

PhD Project Description

School/Department:	Dept Internal Medicine-Endocrinology, Erasmus MC
Supervisor information:	<ul style="list-style-type: none"> • Prof dr. M.C. (Carola) Zillikens; Email: m.c.zillikens@erasmusmc.nl Website: <ul style="list-style-type: none"> • http://glimdna.org/ • https://www.erasmusmc.nl/en/research/groups/genetic-laboratory-of-internal-medicine • https://www.erasmusmc.nl/en/research/researchers/zillikens-carola • https://www.erasmusmc.nl/en/research/groups/laboratory-for-calcium-and-bone-metabolism • Grants: <ul style="list-style-type: none"> - Several grants from Dutch and Australian Government and private foundations • Most important publications: <ol style="list-style-type: none"> 1. Waqas K, Chen J, et al. J Bone Miner Res. 2020 May 28. doi: 10.1002/jbmr.4096. 2. van den Beld AW. Lancet Diabetes Endocrinol. 2018 Aug;6(8):647-658 3. Jiang X, et al. Nat Commun. 2018 Jan 17;9(1):260. 4. Zillikens MC*, et al Nature Commun 2017 Jul 19;8(1):80. Erratum in: Nat Commun. 2017 Nov 7;8(1):1414. 5. Zheng HF, et al. Nature. 2015 Oct 1;526(7571):112-7 6. Locke AE, et al. Nature. 2015 Feb 12;518(7538):197-206. 7. Shungin D, et al. Nature. 2015 Feb 12;518(7538):187-96. 8. van Dijk FS*, Zillikens MC*, et al. N Engl J Med. 2013 Oct 17;369(16):1529-36. 9. Zhu H, et al. Cell. 2011 Sep 30;147(1):81-94 10. Kilpelainen TO, et al. Nat Genet. 2011 Aug;43(8):753-60
Project Title:	Advanced glycation end products in relation to ageing and age-related diseases
Abstract:	<p>Advanced glycation end products (AGEs) are heterogeneous glycosylated products that accumulate in the body over lifetime as part of normal ageing but increased under certain conditions. It is becoming more and more clear that they are involved in age-related diseases as evidence from population studies and wet-lab studies accumulates (Singh et al. 2001). AGEs (e.g. glucospane, pentosidine and carboxymethyllysine) are produced after glycation of protein amino acid residues, lipids or nucleic acids and sometimes through oxidation without enzymatic catalysis (Vistoli et al. 2013). They tend to accumulate in long-lived tissues because of irreversible formation and limited clearance. In diseases such as diabetes and renal failure, the accumulation of AGEs is accelerated and lifestyle factors such as smoking and diet also contribute to the accumulation (van Waateringe et al. 2016). AGEs can exert influence through several mechanisms, e.g., through formation of cross-links in extracellular matrix or binding to its transmembrane receptor RAGE. Several studies have found some evidence of an association between AGEs and type 2 diabetes and complications, cardiovascular diseases, and neurodegenerative diseases (Chaudhuri et al. 2018). However, large-scale population based studies are scarce.</p> <p>Within the Rotterdam Study - a large population-based prospective cohort study in the Netherlands - we have assessed AGEs accumulation level in the skin as a reflection of AGEs accumulation in long-lived tissues using a device called the AGE Reader™. It measures the skin fluorescence based on the fluorescent property of several AGEs and so far 3009 participants had the measurement from 2013-2016. We have shown cross-sectional associations between skin AGEs and several traits including vitamin D levels (Chen J et al. 2018), bone fractures (Waqas K 2020), cognition (Chen J et al unpublished, Mooldijk et al 2020) and cardiovascular diseases (Chen J. et al unpublished). We also have estimated dietary AGEs intake from previous visits and have shown a weak relation with skin AGEs (Chen J et al. 2020) and with stool microbiome (Chen J et al. unpublished) and fractures (Waqas K et al. 2020). Follow-up data on incident diseases are being collected every 3-5 years. Repeated measurements of skin AGEs are planned for 2021. We plan to also measure levels of AGEs in serum. In the current project, we aim to study the association between skin AGEs and serum and dietary AGEs using prospective data on incident disease events and perform repeated measurements of skin AGEs. We also plan genetic studies performing GWAS on skin AGEs and through Mendelian Randomisation (MR) techniques we want to study whether the observed associations are causal. We plan to do this in international consortia, where the Rotterdam Study group has leading roles.</p> <p>The Rotterdam Study has been designed by the Department of Epidemiology of Erasmus MC, featured with densely and deeply phenotyped baseline and follow-up information on incident diseases, multi-layer omics data including genome-wide association studies, whole exome sequencing, transcriptomics, methylation and microbiome data as well as detailed life style information including dietary information, medical history and medication use.</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:

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

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| | <ul style="list-style-type: none">○ <i>English speaking countries & Netherlands: no requirement</i>○ <i>Other countries: IELTS 7.0 (min 6.0 for all subs), TOEFL 100 (min 20 for all subs)</i> |
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Application requirements & Deadlines:

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

Erasmus MC, ranked world

** 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>