ERASMUS UNIVERSITEIT ROTTERDAM

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Genetics
Project Title:	"The development of bio-informatics approaches to identify DNA damage response defects in human cancer".
Abstract:	Cancer is a disease of the genes. One of the hallmarks of cancer is genome instability, which is the result of defects in DNA repair or other DNA damage response (DDR) genes. Identification of specific DDR defects in tumor samples however, is comparable to finding the needle in the haystack, taking into account that the class of DNA repair and DDR genes already consists of a few hundred genes. Identification of DDR defects in human tumors is important to select the best therapy to avoid genotoxic cancer therapy resistance and develop novel therapeutic strategies. Over the past years, complete genome sequences of many tumors have been generated, but also enormous amounts of gene and microRNA expression datasets. These resources have not yet been used to their full potential regarding the DDR. The PhD student will develop novel bio-informatics approaches using large micro-array and next generation datasets from human tumors and cells exposed to various genotoxic stresses to identify DDR defects in cancer and mechanisms that render cancer cells resistant to genotoxic cancer treatments. These findings are important for better understanding of carcinogenesis, improved cancer treatment and prevention.
Requirements of candidate:	Background: The candidate should have a background in bio-informatics, programming skills and knowledge of molecular cell biology. Experience in analyzing next generation sequencing and micro-array datasets is an advantage, but not mandatory. Master degree: Yes IELTS Grade: 7.0 *(minimal 6.0 per component)* *or* TOEFL: *100 (minimal 20 per component)*

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Supervisor information:	Prof. Dr. Jan H.J. Hoeijmakers / Dr. J. Pothof Email address: j.pothof@erasmusmc.nl Personal website: http://www.erasmusmc.nl/genetica/research/ Recent publication list, preferably last 3-5 years (1-2 pages) J.H. Hoeijmakers (2009) DNA Damage, aging, and cancer, **NEJM** 361, 1475-1485 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**. 11, 604-615 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. 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. 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. B. Schumacher, I. van der Pluijm, M.J. Moorhouse, T. Kosteas, A.R. Robinson, Y. Suh, T.M. Breit, H. van Steeg, L.J. Niedernhofer, W. van IJcken, A. Bartke, S.R. Spindler, J.H. Hoeijmakers, G.T. van der Horst, G.A. Garinis. Delayed and accelerated aging share common longevity assurance mechanisms. **PLoS Genetics** 15, e1000161 (2008) I. van der Pluijm, G.A. Garinis, R.M.C. Brandt, T.G.M.F. Gorgels, S.W. Wijnhoven, K.E.M. Diderich, J. de Wit, J.R. Mitchell, C. van Oostrom, R. Beems, L.J. Niedernhofer, S. Velasco, E.C. Friedberg, K. Tanaka, H. van Steeg, J.H.J. Hoeijmakers, G.T.J. van der Horst. Impaired genome maintenance suppresses the GH/IGF1 axis in Cockayne syndrome mice. **PLoS Biol.** 5, 23-38 (2007) L.J. Niedernhofer, G.A. Garinis, A. Raams, S.A. Lalai, A.R. Robinson, E. Appeldoorn, H. Odijk, R. Oostendorp, A. Ahmad, W. van Leeuwen, A. Theil, W. Vermeulen, G.T. van der Horst, P. Meinecke, W. Kleijer, J. Vijg, N.G.J. Jaspers and J.H.J. Hoeijmakers. A new progeriod

	syndrome reveals that genotoxic stress suppresses the somatotroph axis. **Nature** 444, 1038-1043 (2006) (see also accompanying 'News and Views', Kirkwood) de Graaf EL, Vermeij WP, de Waard MC, Rijksen Y, van der Pluijm I, Hoogenraad CC, Hoeijmakers JH, Altelaar AF, Heck AJ. Spatio-temporal analysis of molecular determinants of neuronal degeneration in the aging mouse cerebellum. **Mol Cell Proteomics.** 2013 May;12(5):1350-62. doi: 10.1074/mcp.M112.024950. Epub 2013 Feb 11. Giglia-Mari G, Theil AF, Mari PO, Mourgues S, Nonnekens J, Andrieux LO, de Wit J, Miquel C, Wijgers N, Maas A, Fousteri M, Hoeijmakers JH, Vermeulen W. Differentiation driven changes in the dynamic organization of Basal transcription initiation. **PLoS Biol**. 2009 Oct;7(10):e1000220. 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.