ERASMUS UNIVERSITEIT ROTTERDAM

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Erasmus Medical Center Department of Pathology
Project Title:	**The role of endothelial-mesenchymal transition (EndMT) in human cancers**
Abstract:	The tumor microenvironment (TME) is the reactive cellular and humoral environment of a tumor (also designated as "tumor reactive stroma"). The TME includes the surrounding blood vessels, various cell types and components among which immune cells, fibrocytes, fibroblasts, myofibroblasts, the extracellular matrix (ECM) and the humoral milieu of signaling molecules, growth factors, chemokines and cytokines where these cells reside. The TME plays a critical role in tumor initiation and progression. The properties of the TME may limit the access of therapeutics to the tumor, may alter drug metabolism and may contribute to the development of drug resistance. As a consequence, the tumor microenvironment has a profound effect on tumor development, plasticity and response to therapy. The cellular and/or molecular stromal components of the TME are of paramount importance for biological significance and offer attractive therapeutic targets. The tumor and its surrounding microenvironment are closely related and interact constantly. The components of the TME are influenced by local as well as systemic factors. Tumor cells may adopt particular phenotypical and genotypical characteristics dependent on the environment in which the cells reside. Therefore, if tumor cells leave their microenvironment, or if the environment changes, the tumor cells may adopt completely new properties. Clearly, the TME is a complex environmental constellation with specific spatiotemporal and dynamic properties, which are defined by the in vivo situation and which cannot simply be reproduced in in vitro models. The population of fibroblasts in cancers (cancer-associated fibroblasts, CAF) is a prominent component of the TME and is supposed to have a profound effect on the tumor cells and other stromal cells in most types of solid tumors. The possible origins of CAFs include epithelial-mesenchymal transition (EMT), adipose-derived stem cells (ASCs) or carcinoma-associated adipocytes (CAAs), endothelial-mesenchymal transition (EndMT), bone marrow-derived cells and more. The endothelial-mesenchymal transition (EndMT) has largely been investigated in tissue fibrosis, not in cancers, and its role in human cancers remains largely unclear. In this PhD project, we will focus on the EndMT in human cancers and investigate the association of EndMT with motility and proliferation of the tumor cells, since cell migration and cell proliferation of cancer cells are the two key cellular phenomena for any types of cancer development and progression, irrespective of their molecular characteristics. In order to study this association with human relevance, human tumor tissues and/or xenograft animal models are required. The Department of Pathology of the Erasmus MC is equipped with a large arsenal of

	techniques, including molecular methods for DNA, RNA, proteins, cyto-histologic analysis, PALM laser-capture microdissection systems, tissue culture facilities, and a variety of microscopes & imaging systems among which fluorescent microscopy, confocal laser scanning microscopy, (immune) electron microscopy, and more. There is a tissue bank in the department encompassing a large variety of tumor types. There are experiences with zebrafish modelling of development and diseases (collaboration with the Dept. of Clinical Genetics). A zebrafish model can be developed accordingly.
Requirements of candidate:	Master degree: Yes (Academic) Background: MD degree, preferably with interest in cancer biology and pathology. Strong motivation to obtain a PhD-degree within four years. IELTS Grade: 7.0 *(minimal 6.0 per component)* *or* TOEFL: *100 (minimal 20 per component)*
Supervisor information:	**Dr. P.P. Zheng (MD, PhD) / Prof. J.M. Kros (MD, PhD)** *Email address:* p.zheng.1@erasmusmc.nl *;* j.m.kros@erasmusmc.nl **Selected publications:** 1. **Kros JM**, Mustafa DM, Dekker LJ, Sillevis Smitt PA, Luider TM and **Zheng PP.** Circulating glioma biomarkers. *Neuro Oncol*. 2014. DOI: 10.1093/neuonc/nou207 [Epub ahead of print] 2. **Zheng PP,** van der Weiden M and **Kros JM.** Fast tracking of co-localization of multiple markers by using the nanozoomer slide scanner and NDPViewer. *J Cell Physiol*. 2014;229:967-73. 3. **Zheng PP,** van der Weiden M, van der Spek PJ, Vincent AJ and **Kros JM.** Intratumoral, not circulating, endothelial progenitor cells share genetic aberrations with glial tumor cells. *J Cell Physiol*. 2013;228:1383-90. 4. **Zheng PP**, van der Weiden M and **Kros JM.** Video-Coupled Laser Capture Microdissection Using the PALM MicroBeam: A Powerful Approach for Live Digital Data Communications in Biomedical Research and Education. *J Mol Genet Med* 2013;7. DOI: 10.4172/1747-0862.1000069 5. **Zheng PP**, van der Weiden M, van der Spek PJ, Vincent AJ and **Kros JM**. Isocitrate dehydrogenase 1R132H mutation in microglia/macrophages in gliomas: indication of a significant role of microglia/macrophages in glial tumorigenesis. *Cancer Biol Ther*. 2012;13:836-9. 6. **Zheng PP**, van der Spek PJ, Dirven CM, Willemsen R and **Kros JM**. Sinus venosus defect (SVD) identified in zebrafish Glut1 morphants by video imaging. *Int J Cardiol*. 2012;154:e60-1. 7. **Zheng PP**, Romme E, van der Spek PJ, Dirven CM, Willemsen R and **Kros JM**. HeNe laser (633 nm)-coupled confocal microscope allows simulating magnetic resonance imaging/computed tomography scan of the brain and eye: a noninvasive optical approach applicable to small laboratory animals. *Zebrafish*. 2011;8:83-5. 8. **Zheng PP**, Romme E, van der Spek PJ, Dirven CM, Willemsen R and **Kros JM**. Defect of development of ocular vasculature in Glut1/SLC2A1 knockdown in vivo. *Cell Cycle*. 2011;10:1871 - 1872.

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