

PhD Project Description

School/Department:	Department of Pathology Erasmus MC
Supervisor information:	<ul style="list-style-type: none"> • Prof dr Adriaan B. Houtsmuller Assoc. Prof dr Timo L.M. ten Hagen Dr. Ann L.B. Seynhaeve • Email: a.houtsmuller@erasmusmc.nl t.l.m.tenhagen@erasmusmc.nl a.seynhaeve@erasmusmc.nl • Website: www.erasmusmc.nl , www.molmed.nl • Grants: Mrace • Most important publications: <ol style="list-style-type: none"> 1) Seynhaeve ALB, ten Hagen TL, Theranostics. 2020 2) Seynhaeve ALB, ten Hagen TL. Sci Rep. 2018 3) ten Hagen TL, Oncotarget. 2016 4) ten Hagen TL, Nat. Protoc. 2015 5) Seynhaeve AL, ten Hagen TL, J. Controlled Release. 2013 6) Seynhaeve AL, ten Hagen TL, Cancer res. 2008 7) Houtsmuller AB. Sci Rep. 2019 8) Houtsmuller AB, Nat Commun. 2016 9) Houtsmuller AB, Sci Rep. 2015
Project Title:	Investigation the association between endothelial cells and mural cells in angiogenesis
Abstract:	<p>Angiogenesis, the formation of new blood vessels, is essential for the proper development of tissues. Endothelial cells form the inner lining providing a dynamic barrier between underlying tissue and blood. Vascular mural cells are wrapped around the endothelial tube and are considered as stabilizing cells: control contractility and regulate endothelial proliferation. Vascular mural cells can be subdivided in vascular smooth muscle cells (vSMC), surrounding the larger vessels, and pericytes in smaller capillaries although some vessels have mural cells with properties between vSMC and pericytes. This distinction is more difficult in the tumor as typical properties separating arteries and veins are lost due to the more rapid and chaotic vessel growth. The study of angiogenesis is predominantly focused on endothelial cells and much less is known of mural cells. However, mural cells play a fundamental role in normal as well as pathological angiogenesis and are crucial for endothelial survival. The complex molecular association between both cells suggests that pericytes are more than just supporting cells. Functionality, ontogeny and identity are not fully understood and as there is no single common marker available to define vSMC and pericytes this makes it a more challenging cell type to investigate. We argue that mural cells are equally important to establish a functional vascular network and the cellular and molecular interaction between these cells will be studied. To do this we developed intravital microscopy using transgenic mice in which we can follow the dynamic nature of these cells in a 4D (XYZ+T, time dimension) manner. Also 2D and 3D in vitro cell cultures and ex vivo material will be used to study all steps in angiogenesis.</p> <p>Figure: High resolution 4D intravital imaging of sprouting endothelial cells and pericytes. (a) Shown are 70 μm subsequential maximal projections of endothelial cells (eNOSTagGFP in green) and pericytes (Cspg4-DsRed in red) in a B16BL6 melanoma tumor. (ai, aii) Zoom-in showing endothelial cell and pericyte spatial and temporal dynamics. x represent reference points in the vasculature. Scale bar represent 100 μm.</p>
Requirements of candidate:	<ul style="list-style-type: none"> • We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. As mice models are a major part of the experimental set-up affinity to work with animals is required. • Master degree or MD • Scholarship that will, at least, cover subsistence allowance and international air plane

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	<p>ticket (we could help with the scientific part of your scholarship proposal)</p> <ul style="list-style-type: none">• English language requirement:• <i>English speaking countries & Netherlands</i>: no requirement• <i>Other countries</i>: IELTS 7.0 (<i>min 6.0 for all subs</i>), TOEFL 100 (<i>min 20 for all subs</i>)
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Application requirements & Deadlines:

<https://www.eur.nl/en/about-eur/erasmus-university-china-centre/csc-scholarship>

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** No.32 for Clinical Medicine US News 2020:*

<https://www.usnews.com/education/best-global-universities/clinical-medicine?page=3>

** No. 30 Nature Index for Biomedical Sciences 2019:*

<https://www.natureindex.com/supplements/nature-index-2019-biomedical-sciences/tables/healthcare>