

PhD Project Description

School/Department:	Department of Clinical Genetics Erasmus MC
Supervisor information:	<ul style="list-style-type: none"> • Stefan Barakat, M.D., Ph.D., MSc., principal investigator • Email: t.barakat@erasmusmc.nl <ul style="list-style-type: none"> • Website: https://www.erasmusmc.nl/en/research/groups/barakat-lab-non-coding-genome-in-clinical-genetics • Personal Grants: Niels Stensen Fellowship (2014); EMBO Long-Term Fellowship (2014); Marie Skłodowska-Curie Individual Fellowships (IF-EF) (2015); Human Frontiers Science Project Long-Term Fellowship (2015); Wellcome Trust ISSF2 award (2015); NARSAD Young Investigator Award (2016); ZonMW VENI award (2016); Erasmus MC fellowship (2017); EMC Human Disease Model Award (2018) • Awards: American Society of Human Genetics (ASHG) Charles J. Epstein Award for Excellence in Human Genetics Research (2015); International Society for Differentiation Beverly Kerr McKinnel Award, for outstanding research as a PhD student (2012) • Most important publications: (H-index:14; total citations:>1320) (sep 2020) Nature Reviews Neurology doi: 10.1038/s41582-020-0395-6 (IF: 27.0) (apr 2020) Acta Neuropathologica doi: 10.1007/s00401-020-02128-8 (IF:18.2) (dec 2019) Acta Neuropathologica doi: 10.1007/s00401-019-02109-6 (IF:18.2) (aug 2018) Cell Stem Cell doi: 10.1016/j.stem.2018.06.014 (IF:23.3) (aug 2015) Genome Biology doi: 10.1186/s13059-015-0698-x (IF:11.9) (mar 2014) Molecular Cell doi: 10.1016/j.molcel.2014.02.006 (IF:14.7) (mar 2013) Cell Reports doi: 10.1016/j.celrep.2013.02.018 (IF:8.3) (apr 2012) Nature doi: 10.1038/nature11070 (IF:40.1) (jun 2012) Molecular Cell doi: 10.1016/j.molcel.2012.04.003 (IF:14.7) (oct 2011) Nucleic Acid Research doi: 10.1093/nar/gkr550 (IF:9.2) (jun 2010) Cell Stem Cell doi: 10.1016/j.stem.2010.05.003 (IF:23.3) (nov 2009) Cell doi: 10.1016/j.cell.2009.10.034 (IF:30.4) For full list see: https://www.ncbi.nlm.nih.gov/pubmed/?term=tahsin+stefan+barakat
Project Title:	Deciphering the role of Non-Coding DNA sequences in the genetics of neurodevelopmental disorders
Abstract:	<p>Despite the fact that we know that the majority of DNA sequences (~98%) in the human genome do not encode protein-coding genes, our understanding of those sequences and why they are important is still far from complete. An important group of non-coding genome elements are enhancers that are crucial for the proper regulation of spatiotemporal gene expression. The clinical genetic work-up of patients suffering from neurodevelopmental disorders currently focusses almost completely on exons. An attractive hypothesis is that currently genetically unexplained patients might have mutations in regulatory elements such as enhancers that might cause their phenotype, but before this hypothesis can be tested on a large scale it is crucial to identify regulatory elements involved in brain development.</p> <p>In my lab, we are trying to understand the role of regulatory elements in brain development using several approaches. We are using state-of-the-art techniques to profile the epigenome of cerebral organoids using ChIP-seq, ATAC-seq, and single cell RNA-seq to identify putative regulatory elements. Using ChIP-STARR-seq, a novel type of massively parallel reporter assay system that we have developed, we are generating genome-wide enhancer activity maps of various brain related cell types. Using functional genomics and CRISPR-Cas9 mediated screens, we validate putative enhancers. Integrative computational analysis and data mining further helps us to identify crucial regulatory elements, that we sequence in a large cohort of genetically unexplained patients. Using iPSC technology combined with genome-engineering, we validate our findings. In addition, we perform disease modeling for novel genetic neurodevelopmental disorder. Ultimately, our efforts will lead to an enhanced understanding of the brain regulome and will lead to novel diagnostic approaches for patients suffering from neurodevelopmental disorders.</p>
Requirements of candidate:	<ul style="list-style-type: none"> • We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. • Master degree or MD • Scholarship that will, at least, cover subsistence allowance and international air plane ticket (we could help with the scientific part of your scholarship proposal) • English language requirement: • <i>English speaking countries & Netherlands:</i> no requirement • <i>Other countries:</i> IELTS 7.0 (min 6.0 for all subs), TOEFL 100 (min 20 for all subs)

Erasmus MC, ranked world no. 32 for [Clinical Medicine US News 2020](#) no. 30 [Nature Index for Biomedical Sciences 2019](#)

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Application requirements & Deadlines:

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

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** No.32 for Clinical Medicine US News 2020:*

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

** No. 30 Nature Index for Biomedical Sciences 2019:*

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