


PhD Project Description

Department:	Department of Medical Oncology. Erasmus MC
Supervisor information:	<ul style="list-style-type: none"> • Prof dr. John Martens (supervisor) • Dr. Harmen van de Werken & Dr. Martijn Lolkema (co-supervisors) • Email: j.martens@erasmusmc.nl and/or ccbc@erasmusmc.nl • Website: ccbc.erasmusmc.nl • Personal Grants: <ul style="list-style-type: none"> DDHF CCBC (2014 & 2018) Astellas (ML; 2014) NKB EMCR (2014) • Most important recent publications: <ol style="list-style-type: none"> 1. Priestley, Peter, Jonathan Baber, Martijn P. Lolkema, ..., Edwin Cuppen. 2019. "Pan-Cancer Whole Genome Analyses of Metastatic Solid Tumors." <i>Nature</i> 575(7781):210-216 2. Lindsay Angus, ..., Martijn P. Lolkema, ..., Harmen J.G. van de Werken, ..., John W.M. Martens 2019. "Genomic landscape of metastatic breast cancer and its clinical implications". <i>Nature Genetics</i> 51(10):1450-1458.. 3. Dessel, Lisanne F. van, ..., Harmen J. G. van de Werken, ..., John W.M. Martens, ... and Martijn P. Lolkema. 2019. "The Genomic Landscape of Metastatic Castration-Resistant Prostate Cancers Using Whole Genome Sequencing Reveals Multiple Distinct Genotypes with Potential Clinical Impact." <i>Nature Communication</i> 10(1):5251 4. Nik-Zainal, Serena, ... John W. M. Martens, ..., and Michael R. Stratton. 2016. "Landscape of Somatic Mutations in 560 Breast Cancer Whole-Genome Sequences." <i>Nature</i> 534(7605):47–54. 5. Smid, Marcel, .., John W. M. Martens. 2016. "Breast Cancer Genome and Transcriptome Integration Implicates Specific Mutational Signatures with Immune Cell Infiltration." <i>Nature Communications</i> 7:12910. 6. Queirós, Ana C.,..., Harmen J. G. van de Werken, ... and José I. Martín-Subero. 2016. "Decoding the DNA Methylome of Mantle Cell Lymphoma in the Light of the Entire B Cell Lineage." <i>Cancer Cell</i> 30(5):806–21. 7. van de Werken, Harmen J. G., 2012 et al. "Robust 4C-Seq Data Analysis to Screen for Regulatory DNA Interactions." <i>Nature Methods</i> 9(10):969–72. 
Project Title:	Cancer Computational Biology and its Clinical Value using Multiple State-of-the-art Omics Data of Prostate and Breast Cancer Patients.
Abstract:	<p>Cancer onset, progression and drug resistance mechanisms are driven by hereditary and somatically acquired genomic aberrations. Many cancer driver genes and their coding changes are currently known. However more than 98% of the somatic DNA mutations in cancer occur in non-coding areas of the human genome and their contribution towards cancer cell behavior is still enigmatic. In this project we will interrogate the entire cancer genome with a focus on its regulatory part including promoters, enhancers, silencers and regions generating non-coding RNAs to gain insight in their contribution to cancer progression and mechanisms of drug-resistance. Moreover, we aim to develop novel tools that may improve patient stratification.</p> <p>Currently, we possess world-wide the largest metastatic Whole Genome Sequencing data sets from breast (Currently, n > 600) and prostate cancer patients (n > 400)^{1,2,3} and matched RNA-seq data. These comprehensive data sets will give us the opportunity to unravel novel biology including interaction of DNA elements and regulatory mechanisms. We will apply next to state-of-the-art bioinformatics and statistical analyses, Machine Learning methods to interrogate this rich data source. We will compare the results to primary cancer^{4,5} and integrate our data with publicly available data sources from ChIP-seq and 3D chromosome conformation capture assays⁷ to reveal non-coding drivers of cancer initiation and progression and importantly drug-resistance^{3,6}. Ultimately, we will apply this gained knowledge to improve patient stratification.</p> <p>The PhD student will be supervised by a team of molecular biologists, clinicians and computational biologists headed by respectively prof. J. Martens, dr. M. Lolkema and dr. H. van de Werken. The student will be housed in the Erasmus MC CCBC (https://ccbc.erasmusmc.nl/). The PhD-student will be engaged in the excellent educational PhD and career guidance program at Erasmus MC.</p>

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Requirements of candidate:	<ul style="list-style-type: none">• We are looking for a candidate with strong analytical and problem solving skills, being highly motivated and having excellent communication and writing skills and able to work independently. A background in cancer biology is of significant added value.• Master degree in bioinformatics, computational biology, statistics or a related field.• The candidate should have demonstrated excellent scientific writing and software engineering skills in R and Perl or Python and preferably in Java.• Scholarship that will, at least, cover subsistence allowance and international air plane ticket (we could help with the scientific part of your scholarship proposal)• The student should be fluent in English (English speaking countries & Netherlands): no requirement; Other countries: IELTS 7.0 (min 6.0 for all subs), TOEFL 100 (min 20 for all subs).
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Application requirements & Deadlines:

<https://www.eur.nl/en/about-eur/erasmus-university-china-centre/csc-scholarship>

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<https://www.usnews.com/education/best-global-universities/clinical-medicine?page=3>

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<https://www.natureindex.com/supplements/nature-index-2019-biomedical-sciences/tables/healthcare>