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Hereditary haemorrhagic telangiectasia: from physiopathology to future treatments

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List of publications

1. Imaging and Quantification of the Hepatic Vasculature of Mice Using Ultrafast Doppler Ultrasound. Stripling K, Timmermans F, Décombas-Deschamps S, **Thalgott JH**, Lemonnier D, de Vries MR, Rabelink TJ, Tanter M, Deffieux T, Lebrin FPG. J Vis Exp. 2024.
2. Thresholds of Endoglin Expression in Endothelial Cells Explains Vascular Etiology in Hereditary Hemorrhagic Telangiectasia Type 1. Galaris G*, Montagne K*, **Thalgott JH***, Goujon GJPE, van den Driesche S, Martin S, Mager HJ, Mummery CL, Rabelink TJ, Lebrin F. Int J Mol Sci, 2021. *co-author.
3. In vitro Three-Dimensional Sprouting Assay of Angiogenesis using Mouse Embryonic Stem Cells for Vascular Disease Modeling and Drug Testing. Galaris G, **Thalgott JH**, Teston E, Lebrin FPG. J Vis Exp, 2021.
4. Pericyte in Hereditary Hemorrhagic Telangiectasia. Galaris G, **Thalgott JH**, Lebrin FPG. Review: Adv Exp Med Biol, 2019.
5. Decreased expression of VEGFR1 contributes to the pathogenesis of Hereditary Hemorrhagic Telangiectasia 2. **Thalgott JH**, Dos-Santos-Luis D, Hosman AE, Martin S, Lamandé N, Bracquart D, Srun S, Galaris G, de Boer HC, Tual-Chalot S, Kroon S, Arthur HM, Cao Y, Snijder RJ, Disch F, Mager JJ, Rabelink AJ, Mummery CL, Raymond K, Lebrin F. Circulation, 2018.
6. A New Wnt1-CRE TomatoRosa Embryonic Stem Cell Line: A Tool for Studying Neural Crest Cell Integration Capacity. Acuna-Mendoza S, Martin S, Kuchler-Bopp S, Ribes S, **Thalgott JH**, Chaussain C, Creuzet S, Lesot H, Lebrin F*, Poliard A*. Stem cells dev., 2017. *co-author.
7. The TGF β pathway is a key player for the endothelial-to-hematopoietic transition in the embryonic aorta. Lempereur, A, Canto P.Y. Richard, C, Martin, S, **Thalgott JH**, Raymond K, Lebrin, F, Drevon, C, Jaffredo, T. Developmental biology, 2017.
8. Interaction Between ALK1 Signaling and Connexin40 in the Development of Arteriovenous Malformations. Gkatzis K, **Thalgott JH**, Dos-Santos-Luis D, Martin S, Lamandé N, Carette MF, Disch F, Snijder RJ, Westermann CJ, Mager JJ, Oh SP, Miquerol L, Arthur HM, Mummery CL, Lebrin F. ATVB, 2016.
9. Pericytes as targets in Hereditary Hemorrhagic Telangiectasia. **Thalgott JH**, Dos-Santos-Luis D, Lebrin F. Review: Frontier genetics, 2015.

In revision

10. Non-invasive detection and functional characterization of pericyte-induced cerebral small vessel disease using super-resolution ultrasound. **Thalgott**

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JH*, Zucker N*, Deffieux T, Koopman MS, Dizeux A, Avramut CM, Koning RI, Mager JJ, Rabelink AJ, Tanter M and Lebrin F. *co-author. Nat Biomed Eng.

In preparation

11. Chemical modifications of the Phthaloyl ring determine the vascular protective effects of thalidomide and its analogs. **Thalgott JH***, Soussain C*, Dekkers S, Zamfirov L, Koster J, Martin S, Dos-Santos-Luis D, Goujon G, Teston E, Ijzerman A, Delfieux T, Tanter M, Rabelink AJ, Lebrin F
12. Akt inhibition prevents AVM formation in Hereditary Hemorrhagic Telangiectasia. **Thalgott JH**, Pollenus T, Goujon GJPE, Lebrin F.

List of patents

1. Use of thalidomide or analogs thereof for preventing neurologic disorders induced by brain irradiation. WO2015107196A1. Lebrin F, Soussain C, **Thalgott JH**. 2015.
2. Phthalimide and derivatives thereof for vascular dysfunction treatment. **Thalgott JH**, Lebrin F, Dekkers S, Ijzerman A. 2023.

Curriculum vitae

Jérémy Hervé Thalgot was born on February 13, 1988, in Cholet, France. He initially aspired to become a motorcycle mechanic, and so he entered the Lycée professionnel Albert Chassagne, Paimboeuf, France and obtained a professional diploma (brevet d'enseignement professionnel) in 2005, followed by a higher professional diploma (diplôme du Baccalauréat professionnel) from the Centre de Formation d'Apprentis de la Chambre de Commerce et d'Industrie Le Mans Sarthe, France in 2007, both in vehicle maintenance with a specialization in motorcycles. During this time, his interest in internal combustion engines and related manufacturing processes continued to grow. As a result, he continued to study and received an Industrial Science and Technology Baccalaureate in 2009. Subsequently, he studied mechanical engineering and manufacturing processes at the University Institute of Technology in Nantes, France, and received a bachelor's degree in 2011. Afterwards, he enrolled at the Ecole d'ingénieurs de l'Université d'Angers (Institut des Sciences Techniques de l'Ingénieur d'Angers), Angers, France to explore the creation and development of innovative products and processes, alongside intellectual property, and project management. His interest in engines slowly diminished, and he became more interested in another fascinating machine: the human body. To pursue his interest, he completed an internship at the research group of Dr. Franck Lebrin at the Center for Interdisciplinary Research in Biology at Collège de France in Paris, France. While there, he discovered the academic environment and biology. He setup an electrostimulation system to evaluate the ability of pericytes to induce vascular constriction during this first internship. For his work, he received the best poster presentation prize at the 10th HHT Scientific Conference, Cork, Ireland. As this internship sparked his interest for scientific research, he started, directly after his master graduation in 2014, his PhD research at the Lebrin group in the beginning of 2015. When Dr. Franck Lebrin moved with his group to The Netherlands, Jérémy decided to join and continued his PhD research at the Einthoven Laboratory for Vascular and Regenerative Medicine within the Department of Internal Medicine at the Leiden University Medical Center, The Netherlands. His PhD project was conducted under the supervision of Prof. Dr. A.J. Rabelink and Dr. F. Lebrin.

Jérémy's PhD research made significant strides in understanding HHT and translating scientific findings into practical applications. His work contributed to the creation of Rouge Therapeutics company, a startup dedicated to developing innovative therapies for HHT and vascular disorders, where he serves as a scientific founder and director of innovation.

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Throughout his career, J  r  my has presented his research at a number of biomedical conferences, winning several travelling awards and the prize for best presenter at the HHT Scientific Conference. The results of his extensive research, which he completed in 2024, are presented in this thesis. Throughout his academic and professional career, J  r  my's transition from engineering to biology illustrates a deep-rooted passion for innovation and discovery. His interdisciplinary expertise allows him to approach biological problems from a unique perspective, combining engineering principles with the biological sciences to pioneer new solutions in the field of vascular biology. J  r  my's career continues to be defined by his commitment to advancing science and his dedication to translating research into real-world applications that can make a tangible difference to people's lives.

