ERASMUS UNIVERSITEIT ROTTERDAM

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Erasmus MC Department of Surgery, Division of Surgical Oncology
Project Title	A helping hand in personalized melanoma staging and treatment planning through characterization of melanoma cell biology of individual patients
Abstract:	Melanoma incidence has risen steadily during the last century, especially among young individuals. Importantly, melanoma presents a high degree of malignancy and aggressiveness, with an impressive viability and resistance to chemotherapy. Classically melanoma staging is based on TNM nomenclature, describing parameters such as tumor thickness and ulceration, involvement of lymph nodes and presence of distant metastasis. Based on these clinical parameters patients are staged at 4 levels with a number of substages. Staging of melanoma patients and treatment decision making is imprecise at the moment. The average expected survival indicated by the staging does not nearly reflect the true survival of the individual patient, mainly because of the very wide ranges. This is especially true in the so called stage III melanoma patients. The range of 5 year survival rates in this specific stage varies from 20% to 95%. In this project we hypothesize that we can improve staging, and thus prognosis and treatment planning, of melanoma patients by characterization of the biological capacities of melanoma cells per individual patient. To do so, melanoma cells are isolated from biopsies and tested ex vivo. The acquired biological data is used to cluster the patients. Using genetic analysis we provide possible markers which could replace the biological screening. Finally, we will perform functional assays on melanoma material cultured ex vivo to test new methods to improve sensitivity to anti-melanoma compounds.
Requirements of candidate:	Background: For this project we need an enthusiastic and highly motivated young scientist who has recently completed his/her MSc degree in (Molecular/Medical) Biology, Pharmaceutical Sciences or Medicine with strong emphasis for basic cell biology or a similar discipline. The candidate should preferably have experience in cell biological research and have a legal qualification as an animal experimentalist or is willing to obtain this qualification. Candidates English should meet following level: IELTS Grade: 7.0 (minimal 6.0 per component) or TOEFL: 100 (minimal 20 per component). The project should result in writing of a PhD thesis. Master degree: Yes

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	IELTS Grade: 7.0 *(minimal 6.0 per component)* *or* TOEFL: *100 (minimal 20 per component)* *or* PETS-5 level If the candidate does not hold any of these certificates an interview and a writing assignment maybe considered by the supervisor to establish the level of English.
Supervisor information:	Timo L.M. ten Hagen, PhD Associate Professor Laboratory Experimental Surgical Oncology Section Surgical Oncology Department of Surgery Erasmus MC Room Ee 0104a POBox 1738 3000 DR Rotterdam the Netherlands tel. +31 (0)10 70 43682 / 44568 mob. +31(0)6 14 37 58 63 fax. +31 (0)10 70 44746 postal address: Dr. Molewaterplein 50 3015 GE Rotterdam t.l.m.tenhagen@erasmusmc.nl http://www.surgical-oncology.nl *Recent publication list, 2013-2014* *Kaščáková S, Hofland LJ, De Bruijn HS, Ye Y, Achilefu S, van der Wansem K, van der Ploeg-van den Heuvel A, van Koetsveld PM, Brugts MP, van der Lelij AJ, Sterenborg HJ, Ten Hagen TL, Robinson DJ, van Hagen MP. Somatostatin analogues for receptor targeted photodynamic therapy. PLoS One. 2014 Aug 11;9(8):e104448. doi: 10.1371/journal.pone.0104448. eCollection 2014. PubMed PMID:*

	25111655; PubMed Central PMCID: PMC4128677. *Dicheva BM, Ten Hagen TL, Schipper D, Seynhaeve AL, van Rhoon GC, Eggermont AM, Koning GA. Targeted and heat-triggered doxorubicin delivery to tumors by dual targeted cationic thermosensitive liposomes. J Control Release. 2014 Aug 29. pii:S0168-3659(14)00578-1. doi: 10.1016/j.jconrel.2014.07.058. [Epub ahead of print]* *Pool SE, Kam BL, Koning GA, Konijnenberg M, Ten Hagen TL, Breeman WA, Krenning EP, de Jong M, van Eijck CH. [(111)In-DTPA]octreotide Tumor Uptake in GEPNET Liver Metastases After Intra-Arterial Administration: An Overview of Preclinical and Clinical Observations and Implications for Tumor Radiation Dose After Peptide Radionuclide Therapy. Cancer Biother Radiopharm. 2014 May;29(4):179-87.* *Seynhaeve AL, Rens JA, Schipper D, Eggermont AM, Ten Hagen TL. Exposing endothelial cells to tumor necrosis factor-α and peripheral blood mononuclear cells damage endothelial integrity via interleukin-1ß by degradation of vascular endothelial-cadherin. Surgery. 2014 Mar;155(3):545-53.* *Gül N, Babes L, Siegmund K, Korthouwer R, Bögels M, Braster R, Vidarsson G, ten Hagen TL, Kubes P, van Egmond M. Macrophages eliminate circulating tumor cells after monoclonal antibody therapy. J Clin Invest. 2014 Feb 3;124(2):812-23.* *Li L, ten Hagen TL, Haeri A, Soullié T, Scholten C, Seynhaeve AL, Eggermont AM, Koning GA. A novel two-step mild hyperthermia for advanced liposomal chemotherapy. J Control Release. 2014 Jan 28;174:202-8.* *Das AM, Seynhaeve AL, Rens JA, Vermeulen CE, Koning GA, Eggermont AM, Ten Hagen TL. Differential TIMP3 expression affects tumor progression and angiogenesis in melanomas through regulation of directionally persistent endothelial cell migration. Angiogenesis. 2014 Jan;17(1):163-77.* *Seynhaeve AL, Dicheva BM, Hoving S, Koning GA, ten Hagen TL. Intact Doxil is taken up intracellularly and released doxorubicin sequesters in the lysosome: evaluated by in vitro/in vivo live cell imaging. J Control Release. 2013 Nov 28;172(1):330-40.* *Bakker ER, Das AM, Helvensteijn W, Franken PF, Swagemakers S, van der Valk MA, ten Hagen TL, Kuipers EJ, van Veelen W, Smits R. Wnt5a promotes human colon cancer cell migration and invasion but does not augment intestinal tumorigenesis in Apc1638N mice. Carcinogenesis. 2013 Nov;34(11):2629-38* *Seynhaeve AL, Dicheva BM, Hoving S, Koning GA, Ten Hagen TL. Intact Doxil is taken up intracellularly and released doxorubicin*

	sequesters in the lysosome: Evaluated by in vitro/in vivo live cell imaging. J Control Release. 2013 Sep 4;172(1):330-340. *Pedrosa LR, van Hell A, Süss R, van Blitterswijk WJ, Seynhaeve AL, van Cappellen WA, Eggermont AM, Ten Hagen TL, Verheij M, Koning GA. Improving intracellular Doxorubicin delivery through nanoliposomes equipped with selective tumor cell membrane permeabilizing short-chain sphingolipids. Pharm Res. 2013 Jul;30(7):1883-95.* *Alic L, van Vliet M, Wielopolski PA, Ten Hagen TL, van Dijke CF, Niessen WJ, Veenland JF. Regional heterogeneity changes in DCE-MRI as response to isolated limb perfusion in experimental soft-tissue sarcomas. Contrast Media Mol Imaging. 2013 Jul;8(4):340-9.* *Li Li, Timo L.M. ten Hagen, Martin Hossann, Regine Suss, Gerard C. van Rhoon, Alexander M.M. Eggermont, Dieter Haemmerich, and Gerben A. Koning. Mild hyperthermia triggered doxorubicin release from optimized stealth thermosensitive liposomes improves intratumoral drug delivery and efficacy. J Control Release. 2013 Jun 10;168(2):142-50.* *Li L, Ten Hagen TL, Bolkestein M, Gasselhuber A, Yatvin J, van Rhoon GC, Eggermont AM, Haemmerich D, Koning GA. Improved intratumoral nanoparticle extravasation and penetration by mild hyperthermia. J Control Release. 2013 Feb 4;167(2):130-137.* *Ten Hagen TL, Seynhaeve AL, Aan de Wiel-Ambagtsheer G, de Bruijn EA, van Tiel ST, Ruegg C, Meyring M, Grell M, Goodman SL, Eggermont AM. The αVβ3/αVβ5 integrin inhibitor cilengitide augments tumor response to melphalan isolated limb perfusion in a sarcoma model. Int J Cancer. 2013 Jun 1;132(11):2694-704.* *van Horssen R, Hollestelle A, Rens JA, Eggermont AM, Schutte M, Ten Hagen TL. E-cadherin promotor methylation and mutation are inversely related to motility capacity of breast cancer cells. Breast Cancer Res Treat. 2012 Nov;136(2):365-77.* *Manzoor AA, Lindner LH, Landon CD, Park JY, Simnick AJ, Dreher MR, Das S, Hanna G, Park W, Chilkoti A, Koning GA, Ten Hagen TL, Needham D, Dewhirst MW. Overcoming limitations in nanoparticle drug delivery: triggered, intravascular release to improve drug penetration into tumors. Cancer Res. 2012 Nov 1;72(21):5566-75.* *van der Zee JA, Ten Hagen TL, Hop WC, van Dekken H, Dicheva BM, Seynhaeve AL, Koning GA, Eggermont AM, van Eijck CH. Bcl-2 associated anthanogen-1 (Bag-1) expression and prognostic value in pancreatic head and periampullary cancer. J Cancer. 2013 Jan;49(2):323-8.* *.*

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