

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Genetics
Project Title:	Ex vivo investigation of DNA damage response defects in prostate and bladder cancer
Abstract:	Genetic instability is a hallmark tumors. This can be the result of defects in DNA repair or other DNA damage response genes. Better understanding of these defects in individual tumors will aid in selecting the best therapy for these tumors and to develop novel therapeutic strategies. We already developed assays to assess the DNA repair status in breast and ovarian cancers and showed that a sizeable fraction of these tumors shows a defect in the homologous recombination pathway of DNA double strand break repair. We are currently extending these studies to bladder and prostate cancer. In collaboration with the Department of Urology we are setting up procedures for bladder cancer and prostate cancer cultures. The PhD student will set up and extend these studies using fresh tumor material from the clinic and material from mouse xenografts.
Requirements of candidate:	<p>Background: The candidate should have thorough knowledge of molecular cell biology. Experience in handling fresh primary cells or tumor tissue is an advantage, but not a mandatory. Flexibility in working hours is part of this project, as fresh tumor material from the clinic should be processed when it becomes available.</p> <p>Master degree: Yes IELTS Grade: 7.0 (<i>minimal 6.0 per component</i>) or TOEFL: 100 (<i>minimal 20 per component</i>)</p>
Supervisor information:	<p>Prof. dr. Jan H.J. Hoeijmakers / Dr. Dik C. van Gent Email address: d.vangent@erasmusmc.nl Personal website: http://www.erasmusmc.nl/genetica/research/vanGent/ http://www.erasmusmc.nl/genetica/research/</p> <p>Recent publication list, preferably last 3-5 years (1-2 pages)</p> <p>Van der Burg, M., IJspeert, H., Verkaik, N.S., Turul, T., Wiegant,</p>

	<p>W.W., Morotomi-Yano, K., Mari, P.O., Tezcan, I., Chen, D.J., Zdzienicka, M.Z., van Dongen, J.J.M. and van Gent, D.C. (2009) DNA-PKcs Mutation In a T-B-SCID Patient Inhibits Artemis Activation and Non-Homologous End-Joining. J. Clin. Invest., 119, 91-98.</p> <p>J.H. Hoeijmakers (2009) DNA Damage, aging, and cancer, NEJM <u>361</u>, 1475-1485</p> <p>G.A. Garinis, L.M. Uittenboogaard, H. Stachelscheid, M. Fousteri, W. van IJcken, T.M. Breit, H. van Steeg, L.H. Mullenders, G.T. van der Horst, J.c. Brüning, C.M. Niessen, J.H. Hoeijmakers, B. Schumacher (2009) Persistent transcription-blocking DNA lesions trigger somatic growth attenuation associated with longevity, Nat Cell Biol. <u>11</u>, 604-615</p> <p>Weterings, E., Verkaik, N.S., Keijzers, G., Florea, B.I., Wang, S.Y., Ortega, L.G., Uematsu, N., Chen, D.J. and van Gent, D.C. (2009) The Ku80 carboxy-terminus stimulates Joining and Artemis-mediated processing of DNA ends. Mol. Cell. Biol., 29, 1134-1142.</p> <p>Pothof, J., Verkaik, N.S., van IJcken, W., Wiemer, E.A.C., Ta, V.T.B., van der Horst, G.T.J., Jaspers, N.G.J., van Gent, D.C., Hoeijmakers, J.H.J. and Persengiev, S.P. (2009) MicroRNA-mediated Gene Silencing Modulates the UV-induced DNA Damage Response. EMBO J. 28, 2090-2099.</p> <p>Pothof, J., Verkaik, N.S., Hoeijmakers, J.H.J. and van Gent, D.C. (2009) MicroRNA responses and stress granule formation modulate the DNA damage response. Cell Cycle, 8, 3462-3468.</p> <p>J.R. Mitchell, M. Verweij, K. Brand, M. van de Ven, N. Goemaere, S. van den Engel, T. Chu, F. Forrer, C. Müller, M. de Jong, W. van IJcken, J.N. IJzermans, J.H. Hoeijmakers, R.W. de Bruin (2010) Short-term dietary restriction and fasting precondition against ischemia reperfusion injury in mice, Aging Cell 1, 40-53.</p> <p>Wouters, M.D., van Gent, D.C., Hoeijmakers, J.H.J., Pothof, J. (2011) MicroRNAs, the DNA damage response and cancer. Mutat Res. 717, 54-66.</p> <p>Pothof, J., and van Gent, D.C. (2011) Spatiotemporal aspects of MicroRNA mediated gene regulation. In: RNA infrastructure and networks, L.J. Collins (ed.), Landes Bioscience and Springer, Austin, TX, USA.</p> <p>H. Menoni, J.H. Hoeijmakers, W. Vermeulen (2012) Nucleotide excision repair-initiating proteins bind to oxidative DNA lesions in vivo. J Cell Biol. 199(7):1037-46.</p> <p>P. Schwertman, A. Lagarou, D.H. Dekkers, A. Raams, A.C. van der Hoek, C. Laffeber, J.H. Hoeijmakers, J.A. Demmers, M. Fousteri, W. Vermeulen, J.A. Marteijn. (2012) UV-sensitive syndrome protein UVSSA recruits USP7 to regulate transcription-coupled repair. Nat</p>
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	<p>Genet. 44(5):598-602.</p> <p>Naipal, K.A.T., Verkaik, N.S., Ameziane, N., van Deurzen, C.H.M., ter Brugge, P., Meijers, M., Sieuwerts, A.M., Martens, J.W., O'Connor, M.J., Vrieling, H., Hoeijmakers, J.H.J., Jonkers, J., Kanaar, R., de Winter, J.P., Vreeswijk, M.P., Jager, A., van Gent, D.C. (2014) Functional <i>ex vivo</i> assay to select Homologous Recombination deficient breast tumors for PARP inhibitor treatment. Clin. Cancer Res., <i>in press</i>.</p> <p>Marteijn J.A., Lans H., Vermeulen W., Hoeijmakers J.H.J.(2014) Understanding Nucleotide Excision Repair and its roles in Cancer and Ageing. Nature Rev Mol Cell Biol; 15, 465-481.</p>
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