

School/Department:	Department of Genetics
Project Title:	Investigating Transcription Coupled Repair from an RNA Polymerase point of view
Abstract:	<p>Accurate transcription and transmission of genetic information is vital for organism and requires an intact genome. However, DNA is continuously damaged by e.g UV-radiation, environmental chemicals and cellular metabolites that induce mutations and chromosomal aberrations, which are at the basis of oncogenic transformation. Moreover, DNA damage blocks transcription, causing cellular dysfunction or even apoptosis, resulting in DNA damage-induced aging [1]*. The cytotoxic damage-induced stalled RNA polymerase 2 (RNAP2) are removed by transcription-coupled repair (TCR). The severe symptoms associated with inherited TCR defects underscore its importance, but are also strikingly diverse, ranging from mild photosensitivity to severe progeria. Despite detailed information on factors involved in TCR, surprisingly little is known about the fate of lesion-stalled RNAP2 and how transcription is re-initiated after repair. Our recent data point to a central role for regulation of both by the post-translational modifier ubiquitin [3,4]*. To fully understand how cells deal with transcription blocking DNA damage we will use a multi-disciplinary approach including live cell imaging of fluorescent tagged RNAP2 and quantitative proteomics to: (1) analyse the fate of lesion-stalled RNAP2, (2) characterize transcription inhibition on different types of DNA damage and the proteins involved, (3) identify proteins that regulate transcription recovery after DNA repair (4) determine the ubiquitin-mediated regulation of these processes. This ambitious project will advance our understanding on the mechanism and biological impact of TCR and its role in DNA damage induced aging.</p> <p>Our recent identification of the causative gene for the last unresolved TCR disorder [4]* and the uncovering of a dynamic chromatin remodelling process that promotes re-initiation of stalled transcription [2]* indicates that our lab offers candidates ample expertise and state-of-the-art equipment to address these questions. Our lab hosts a group of international PhD students and Post-docs which, together with our departmental PhD training program, ensures intensive supervision of PhD students.</p>



ERASMUS UNIVERSITEIT ROTTERDAM

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

<p>Requirements of candidate:</p>	<p>Background: The candidate should have thorough knowledge of molecular and cellular biology. Experience in live cell imaging and image analysis and/or proteomics is an advantage, but not mandatory.</p> <p>Master degree: Yes</p> <p>IELTS Grade: 7.0 (<i>minimal 6.0 per component</i>) or TOEFL: 100 (<i>minimal 20 per component</i>)</p>
<p>Supervisor information:</p>	<p>Supervisors: Dr. J.A.F Marteijn and Prof.dr. W. Vermeulen</p> <p>Email address: J.Marteijn@erasmusmc.nl W.Vermeulen@erasmusmc.nl</p> <p>Personal website: http://www.vermeulenlab.com/</p> <p>Key publications ([x]*) relevant to the project:</p> <ol style="list-style-type: none"> 1. <i>Understanding nucleotide excision repair and its roles in cancer and ageing.</i> Marteijn JA, Lans H, Vermeulen W, Hoeijmakers JH (2014) Nature Review Mol Cell Biol. 2. <i>Enhanced chromatin dynamics by FACT promotes transcriptional restart after UV-induced DNA damage.</i> Dinant C, Ampatzidis-Michailidis G, Lans H, Tresini M, Lagarou A, Grosbart M, Theil AF, van Cappellen WA, Kimura H, Bartek J, Foustieri M, Houtsmuller AB, Vermeulen W and Marteijn JA (2013) Molecular Cell 3. <i>RNF168 Ubiquitinates K13-15 on H2A/H2AX to Drive DNA Damage Signaling.</i> Mattioli F, Vissers JHA, van Dijk WJ, Ikpa P, Citterio E, Vermeulen W, Marteijn JA, Sixma TK. (2012) Cell. 4. <i>UV-sensitive syndrome protein UVSSA recruits USP7 to regulate TCR.</i> Schwertman P, Lagarou A, Dekkers DH, Raams A, van der Hoek AC, Laffeber C, Hoeijmakers JH, Demmers JA, Foustieri M, Vermeulen W, Marteijn JA. (2012) Nature Genetics. <p>Selected other recent publications from the lab:</p> <ol style="list-style-type: none"> 1. Marteijn JA, Bekker-Jensen S, Mailand N, Lans H, Schwertman P, Gourdin AM, Dantuma NP, Lukas J, and Vermeulen W (2009). <i>The</i>

	<p>Journal of Cell Biology 186, 834-847.</p> <ol style="list-style-type: none"> 2. Lans H, Marteijn JA, Schumacher B, Hoeijmakers JH, Jansen G and Vermeulen W (2010) PLoS Genetics, e1000941 3. Anindya R, Mari PO, Fousteri M, Kristensen U, Kool H, Giglia-Mari G, Mullenders LH, Vermeulen W, Egly JM, and Svejstrup JQ (2010) Mol. Cell 38, 637-648. 4. Lans H, Marteijn JA, Vermeulen W (2012) Epig. & Chrom., 5:4. 5. Bergink S, Toussaint W, Luijsterburg MS, Dinant C, Alekseev S, Hoeijmakers JH, Dantuma NP, Houtsmuller AB and Vermeulen W (2012) J. Cell Biology 196, 681-688. 6. Pines A, Vrouwe MG, Marteijn JA, Typas D, Luijsterburg MS, Cansoy M, Hensbergen P, Deelder A, de Groot A, Matsumoto S, Sugasawa K, Thoma N, Vermeulen W, Vrieling H and Mullenders LH (2012) J. Cell Biol., 199: 235-249. 7. Menoni H, Hoeijmakers JH and Vermeulen W (2012) J. Cell Biol., 199: 1037-46. 8. Smeenk G, Wiegant WW, Marteijn JA, Luijsterburg MS, Sroczynski N, Costelloe T, Romeijn RJ, Pastink A, Mailand N, Vermeulen W, van Attikum H (2013) J. Cell Scie., 126: 889-903. 9. Theil AF, Nonnekens J, Steurer B, Mari PO, de Wit J, Lemaitre C, Marteijn JA, Raams A, Maas A, Vermeij M, Essers J, Hoeijmakers JH, Giglia-Mari G, Vermeulen W. (2013) PLoS Genetics, 9:e1003431. 10. Schwertman P, Vermeulen W, Marteijn JA (2013) Chromosoma, 122: 275-84. 11. Bergink S, Theil AF, Toussaint W, De Cuyper IM, Kulu DI, Clapes T, van der Linden R, Demmers JA, Mul EP, van Alphen FP, Marteijn JA, van Gent T, Maas A, Robin C, Philipsen S, Vermeulen W, Mitchell JR and Gutiérrez L (2013) Mol Cell Biol., 33: 3879-3892. 12. Lans H, Lindvall JM, Thijssen K, Karambelas AE, Cupac D, Fensgård Ø, Jansen G, Hoeijmakers JH, Nilsen H and Vermeulen W (2013) Cell Death & Diff. 20: 1709-1718. 13. Mandemaker IK, Vermeulen W, Marteijn JA (2014). Nucleus, 5:203-210 14. Aydin OZ, Marteijn JA, Ribeiro-Silva C, Rodríguez López A, Wijgers N, Smeenk G, van Attikum H, Poot RA, Vermeulen W, Lans H (2014) Nuc. Acid Res., 42: 8473-85
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