MCPS Projects Tracker

Projects are show in order of Start Date with most recent first and those started in the last 3 months are highlighted in pink.
Individual Data Sharing Agreements are no longer available

Mexico City-led

	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Title **Description of Runs of Heterozygosity (ROH) in the MCPS population**							
Status To begin	Oscar Pérez Flores, Jaime Berumen Campos	N/A	01/04/2024	No	N/A	N/A	37

Research Summary/Abstract: Run of Homozygosity (ROH) typically indicates regions of the genome where both alleles are identical by descent, resulting in regions of homozygosity. This can occur through mechanisms such as uniparental disomy (UPD), or copy-neutral loss of heterozygosity (CN-LOH).
In the context of genetic research, the analysis of ROH can provide valuable insights into several aspects in the MCPS population. The presence or absence of ROH regions can reflect historical demographic events, population admixture, or genetic drift. Also, a lack of ROH may indicate recent common ancestry or inbreeding within a population. Inbreeding can lead to the increased frequency of homozygous regions in the genome due to the inheritance of identical alleles from common ancestors. Moreover, the presence of ROH regions in the genome can result in the manifestation of recessive genetic disorders.
This approach will allow the characterization of genetic diversity and population structure of the MCPS population. As well as infer historical demographic events, population migrations, and patterns of admixture.

Further information: N/A

	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Title **Metabolomics and other risk factors involved in prediabetes and undiagnosed diabetes: a window opportunity for prevention.**							
Status Analyses Ongoing	Paulina Baca Peynado, Jaime Berumen Campos	N/A	01/03/2024	No	N/A	N/A	36

Research Summary/Abstract: The influence of fat and lipids on type 2 diabetes has not been well established in Mexico and other regions of the world due to the focus of case-control studies on individuals already diagnosed with diabetes, who often have had the disease for many years. Diabetic individuals commonly experience weight loss and alterations in their lipid profile as the disease progresses. These changes are attributed to peripheral resistance to insulin or decreased insulin secretion by the pancreas, as insulin plays a crucial role in lipid synthesis and storage. This study aims to investigate the impact of total body fat (BMI), fat distribution (WHR), and blood lipids on prediabetes and undiagnosed diabetes. We seek to determine whether these factors exhibit similarities in both conditions and which factors contribute to the progression from prediabetes to type 2 diabetes. Additionally, we aim to determine the percentage of prediabetic individuals who transition to type 2 diabetes and the duration between these two states.
A total of 106,810 individuals (comprising those with available blood lipid data and genetic ancestry) will be included in this analysis. The sample will be classified into four groups: 1) known diabetics, 2) undiagnosed diabetics, 3) prediabetics, and 4) controls. All four groups will be included in the descriptive portion of the study. To identify the factors associated with prediabetes and undiagnosed diabetes, both case-control studies and a case (prediabetes)-case (undiagnosed diabetics) study will be conducted. All factors measured in the metabolomic analysis, as well as fat-related and lifestyle factors, will be included in the analysis. ANOVA analysis will be performed on all quantitative factors, and those showing differences between comparison groups will be selected for further analysis using univariate regression models. Finally, several multivariate models will be constructed as necessary. The percentage of prediabetic patients progressing to type 2 diabetes will be determined by examining data from the ongoing re-survey. The duration between the progression of prediabetes to type 2 diabetes will be indirectly calculated using the frequency distribution of both diseases across age intervals.

Further information: N/A

	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Title **Influence of risk factors and genetic ancestry on metabolic syndrome: analysis of 140,000 Individuals in the Mexico City Prospective Study.**							
Status Analyses ongoing	Paulina Baca Peynado, Jaime Berumen Campos	N/A	01/03/2024	No	N/A	N/A	35

Research Summary/Abstract: Metabolic syndrome (MS) is a group of conditions that together raise the risk of diabetes, coronary heart disease, stroke, and other serious health problems. Metabolic syndrome is also called insulin resistance syndrome. The diagnosis of MS is made when a person has altered 3 or more of the following 5 factors or body measurements: blood sugar, waist circumference (WC), high blood pressure, triglycerides, and low-density lipoprotein (HDL). In this paper we will study the role played by each of the factors involved and genetic ancestry in MS in the cohort of 140,000 Mexicans from Mexico City and their differences between the sexes and appearance before or after the age of 50. A total of 106,810 individuals (those with blood lipid data and genetic ancestry) will be included in this analysis. By definition, we will exclude from the diagnosis of MS individuals who already had diabetes before the study or who were diagnosed during recruitment, as well as those who had a cardiovascular disease (coronary heart disease, stroke), leaving a total of 84,429 (56,779 women and 27,650 men). A descriptive analysis of the MS and its subgroups, the 5 factors involved and the difference in the distribution by degree (quartiles) of Amerindian ancestry in the entire study population and stratified by age and sex will be carried out. It will also be investigated which is the best cut-off value for CC and HDL by means of analysis with ROC curves. Likewise, the effect of each of the factors, ancestry and various factors related to lifestyle on the risk of suffering from MS will be investigated through univariate and multivariate logistic regression models.

Further information: N/A

		MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Title	**Genetic structure of copy number variations (CNVs) and their association with diabetes, obesity and cardiovascular disease: genome analysis of 140,000 Mexicans**							
Status	Analyses ongoing	Georgina Del Vecchyo Tenorio, Fernando Rivas, Jaime Berumen Campos	N/A	01/03/2024	No	N/A	N/A	31
Research Summary/Abstract	CNVs (Copy Number Variations) are structural variations of chromosomes greater than 1000 bp that can intersect with multiple genes, appearing as deletions or duplications, compared to a reference genome. They are an important source of genetic variation with implications from evolution to disease development. They were originally identified in patients with genetic disorders, however, CNVs are present in the human genome of healthy people. With the increase in studies and advances in next-generation sequencing (NGS) technology of the exomic and complete genome, the catalog of CNVs has increased considerably. In a study carried out with data from the UK Biobank where 54 CNVs known for their associations with diseases due to genomic disorders or clinical phenotypes were analyzed, it was determined that these CNVs have effects on health and mortality. Diseases such as diabetes, hypertension, obesity, and kidney damage were also found to be related to CNVs identified in specific genetic regions. Likewise, CNVs can be used as robust tumor biomarkers to subtype and make survival prognoses; they allow identification of how mutations occur and in what order. In Mexico, there have been a few studies of CNVs associated with diseases. The call for CNV variants in data from the Mexico City Prospective Study (MCPS) allows us to investigate how CNVs contribute to population genetic variability and how their presence is associated with specific health conditions and genetic disorders.							
Further information	N/A							
Title	**Genetics of human healthspan and lifespan in the MCPS**							
Status	Analyses ongoing	Paulina Baca Peynado, Jaime Berumen Campos	N/A		No	N/A	N/A	34
Research Summary/Abstract	Age is the most important risk factor in disease development. It is expected that for the first time in human history, there will be more older people than adolescents and young adults combined, result of an improvement in human health care. Unfortunately, the increase in lifespan has not been followed by a parallel increase in healthspan, the morbidity-free lifespan, often termed as “healthspan” as more than 90% of the individuals above 65 years have at least one chronic disease. Thus, it has been hypothesized that addressing aging physiology, as opposed to treating each age-associated disease individually, could delay the appearance of multiple chronic diseases. Recent human genetic studies support this hypothesis showing that the same conserved pathways modulate lifespan and healthspan in humans. Therefore, the identification of genetic variants that affect these phenotypes promises a contribution in the quality of life by increasing the discovery of key genes and pathways that could perform as molecular targets for the development of therapies to prevent and attenuate multiple age-related diseases. The present study aims to identify the loci associated to healthspan and lifespan in the Mexican population.							
Further information	N/A							

	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID

Mexico City MSc & PhD Student

Title **Genome-wide Association Study in Lean and Obese Type 2 Diabetics**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Alberto Zarza Vela	N/A	01/01/2024	No	N/A	N/A	33

Research Summary/Abstract: Type 2 diabetes (T2D) is a heterogeneous illness caused by genetic and environmental factors. A complex pattern of genetic susceptibility and environmental exposures by individual leads to significant heterogeneity in the pathogenesis of T2D between individuals. Most GWAS do not consider the underlying the heterogeneity between cases, but studies that stratify cases have found evidence for different genetic profiles between subgroups of T2D. Cases of T2D have already been stratified according to body mass index in a meta-analysis of previous GWAS findings, revealing a difference in the genetic profile between lean individuals and obese individuals. In the MCPS, T2D cases will be stratified into two subgroups on the basis of BMI, and GWAS will be performed for all T2D cases and for each subgroup relative to controls. We will identify SNP's associated with T2D across the subgroups and test for heterogenous SNP effects within these subgroups.

Further information: N/A

Title **Cognitive impairment at older ages among 8000 men and women living in Mexico City: cross-sectional analyses of a prospective study**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Paper to be submitted to academic journal	Carlos González-Carballo	N/A	01/06/2023	No	N/A	N/A	32

Research Summary/Abstract: Importance: There is limited population-based evidence on the prevalence of cognitive impairment in Mexico, a country with a rapidly aging population and where key risk factors, such as diabetes and obesity, are common.
Design, Setting, and Participants: This cross-sectional population-based study included participants from the Mexico City Prospective Study that recruited 50,000 men and 100,000 women aged ≥35 years from two districts in 1998-2004. In 2015-2019 about 10,000 survivors were resurveyed with identical information from the original survey and additional assessments including a cognitive assessment. The main analyses included those aged 50- 89 years with complete cognitive assessment and covariate data at resurvey. Results: Of the 9,288 participants aged 50-89 years at the 2015-2019 resurvey with complete data, 8,197 reported having at least some years of formal education. Among these (mean age 66 years; 31% men), their mean MMSE score was 26.2 (SD 3.6) points, 1,941 (24%) had cognitive impairment. The sex- and district-standardised prevalence of cognitive impairment increased strongly with age, from 10% in those 50-59 years to 55% in those aged 80-89. After accounting for the effects of age, sex, and district there was little difference in the prevalence of cognitive impairment between participants with or without diabetes, hypertension, overweight or obesity (BMI ≥25 km/m2), or high levels of fat mass.
Conclusion and relevance: In this population of adults aged 50-89 years from two districts of Mexico City, the prevalence of cognitive impairment was high, particularly among women. The extent to which cognitive impairment relates to health outcomes in this population needs to be investigated.

Further information: N/A

Title **Identification of genes associated with type 2 diabetes specific to sex, age at disease onset and BMI: a whole human genome study in 140,000 individuals from Mexico City**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Elizabeth Barrera Sánchez	N/A	01/05/2022	No	N/A	N/A	30

Research Summary/Abstract: Previous studies have identified differences in the association of type 2 diabetes (T2D) genes between men and women, with insulin-related genes having a greater influence in men and insulin resistance in women. However, these associations were based on a limited set of genetic markers. This new study aims to broaden the understanding of T2D by investigating more genes and physiological processes in both sexes. Its objectives include analyzing specific genes and genetic markers based on age of diagnosis, identifying physiological processes based on sex and age of diagnosis, and exploring the relationship between genes and age of diagnosis. To achieve this, the imputed genome of individuals from the MCPS will be analyzed. This study offers an enlightening perspective on the causes and heterogeneity of common diseases like T2D, by revealing genetic associations and physiological processes based on sex and age of diagnosis. Identifying relevant genes and markers could uncover new biological pathways involved in T2D, with potential implications for other common diseases and improved prevention and management strategies.

Further information: N/A

	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Title	**Identification of genetic variants associated with cognitive impairment in Mexican population**						
Status To begin	Carlos González-Carballo	N/A		No	N/A	N/A	38

Research Summary/Abstract: Cognitive decline is one of the major causes of loss of independence and quality of life in the ageing population. Metabolic and cardiovascular diseases have been identified as risk factors for cognitive impairment. There is limited evidence of genetic variants associated with cognitive impairment in the Mexican population. The primary aim of this project is to identify genetic variants that are associated with cognitive impairment in the Mexican population. The aim is to conduct genome-wide association studies (GWAS) to establish the association with cognitive impairment as measured by the MMSE as continuous and categorical (MMSE score of ≤24). Once identified, the genetic variants will be characterized to understand their functional significance and potential role in cognitive impairment. By identifying genetic variants associated with cognitive impairment, the project contributes to understanding the genetic basis of different forms of dementia and cognitive decline in older Mexican population. Focusing on the Mexican population adds to the diversity of genetic data available, helping to uncover ethnic- specific genetic factors that may not be evident in studies focused on other populations. Insights gained from the research can inform public health strategies for early detection, prevention, and management of cognitive impairment in diverse populations.

Further information: N/A

	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID

Oxford-led

Title **Leverage OMICSPRED genetic-based predicted biomarkers to identify molecular trait associations with disease outcomes in MCPS**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Jason Torres	N/A	01/10/2023	No	N/A	N/A	18

Research Summary/Abstract: This project will involve three research directions: 1)Genetic imputation of proteomics, metabolomics and transcriptomics in MCPS and downstream phenome-wide association analysis; 2) Transferability of Nightingale genetic scores between European ancestries and ancestries in Mexico, and training of genetic scores based on MCPS Nightingale data; 3) Methods development to optimise QTL-based imputation in highly structured and admixed populations (MCPS as exemplar).

Further information: N/A

Title **Refining local ancestry for admixture mapping of type 2 diabetes and obesity**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Alejandra Vergara Lope, Eirini Trichia	N/A	01/08/2023	No	N/A	N/A	16

Research Summary/Abstract:

Further information: N/A

Title **Blood pressure and renal mortality**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Doreen Zhu	N/A		No	N/A	N/A	2

Research Summary/Abstract: To use classical epidemiolgical methods to evaluate the association of different measures of blood pressure with kidney-related mortality, and in particular to explore the modifying effects of age, sex and diabetes.

Further information: N/A

Title **GWAS of adiposity and other baseline phenotypes**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Eirini Trichia	N/A		No	N/A	N/A	15

Research Summary/Abstract:

Further information: N/A

Title **Genome wide association study of major lipid traits**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Diego Aguilar-Ramirez	N/A		No	N/A	N/A	14

Research Summary/Abstract: A set of GWAS analyses of major lipid traits (as inferred from NMR measures in 160K participants), with the focus being to identify novel genetic variants influencing lipid levels.

Further information: N/A

Title **Resolving the genetic architecture of type 2 diabetes in Mexico**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Paper being drafted	Jason Torres, Eirini Trichia	N/A		No	N/A	N/A	13

Research Summary/Abstract: An in-depth characterisation of the genetic architecture of type 2 diabetes in the MCPS cohort, with a focus on identifying novel genetic risk factors for T2D susceptibilty.

Further information: N/A

	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Title **Genome wide association study of blood pressure traits**							
Status To be completed when MT returns	Mike Turner	N/A		No	N/A	N/A	12
Research Summary/Abstract A set of GWAS analyses for major blood pressure traits in MCPS, with the primary focus being to identify and replicate novel GWAS associations.							
Further information N/A							
Title **Causal evaluation of diabetes for cause-specific mortality**							
Status Analyses ongoing	Fiona Bragg, Eirini Trichia	N/A		No	N/A	N/A	11
Research Summary/Abstract To use a Mendelian Randomization approach to elucidate the causal effect of diabetes for cause-specific mortality, and to assess associations separately in men and women and at different ages.							
Further information N/A							
Title **MR of BMI and diabetes prevalence**							
Status Paper submitted	Louisa Gnatiuc-Friedrichs, Eirini Trichia	N/A		No	N/A	N/A	10
Research Summary/Abstract							
Further information N/A							
Title **Causal evaluation of body mass index for cause-specific mortality**							
Status To be submitted	Louisa Gnatiuc-Friedrichs	N/A		No	N/A	N/A	9
Research Summary/Abstract To use a Mendelian Randomization approach to elucidate the causal effect of lifelong differences in BMI for cause-specific mortality, and to assess associations separately in men and women and at different ages.							
Further information N/A							
Title **Renal function and cause-specific mortality**							
Status Analyses ongoing	Diego Aguilar-Ramirez	N/A		No	N/A	N/A	5
Research Summary/Abstract To use classical epidemiolgical methods to evaluate the association of eGFR at baseline with cause-specific mortality in the MCPS, with a major focus on diabetes and kidney-related mortality.							
Further information N/A							
Title **Rare variant analysis**							
Status Analyses ongoing	Jason Torres	N/A		No	N/A	N/A	19
Research Summary/Abstract							
Further information N/A							

	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Title **Causal evaluation of blood pressure for cause-specific mortality**							
Status Analyses underway	Mike Turner, Eirini Trichia	N/A		No	N/A	N/A	8
Research Summary/Abstract							
Further information N/A							
Title **Local ancestry-informed GWAS of type 2 diabetes and cardiometabolic traits**							
Status Analyses ongoing	Jason Torres, Eirini Trichia	N/A		No	N/A	N/A	17
Research Summary/Abstract							
Further information N/A							
Title **Alcohol and cause-specific mortality**							
Status Draft paper with JE	Eirini Trichia	N/A		No	N/A	N/A	1
Research Summary/Abstract To use classical epidemiolgical methods to evaluate the association of alcohol consumption (including amount and pattern of drinking) with cause-specific mortality in the MCPS. Diseases emphasised will be those defined a priori to be likely to be increased by alcohol consumption.							
Further information N/A							
Title **Diabetes, Hypertension and Cognitive Impairment**							
Status Paper drafted by Carlos	Diego Aguilar-Ramirez	N/A		No	N/A	N/A	22
Research Summary/Abstract							
Further information N/A							
Title **Physical activity and cause-specific mortality**							
Status Analyses ongoing	Louisa Gnatiuc-Friedrichs	N/A		No	N/A	N/A	26
Research Summary/Abstract To use classical epidemiolgical methods to evaluate the association of regular leisure-time physical activity and cause-specific mortality in the MCPS.							
Further information N/A							
Title **A GWAS atlas of 140+ metabolites in an admixed Mexican cohort**							
Status Analyses ongoing	Diego Aguilar-Ramirez, Eirini Trichia	N/A		No	N/A	N/A	27
Research Summary/Abstract A survey of genome-wide associations for NMR-based metabolites in the MCPS cohort. Key deliverable will be a webpage that will host genome-wide results.							
Further information N/A							

		MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Title	**A pheWAS catalogue of genotype-phenotype assocations for quantitative and disease traits in MCPS**							
Status	Analyses ongoing	Jason Torres, Eirini Trichia	N/A		No	N/A	N/A	28
Research Summary/Abstract	A survey of genetic analysis, including GWAS, ExWAS, gene burden tests, and whole-genome regression analyses, for a range of complex traits in MCPS. Key deliverable will be a webpage hosting an "atlas" of genetic associations.							
Further information	N/A							
Title	**Combined relevance of risk factors to CV mortality**							
Status	Analyses under review	Jon Emberson, Eirini Trichia	N/A		No	N/A	N/A	29
Research Summary/Abstract	To assess the combined relevance of major disease risk factors (age, sex, diabetes, blood pressure, adiposity and smoking) to 10-year and lifetime risk of cardiovascular death, and to present results in terms of absolute risks, relative risks, and expected life years lost.							
Further information	N/A							

	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID

Oxford MSc & DPhil Student

Title **Runs of homozygosity and cardio-metabolic traits in adults from the Mexico City Prospective Study**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Qinfang Lu	N/A	13/05/2024	No	N/A	N/A	24

Research Summary/Abstract: This project will explore the associations between ROHs and cardio-metabolic traits, to further the current understanding of the genetic architecture of the some of the most burdensome diseases in this and other populations.

Further information: N/A

Title **Adiposity and risk of infectious disease mortality in Mexicans**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Lukman Lawal	N/A	13/05/2024	No	N/A	N/A	25

Research Summary/Abstract: The aim of this project is to assess the associations between various markers of adiposity and infective causes of premature mortality in a large cohort of 150,000 Mexican adults.

Further information: N/A

Title **Genetic determinants and cardio-metabolic consequences of kidney disease in a large population-based study of Mexican adults**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Luisa Fernandez-Chirino	N/A	01/10/2023	No	N/A	N/A	20

Research Summary/Abstract: This project will investigate the genetic basis of CKD/eGFR and their downstream impact on cardio-metablolic outcomes .

Further information: N/A

Title **Causal associations between adiposity markers and NMR biomarkers: Mendelian randomisation study in the Mexico City Prospective Study**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Paper to be drafted	Beryl Lin	N/A	01/05/2023	No	N/A	N/A	7

Research Summary/Abstract: To use a Mendelian Randomization approach to elucidate the causal effect of lifelong differences in blood pressure for cause-specific mortality, and to assess associations separately in men and women and at different ages.

Further information: N/A

Title **Development and evaluation of polygenic risk scores for coronary artery disease in an admixed Mexican poplulation**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Tianshu Liu	N/A	01/10/2022	No	N/A	N/A	6

Research Summary/Abstract: Assess external PRS scores for CAD in MCPS, and develop and evaluate novel PRS scores for CAD in MCPS.

Further information: N/A

Title **GWAS of major lipids**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Analyses ongoing	Yunhe Wang	N/A	01/10/2021	No	N/A	N/A	21

Research Summary/Abstract:

Further information: N/A

	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Title **Major blood lipids and cardiovascular mortality**							
Status Analyses ongoing	Yunhe Wang	N/A	01/10/2021	No	N/A	N/A	4

Research Summary/Abstract

Further information N/A

	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID

Oxford Interdepartmental

Title **Estimation of between-ancestry genetic differences from analysis of family data in an admixed population**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Data transferred/accessed	Jason Torres	Prof Peter Visscher	07/12/2023	Yes	19/01/2024	2023-036	117

Research Summary/Abstract: Our proposal is to exploit the segregation of ancestry proportions within families in an admixed population. If a population is admixed and the founder populations differ in their genetic means, then that creates extra genetic variation relative to a non-admixed population. Within families, siblings will differ in the proportions of ancestral population proportions. This information can be used to estimate variance due to between-population mean genetic differences for complex traits. The use of genetic markers within nuclear families allows estimation of ancestry proportions and identity-by-descent proportions among sibling pairs and can obtain unbiased estimates of genetic effects by effectively conditioning on parental genotypes. We propose to use a large sample of siblings from MCPS and estimate within-family variance and between-population variance simultaneously. Peter Visscher is a leading expert in resolving the genetic architecture of complex traits and has pioneered analytical approaches to estimate genetic variation within families from a homogeneous population (Visscher et al. 2006, PLOS Genetics; Visscher et al. 2007, American Journal of Human Genetics; Hemani et al. 2013, American Journal of Human Genetics; Sidorenko et al. 2023, Nature Genetics, under re-review).
Additional analyses of recombinations rate: Multiple studies of the genetics of recombination rates have been conducted and published in the last ~15 years, notably by deCODE Genetics in Iceland. These studies were based upon pedigrees containing both parental and offspring genotypes. However, as a by-product of estimating identity-by-descent (IBD) coefficients among sibling pairs, we can get indirect estimates of the average parental recombination rates, even if the parental genotypes are not known. This is because the genome-wide IBD coefficients are based upon shared genome segments spread throughout the genome. For example, if a pair of siblings share 2 alleles IBD for a one segment of a chromosome and share 1 allele IBD for the next segment, then there must have been a recombination event in one of the parents.
Visscher and colleagues at the University of Queensland have an ongoing research project where they estimated average parental recombination from more than 100,000 sibling pairs of European ancestry and have performed GWAS on recombination rate 'phenotypes'. We propose to perform the same analyses in MCPS, thereby creating a more powerful study and enhancing the study by including results from a non-European population.

Further information: K:\Mexico\Admin\Data Access Policy\Academic data sharing agreement\2023-036 PeterVisscher\Visscher_Torres_MCPS_Research_proposal_6Dec2023.docx

Title **HLA typing, diversity, and association analysis in the Mexico City Prospective Study**

Status	MCPS Researchers	External Principal Invesitgator	Start Date	DSA Required	Date DSA signed	MCPS Data Request ID	ProjectID
Data transferred/accessed	Jason Torres, Paulina Baca Paynado	Dr Yang Luo	16/03/2023	Yes	13/11/2023	2023-012	70

Research Summary/Abstract: Variations of human leukocyte antigen (HLA) genes in the major histocompatibility complex region (MHC) significantly play vital roles in our adaptive immune responses, and influence the risk of many immunological traits, including autoimmune diseases and cancer. The MHC locus is under strong selective pressure to constantly adapt to our ever-changing environment. Owing to population-specific positive selection, the MHC locus harbours unusually high sequence variation, longer haplotypes than most of the genome, and haplotypes that are specific to individual ancestral populations Consequently, the MHC locus is among the most challenging regions in the genome to analyse. Advances in HLA imputation based on genotyping array and HLA typing based on next-generation sequencing have enabled MHC association and fine-mapping studies at the single-gene and long-range haplotype level. We and others have shown that admixed populations with recent ancestry from two or more continents can facilitate rapid adaptive evolution by introducing novel variants and haplotypes at intermediate frequencies. This makes genetic discovery in admixed populations more powerful than in homogeneous ancestral populations. However, when compared to other continental populations, HLA diversity and its association with complex traits remain underexplored in Latin American populations. This makes MCPS a particularly suitable and valuable cohort for improving our understanding of HLA diversity, natural selection, and its disease asssociations. In this study, we propose to: 1. Infer accurate HLA alleles using both exome sequencing and whole-genome sequencing data from the MCPS. 2. Characterise HLA diversity within the MCPS and compare it to other global populations. 3. Study natural selection at the MHC locus in the MCPS. 4. Construct an MCPS HLA imputation reference panel to facilitate future HLA-disease studies in Mexico and in Latin America. 5. Conduct MHC-wide association and fine-mapping study for phenotypes included in the MCPS, such as diabetes, blood pressure and smoking. This work will be instrumental in understanding HLA and its association with complex traits both within Latin America and across global populations. The large effect sizes of the MHC region for a wide range of immune-mediated traits underscore the importance of defining HLA allelic effect sizes to build generally applicable clinical polygenic risk scores for many diseases. As the number of genome-wide genotyping by patients, both by healthcare providers and direct-to-consumer vendors, increases in Mexico and other South American countries, resources like the one we propose in this study will be essential for such applications.

Further information: K:\Mexico\Admin\Data Access Policy\Academic data sharing agreement\2023-012 YangLuo\Luo-MCPS-research-plan-Oct2023.pdf