# Pathophysiology of von Willebrand factor in bleeding and thrombosis

Pagliari, M.T.

# APPENDIX A

ACKNOWLEDGMENTS

CURRICULUM VITAE

PUBLICATION LIST

PHD PORTFOLIO

# ACKNOWLEDGMENTS

Even this adventure has come to the end. Flora, Jeroen, and Frits thank you for giving me the support and instruments to make this dissertation possible. Flora, my thank goes beyond the work done together for this thesis. Jeroen and Frits, it has been a great opportunity to spend a year in the Netherlands, although the pandemic has changed our plans.

I would like to thank Prof. Sforza, coordinator of the PhD in Translational Medicine at the University of Milan, and more generally, all the people from both the University of Milan and LUMC, who made this joint PhD possible.

Thanks to all my colleagues from both Angelo Bianchi Bonomi Haemophilia and Thrombosis Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano and Leiden University Medical Center for the contribution to the realization of these projects. In particular, I would like to thank Luciano, Giovanna, Paola, Eugenia, and Simona for their collaboration. Of course, thanks to VWF Lab in Leiden: Suzan, Annika, Richard, Yvonne, and Bas, you let me feel part of the group from the beginning. Again, thanks Jeroen for your time and valuable advice.

I would have not enjoyed my time in Leiden as well as I did without my officemates Yiman and Ricardo at office C7-112! Thanks to Eugenia and Eleonora for all the nice moments together.

I would like to thank Prof. Mannucci for his constructive comments on my work and for his enthusiasm for conducting research. Ilaria thanks for all conversations and good advice. Thanks to Gigi, my work would not have been so graphically nice without your contribution.

Finally, I thank my family and friends. You have a lot of patience with me.

A

# CURRICULUM VITAE

Maria Teresa Pagliari was born on 29 April 1986 in Crema, Italy. After achieving a technical diploma in Chemistry, she moved to Pavia for her bachelor's degree in Biotechnologies at the Università degli Studi di Pavia. She completed her internship in virology at the Department of Morphological, Eidological, and Clinical Sciences, Section of Microbiology, Università degli Studi di Pavia, focusing on the genotyping of papillomavirus types in HIV-positive women. After graduating in 2008, she started her master in Medical Biotechnologies at the Università degli Studi di Pavia. Her internship focused on cell models and genotyping applied to the characterization of endocrine disorders in the Laboratory for Endocrine Disruptors, directed by Professor Luca Chiovato. She received her Master's degree in September 2010.

Since 2011 she is working as a researcher at A. Bianchi Bonomi Haemophilia and Thrombosis Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano under the supervision of Prof. Flora Peyvandi. Her research focused on the biochemical, molecular, and in vitro characterization of von Willebrand disease and thrombotic disorders, such as deep vein thrombosis.

Maria Teresa started her PhD program in May 2019 as part of a joint PhD between the Leiden University Medical Center and the Università degli Studi di Milano under the supervision of Professor Frits Rosendaal, Professor Jeroen Eikenboom, and Professor Flora Peyvandi. After her PhD defense, Maria Teresa will continue her research activity as a Postdoc in the group directed by Prof. Peyvandi in Milan.

# PUBLICATION LIST

Seidizadeh O, Baronciani L, **Pagliari MT**, Cozzi G, Colpani P, Cairo A, Siboni SM, Biguzzi E, Peyvandi F. Genetic determinants of enhanced von Willebrand factor clearance from plasma. J Thromb Haemost. 2023 Jan 20:S1538-7836(23)00040-5. doi: 10.1016/j.jtha.2023.01.012.

**Pagliari MT**, Budde U, Baronciani L, Eshghi P, Ahmadinejad M, Badiee Z, Baghaipour MR, Hidalgo OB, Biguzzi E, Bodó I, Castaman G, Goudemand J, Karimi M, Keikhaei B, Lassila R, Leebeek FWG, Lopez Fernandez MF, Marino R, Oldenburg J, Peake I, Santoro C, Schneppenheim R, Tiede A, Toogeh G, Tosetto A, Trossaert M, Yadegari H, Zetterberg EMK, Mannucci PM, Federici AB, Eikenboom J, Peyvandi F. von Willebrand factor neutralizing and non-neutralizing alloantibodies in 213 subjects with type 3 von Willebrand disease enrolled in 3WINTERS-IPS. J Thromb Haemost. 2023;21(4):787-799.

Agosti P, Mancini I, Sadeghian S, **Pagliari MT**, Abbasi SH, Pourhosseini H, Boroumand M, Lotfi-Tokaldany M, Pappalardo E, Maino A, Rosendaal FR, Peyvandi F. Factor V Leiden but not the factor II 20210G>A mutation is a risk factor for premature coronary artery disease: a case-control study in Iran. Res Pract Thromb Haemost. 2023 Jan 11;7(1):100048. doi: 10.1016/j.rpth.2023.100048.

Seidizadeh O, Baronciani L, **Pagliari MT**, Cozzi G, Colpani P, Cairo A, Siboni SM, Biguzzi E, Peyvandi F. Phenotypic and genetic characterizations of the Milan cohort of von Willebrand disease type 2. Blood Adv. 2022;6:4031-4040.

**Pagliari MT**, Rosendaal FR, Ahmadinejad M, Badiee Z, Baghaipour MR, Baronciani L, Benítez Hidalgo O, Bodó I, Budde U, Castaman G, Eshghi P, Goudemand J, Karimi M, Keikhaei B, Lassila R, Leebeek FWG, Lopez Fernandez MF, Mannucci PM, Marino R, Oldenburg J, Peake I, Santoro C, Schneppenheim R, Tiede A, Toogeh G, Tosetto A, Trossaert M, Yadegari H, Zetterberg EMK, Peyvandi F, Federici AB, Eikenboom J. Von Willebrand factor propeptide and pathophysiological mechanisms in European and Iranian patients with type 3 von Willebrand disease enrolled in the 3WINTERS-IPS study. J Thromb Haemost. 2022; 20:1106-1114.

**Pagliari MT**, Baronciani L, Cordiglieri C, Colpani P, Cozzi G, Siboni SM, Peyvandi F. The dominant p.Thr274Pro mutation in the von Willebrand factor propeptide causes the von Willebrand disease type 1 phenotype in two unrelated patients. Haemophilia. 2022; 28:292-300

Mancini I, Baronciani L, Artoni A, Colpani P, Biganzoli M, Cozzi G, Novembrino C, Boscolo Anzoletti M, De Zan V, **Pagliari MT**, Gualtierotti R, Aliberti S, Panigada M, Grasselli G, Blasi F, Peyvandi F. The ADAMTS13-von Willebrand factor axis in COVID-19 patients. J Thromb Haemost. 2021; 19:513-521.

**Pagliari MT**, Cairo A, Boscarino M, Mancini I, Martinelli I, Bucciarelli P, Rossi F, Rosendaal FR, Peyvandi F. Role of ADAMTS13, VWF and F8 genes in deep vein thrombosis. Plos One. 2021;16:e0258675.

**Pagliari MT**, Boscarino M, Cairo A, Mancini I, Martinelli I, Bucciarelli P, Rossi F, Rosendaal FR, Peyvandi F. ADAMTS13 activity, high VWF and FVIII levels in the pathogenesis of deep vein thrombosis. Thromb Res. 2021; 197:132-137.

Stufano F, Baronciani L, Bucciarelli P, Boscarino M, Colpani P, **Pagliari MT**, Peyvandi F. Evaluation of a fully automated von Willebrand factor assay panel for the diagnosis of von Willebrand disease. Haemophilia. 2020; 26:298-305

Ferrari B, Cairo A, **Pagliari MT**, Mancini I, Arcudi S, Peyvandi F. Risk of diagnostic delay in congenital thrombotic thrombocytopenic purpura. J Thromb Haemost. 2019 Apr;17(4):666-669.

**Pagliari MT**, Baronciani L, Stufano F, Colpani P, Siboni SM, Peyvandi F. Differential diagnosis between type 2A and 2B von Willebrand disease in a child with a previously undescribed de novo mutation. Haemophilia. 2018; 24:e263-e266.

Fasulo MR, Biguzzi E, Abbattista M, Stufano F, **Pagliari MT**, Mancini I, Gorski MM, Cannavò A, Corgiolu M, Peyvandi F, Rosendaal FR. The ISTH Bleeding Assessment Tool and the risk of future bleeding. J Thromb Haemost. 2018; 6:125-130.

**Pagliari MT**, Baronciani L, Stufano F, Garcia-Oya I, Cozzi G, Franchi F, Peyvandi F. von Willebrand disease type 1 mutation p.Arg1379Cys and the variant p.Ala1377Val synergistically determine a 2M phenotype in four Italian patients. Haemophilia. 2016;22:e502-e511

**Pagliari MT**, Lotta LA, de Haan HG, Valsecchi C, Casoli G, Pontiggia S, Martinelli I, Passamonti SM, Rosendaal FR, Peyvandi F. Next-Generation Sequencing and In Vitro Expression Study of ADAMTS13 Single Nucleotide Variants in Deep Vein Thrombosis. PLoS One. 2016;11:e0165665.

A

Lancellotti S, Peyvandi F, **Pagliari MT**, Cairo A, Abdel-Azeim S, Chermak E, Lazzareschi I, Mastrangelo S, Cavallo L, Oliva R, De Cristofaro R. The D173G mutation in ADAMTS-13 causes a severe form of congenital thrombotic thrombocytopenic purpura. A clinical, biochemical and in silico study. Thromb Haemost. 2016; 115:51-62.

Bucciarelli P, Siboni SM, Stufano F, Biguzzi E, Canciani MT, Baronciani L, **Pagliari MT**, La Marca S, Mistretta C, Rosendaal FR, Peyvandi F. Predictors of von Willebrand disease diagnosis in individuals with borderline von Willebrand factor plasma levels. J Thromb Haemost. 2015; 13:228-36.

**Pagliari MT**, Baronciani L, Garcìa Oya I, Solimando M, La Marca S, Cozzi G, Stufano F, Canciani MT, Peyvandi F. A synonymous (c.3390C>T) or a splice-site (c.3380-2A>G) mutation causes exon 26 skipping in four patients with von Willebrand disease (2A/IIE). J Thromb Haemost. 2013; 11:1251-9.

Scaglione GL, Lancellotti S, Papi M, De Spirito M, Maiorana A, Baronciani L, **Pagliari MT**, Arcovito A, Di Stasio E, Peyvandi F, De Cristofaro R. The type 2B p.R1306W natural mutation of von Willebrand factor dramatically enhances the multimer sensitivity to shear stress. J Thromb Haemost. 2013; 11:1688-98.

Rotondi M, Stufano F, Lagonigro MS, La Manna L, Zerbini F, Ghilotti S, **Pagliari MT**, Coperchini F, Magri F, Bergamaschi R, Oliviero A, Chiovato L. Interferon-β but not Glatiramer acetate stimulates CXCL10 secretion in primary cultures of thyrocytes: a clue for understanding the different risks of thyroid dysfunctions in patients with multiple sclerosis treated with either of the two drugs. J Neuroimmunol. 2011; 234:161-4.

# PHD PORTFOLIO

PhD period: May 2019 - February 2023

Promotores: Prof. Dr H.C.J. Eikenboom, Prof. Dr. F. R. Rosendaal

| Mandatory courses | Year | Hours |
|---|---|---|
| PhD introductory meeting | 2020 | 5 |
| Basic Methods and reasoning in Biostatistics | 2020 | 42 |
| BROK Course (exempted) | - | - |
| **Disciplinary courses** | | |
| International Course on Clinical Epidemiology (Schiermonnikoog) | 2019 | 42 |
| Prediction modelling and intervention research | 2020 | 84 |
| Causal Inference Course | 2020 | 84 |
| Population Health: Study Design (Coursera) | 2020 | 29 |
| Population Health: Responsible Data Analysis (Coursera) | 2020 | 21 |
| Regression Analysis | 2020 | 22 |
| Meta-Analysis | 2021 | 28 |
| Analysis of Repeated Measurements 2021 | 2021 | 42 |
| 2D, 3D and 4D iPSC-derived cellular models to study neuromuscular diseases (University of Milan) | 2021 | 10 |
| Hemostasis and inflammation: from molecular aspects to organ damage (University of Milan) | 2022 | 10 |
| **Other courses and transferable skills*** | | |
| Scopus for the calculation of H-Index | 2021 | 2 |
| Managing your reference using Endnote | 2021 | 3 |
| Research Integrity II, 35° cycle | 2021 | 2 |
| Fundaments of academic Writing, 36° cycle | 2021 | 4 |
| Dal brevetto all'impresa | 2021 | 3 |
| Language coaching: Presentation skills, 36° cycle | 2021 | 4 |
| Communication on new media, 34° cycle | 2021 | 4 |
| Language coaching: Interpersonal Skills- Interview skills, 35° cycle | 2021 | 4 |
| Lezione propedeutica di base su Ip e brevetti, 36°cycle | 2021 | 4 |
| Lezione avanzata sull'utilizzo dell'IP per fare innovazione, 34° cycle | 2021 | 4 |
| Academic Writing: Research Paper, 35° cycle | 2021 | 4 |
| Valorizzare Creando impresa: fare spin-off, 34° cycle | 2021 | 8 |
| Grantsmanship I, 35° cycle | 2021 | 4 |
| Grantsmanship II 35° cycle | 2021 | 4 |
| Open science e valutazione della ricerca, 36° cycle | 2021 | 4 |

PhD Portfolio (continued)

| | Year | Hours |
|---|---|---|
| Self-Branding, 35° cycle | 2021 | 3 |
| 4EU+ Training Session "What is Open Science?" | 2021 | 1.5 |
| 4EU+ Cycle Of Scientific Publication: An Overview | 2021 | 1.5 |
| 4EU+ What are my funders requirements on Open Science? A focus on Plan S | 2021 | 1.5 |
| Behind the Scene of a peer-reviewed Journal | 2021 | 3 |
| 4EU+ Strategies for publishing in Open Access Journals. | 2021 | 1.5 |
| 4EU+ Training: Data management plans, one tool with many applications | 2022 | 1.5 |
| Laboratorio per la preparazione di un piano di disseminazione | 2022 | 2 |
| 4EU+ Training: Research Data Management-Introduction to FAIR and Open Data | 2022 | 1.5 |
| 4EU+ Open Research Software | 2022 | 1.5 |
| Data Management | 2022 | 3 |
| 4EU+ Citizen Science: producing data with people for innovating research | 2022 | 1.5 |
| CV e tecniche di selezione: come compilare un buon CV e approcciarsi alle tecniche di selezione aziendale | 2022 | 3 |
| **Other activities** | | |
| Attendance Rembrandt Symposium 2019 | 2019 | 9 |
| Attendance Rembrandt Symposium 2020 | 2020 | 9 |
| Managing your references using Mendeley | 2021 | 3 |
| Seminars on reproducible results: Rational and benefits | 2021 | 2 |
| Seminars on reproducible results: Theoretical session | 2021 | 2 |
| Conoscere E Difendersi Dal Nuovo Coronavirus Sars-Cov-2 | 2021 | 4 |
| Il Decreto Legislativo n. 81/08 –Formazione Specifica Profilo di rischio A Sanitari | 2021 | 14 |
| **Congress presentation and posters** | **Year** | |
| ISTH 2019 Oral Presentation and poster | 2019 | |
| ISTH 2020 Poster Presentation (virtual) | 2020 | |
| **Prizes, Awards and Grants** | **Year** | |
| Young Investigator Award, 58th Scientific and Standardization Committee of the ISTH; Liverpool, UK | 2012 | |
| Ricerca Finalizzata Giovani Ricercatori (GR-2011-02351977), Italian Ministry of Health. Principal Investigator | 2016-2019 | |
| Early Career Travel Grant. ISTH 2019; Melbourne, Australia. | 2019 | |
| Prize Guelfo Marcucci (Kedrion Biopharma and Carlo Erba Foundation) | 2020 | |

* Seminaries, lectures, workshops attended as request by the University of Milan PhD regulations.