, Hetty, Catelijne, Bernard, Roel, Marten** each of you has given of your time, energy, and expertise and I am grateful for it.

All the past **Carolien, Margien, Danielle, Jonna, ChunYu, Bram, Ruben** and present members of C7 Island: What welcoming people you are.

K5 Island: **Sophie, Dianne, Franca, Gesa, Barend, Jurjen, Huayu, Gangqi** you are the dream team. I would like to thank you all for your support in my work and also when I had personal troubles.

D2 Island: **Jaq, Anne-Marie, Wendy Sol, Wendy Stam, Loes. People from thrombosis and hemostasis department. Wonderful colleagues from D3 Island.** Former P1 Island: **Erna, Rob;**

I know that I could always ask them for advice and opinions on lab related issues and they are always there to help me.

I would like to thank my colleagues **Dong, Jennifer, Danny, Zhang, Jun, LeeAnn** from my internship at UCLA for their wonderful collaboration.

Yury Shebzukhov, my first science-coach and one of the most creative scientists with a great sense of humor I have ever met. Thank you for enlightening upon me the first glance on real science.

Here, there are my friends.

Russian block:

Lenoki Puris, my forever interested, cheering and always enthusiastic real friend. One of the few people who were always keen to know what I was doing and how I was proceeding with my science.

To my soul mates, **Iriza and Tanjuk.** Thank you for your thoughts, well-wishes, texts, visits, and being there whenever I needed a friend.

My former study mates 15-16 and kozyavki crew.

Amsterdam block:

Ilusha, Ksju, Irisha and Oksana

Berlin block:

Dan. Does not matter where you are or what you are up to, we are always on the same frequency.

Los Angeles block:

Anna Tarasyuk and Mike Miroshnikov, true angels I found in LA. Thank you for taking care.

Basti and Sam, thank you for your support and for showing me beautiful California state and beyond.

Cary for your hospitality and making me feel home.

Finally, there is my family.

My grandfather **Ivan Bezhaev** (dedushka Vanya) who was always truly appreciating any of my achievements. I am sure that he would be one of the few people who would read this thesis from the beginning until the end although it is likely that he would not have grasped what it was all about!

Nicolino a true and great supporter. It is very important for me, to have you - the person with whom I can share my thoughts and doubts. Thank you for making home a place where you want to come back.

My eternal cheerleader and my best friend, my sister **Olyas** and her family **Mills** and **Hugh** who have provided for me through moral and emotional support in my life. Olyas has always faith in me and my intellect. Thank you for being non-judgmental and accepting all my freak-ins and outs.

I am especially grateful to my parents, **maman- Irina Bezhaeva** and **papan- Rostislav Bezhaev** who supported me emotionally and financially. I always knew that you wanted the best for me.

Thank you very much, everyone!

