

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Erasmus Medical Center, Department of Epidemiology
Project Title:	Identifying metabolomics signature of Type-2 Diabetes Mellitus
Abstract:	<p>Type 2 diabetes (T2DM) is common metabolic disease with increased risk of cardiovascular events and high comorbidity to other disorders. Recent developments in the metabolomics profiling method enable the researchers to assess global metabolomics changes related to T2DM and its subclinical markers. So far carnitines, some phospholipids and branch chain amino-acids have been found associated to T2DM. Such data of high resolution metabolomic (563 metabolites) profiles are available in the Erasmus Rucphen Family (ERF) population (n=3000), measured by 5 different platforms, either by mass spectrometry or nuclear magnetic resonance. The aim of the study is to:</p> <ol style="list-style-type: none"> 1. Determine which metabolites associate with T2DM related quantitative measurements such as insulin, HOMA-IR, triglycerides and glucose in non-diabetic population. 2. Select a metabolic risk profiles and predict incident T2DM in ERF. 3. Test which metabolites are causally related to T2DM using Mendelian Randomization (MR). In the PhD program, the student will analyse the metabolomic data with R under Linux, and use statistical and genetic methods to research on metabolite profiles of T2DM and relate this information to metabolic pathways. Findings will be validated in the international MAGNETICS Consortium, as well as in the Rotterdam Study (totaling approximately 15,000 subjects).
Requirements of candidate:	<p>Background: Medical Student, experience with Epidemiology of common endocrinologic diseases, such as type-2 diabetes and metabolic syndrome. Experience with metabolomics datasets, Linux, R statistical computing, SPSS, SAS. From 211 and 985 University.</p> <p>Study Score more than 3.7/4 as an undergraduate student, or more than 2.85/3 as a master student. The candidate should have at least one publication.</p> <p>Master degree: Not necessary IELTS Grade: 6.5</p>

<p>Supervisor information:</p>	<p>Prof. Cornelia M van Duijn e-mail: c.vanduijn@erasmusmc.nl Recent publication list, preferably last 3-5 years (1-2 pages)</p> <ol style="list-style-type: none"> 1. Ling Y, ... van Duijn CM, Gao X, Sijbrands EJ. A genetic variant in SLC6A20 is associated with Type 2 diabetes in white-European and Chinese populations. Diabet Med. 2014 Jun 23. 2. DIAbetes Genetics Replication And Meta-analysis (DIAGRAM) Consortium, ... van Duijn CM, ...Morris AP. Genome-wide trans-ancestry meta-analysis provides insight into the genetic architecture of type 2 diabetes susceptibility. Nat Genet. 2014 Mar;46(3):234-44. 3. Lange LA, ...van Duijn CM,...Willer CJ; NHLBI Grand Opportunity Exome Sequencing Project. Whole-exome sequencing identifies rare and low-frequency coding variants associated with LDL cholesterol. Am J Hum Genet. 2014 Feb 6;94(2):233-45. 4. Versmissen J, ...van Duijn CM, ... Sijbrands EJ. Identifying genetic risk variants for coronary heart disease in familial hypercholesterolemia: an extreme genetics approach. Eur J Hum Genet. 2014 Jun 11. 5. Peloso GM, ... van Duijn CM,...Cupples LA. Association of low-frequency and rare coding-sequence variants with blood lipids and coronary heart disease in 56,000 whites and blacks. Am J Hum Genet. 2014 Feb 6;94(2):223-32. 6. Global Lipids Genetics Consortium, Willer CJ, ...van Duijn CM, Abecasis GR. Discovery and refinement of loci associated with lipid levels. Nat Genet. 2013 Nov;45(11):1274-83. 7. Yaghootkar H, ...van Duijn CM, ...,Frayling TM. Mendelian randomization studies do not support a causal role for reduced circulating adiponectin levels in insulin resistance and type 2 diabetes. Diabetes. 2013 Oct;62(10):3589-98. doi: 10.2337/db13-0128. Epub 2013 Jul 8. Review. 8. Fall T, ... van Duijn CM, ... European Network for Genetic and Genomic Epidemiology (ENGAGE) consortium. The role of adiposity in cardiometabolic traits: a Mendelian randomization analysis. PLoS Med. 2013;10(6):e1001474. 9. Rivera NV, ...van Duijn CM, ... Briguori C. Assessment of the 9p21.3 locus in severity of coronary artery disease in the presence and absence of type 2 diabetes. BMC Med Genet. 2013 Jan 23;14:11. 10. Scott RA, ...van Duijn CM, ...Barroso I. Large-scale association analyses identify new loci influencing glycemic traits and provide insight into the underlying biological pathways. Nat Genet. 2012 Sep;44(9):991-1005. 11. Morris AP, ... van Duijn C, ...McCarthy MI; DIAbetes Genetics tion And Meta-analysis (DIAGRAM) Consortium. Large-scale association analysis provides
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	<p>insights into the genetic architecture and pathophysiology of type 2 diabetes. Nat Genet. 2012 Sep;44(9):981-90.</p> <p>12. Manning AK, ..., van Duijn CM, ...Langenberg C. A genome-wide approach accounting for body mass index identifies genetic variants influencing fasting glycemic traits and insulin resistance. Nat Genet. 2012 May 13;44(6):659-69.</p> <p>13. Dastani Z...,van Duijn C...,Kathiresan S. Novel loci for adiponectin levels and their influence on type 2 diabetes and metabolic traits: a multi-ethnic meta-analysis of 45,891 individuals. PLoS Genet. 2012;8(3):e1002607.</p> <p>14. Demirkan A, van Duijn CM, ... Schmitz G; EUROSPAN consortium. Genome-wide association study identifies novel loci associated with circulating phospho- and sphingolipid concentrations. PLoS Genet. 2012;8(2):e1002490.</p> <p>15. Palmer ND, van Duijn CM, ...Genome-wide association study identifies loci influencing concentrations of liver enzymes in plasma. Nat Genet.2011 Oct 16;43(11):1131-8.</p> <p>16. Willems SM, Mihaescu R, Sijbrands EJ, van Duijn CM, Janssens AC. A methodological perspective on genetic risk prediction studies in type 2 diabetes: recommendations for future research. Curr Diab Rep. 2011 Dec;11(6):511-8.</p> <p>17. Janssens AC, ...van Duijn CM, Mackenbach JP. Accuracy of self-reported family history is strongly influenced by the accuracy of self-reported personal health status of relatives. J Clin Epidemiol. 2012 Jan;65(1):82-9.</p> <p>18. Kanoni S, ... van Duijn CM, ... Franks PW, Dedoussis GV. Total zinc intake may modify the glucose-raising effect of a zinc transporter (SLC30A8) variant: a 14-cohort meta-analysis. Diabetes. 2011 Sep;60(9):2407-16.</p> <p>19. Kilpeläinen TO, ... van Duijn CM,...Loos RJ. Genetic variation near IRS1 associates with reduced adiposity and an impaired metabolic profile. Nat Genet. 2011 Jun 26;43(8):753-60.</p> <p>20. van Hoek M, ... van Duijn CM,...Sijbrands EJ. Association of an APOC3 promoter variant with type 2 diabetes risk and need for insulin treatment in lean persons. Diabetologia. 2011 Jun;54(6):1360-7.</p> <p>21. Nettleton JA, ...van Duijn CM, Meigs JB. Interactions of dietary whole-grain intake with fasting glucose- and insulin-related genetic loci in individuals of European descent: a meta-analysis of 14 cohort studies. Diabetes Care. 2010 Dec;33(12):2684-91.</p> <p>22. : Schuur M, Henneman P, van Swieten JC, Zillikens MC, de Koning I, Janssens AC, Witteman JC, Aulchenko YS, Frants RR, Oostra BA, van Dijk KW, van Duijn CM.Insulin-resistance and metabolic syndrome are related to executive function in women in a large family-based study. Eur J Epidemiol. 2010 Aug;25(8):561-8.</p>
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