2022 POPGEN CONFERENCE

Population Genetics from the Baltic Perspective:

Microevolutionary Processes of the Lithuanian Genomes

Faculty of Medicine

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LIETUVOS MOKSLŲ AKADEMIJA

20-21 May 2022, Vilnius, Lithuania

Venue: National Museum – Palace of the Grand Dukes of Lithuania

PROGRAMME

2022 POPGEN CONFERENCE

Population Genetics from the Baltic Perspective:

Microevolutionary Processes of the Lithuanian Genomes

Date: 20-21 May 2022

Place: Vilnius, Lithuania (hybrid with virtual participation according to the epidemiological situation)

Venue: National Museum – Palace of the Grand Dukes of Lithuania

20th May, 2022; Friday

12:45 – 13:00	Welcome/registration
13:00 – 13:10	Prof. habil. dr. Vaidutis Kučinskas, Vilnius University, FM LAS Prof. habil. dr. Jūras Banys, Lithuanian Academy of Sciences, FM LAS Prof. (HP) dr. Edita Sužiedėlienė, Vilnius University Welcome message
13:10 – 13:30	Dr. Laima Ambrozaitytė, Vilnius University Population genetics research of Lithuania
13:30 – 14:15	Prof. Johannes Krause, Max Planck Institute for Evolutionary Anthropology The genetic history of Europe: Migration and adaptation in prehistory
14:15 – 14:45	Dr. Alina Urnikytė, Vilnius University Inferring microevolutionary processes in the Lithuanian population
14:45 – 15:00	Coffee break
15:00 – 15:45	Prof. Guido Barbujani, Ferrara University Inferring the evolution of skin colour from ancient DNA
15:45 – 16:15	Dr. Ingrida Kavaliauskienė, Vilnius University Map of the Lithuanian population: distribution of genetic markers
16:15 – 16:45	Kristina Grigalionienė, Vilnius University Pathogenic and rare mitochondrial DNA variants in the Lithuanian population
16:45 – 17:00	Coffee break
17:00 – 17:45	Prof. Rimantas Jankauskas, Vilnius University, FM LAS Paleogenetics in Lithuania: synopsis of data and perspectives for future

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21st May, 2022; Saturday

9:00 – 9:45	Assoc. prof. Alena Kushniarevich, Tartu University The genetic making of the (northern) Baltics
9:45 – 10:15	Prof. Janis Klovins, the Latvian Biomedical Research and Study Center First insight in Latvian genome diversity from the whole-genome sequencing data
10:15 – 10:45	Dr. Laura Pranckėnienė, Vilnius University The turnover of the relative fitness for the whole-genome variants in the Lithuanian population
10:45 – 11:00	Coffee break
11:00 – 11:30	Dr. Ingrida Domarkienė, Vilnius University Inferring whole-genome sequencing structural variation data in the Lithuanian population
11:30 – 12:00	Gabrielė Žukauskaitė, Vilnius University Genomic signatures of adaptation in the cohort of Chernobyl Catastrophe Clean-up Workers from Lithuania
12:00 – 12:30	Dr. Tautvydas Rančelis, Vilnius University The omnigenic model of the behaviour traits in the Lithuanian and other populations
12:30 – 13:00	Discussion
13:00 – 14:00	Guided tour around the Palace of the Grand Dukes of Lithuania, Route I - HISTORY, ARCHAEOLOGY, ARCHITECTURE

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ABSTRACTS

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POPULATION GENETICS RESEARCH OF LITHUANIA

Dr. Laima Ambrozaitytė

Department of Human and Medical Genetics, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University

Much remains to be understood about the extent and structure of genetic variation in our species and how it was shaped by past population separations, admixture, adaptation, size changes, and gene flow from archaic human groups. Genome sequences from diverse human groups are needed to understand the structure of genetic variation in our species and the history of and relationships between different populations.

What were the main microevolutionary forces which formed the genomic diversity in the Lithuanian population? The research of the Lithuanian population since 1970s has shown that genetic drift, migration, mating choices and effective population size, selection pressure, mutation pressure were and still are operating in the contemporary Lithuanian population. To reassure their importance, both old and new genetic/genomic markers are necessary and big data must be generated. In an era where new genome analysis technologies are emerging, established population genetics principles will be applied to reveal more detailed migration history, population history, and mechanisms of selection pressure, particularly in small ethnic populations.

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THE GENETIC HISTORY OF EUROPE: MIGRATION AND ADAPTATION IN PREHISTORY

Prof. Johannes Krause

Max Planck Institute for Evolutionary Anthropology

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INFERRING MICROEVOLUTIONARY PROCESSES IN THE LITHUANIAN POPULATION

Dr. Alina Urnikytė

Department of Human and Medical Genetics, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University

Lithuania is geographically specific region where the most archaic Indo-European language is spoken. The current Lithuanian population resulted from a complex amalgam between the former Baltic tribes each with potentially different contributions from Finno-Ugric and Slavic sources. Moreover, since the Neolithic, the native population of what would become Lithuania has not been substituted by other peoples. Thus, the origin of the contemporary Lithuanian population may be traced back to the Neolithic settlers, with little admixture hereafter. The Lithuanian population is partially isolated with genetic distinctiveness within the European context. Moreover, Lithuanians preserve one of the highest proportions of western, Scandinavian and eastern hunter-gather ancestry components found in European populations but also that of an steppe Early to Middle Bronze Age pastoralists, which together configure the genetic distinctiveness of the Lithuanian population.

Signals of positive selection could be identified in the lithuanians using different statistical approaches for recent and old classical selective sweeps.

In addition the high-coverage WGS data will be reported for the Lithuanian population for the first time.

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INFERRING THE EVOLUTION OF SKIN COLOUR FROM ANCIENT DNA

Prof. Guido Barbujani

Department of Life Sciences and Biotechnology, Ferrara University

Human pigmentation is a complex trait. At least 70 genes are involved in the synthesis of melanins – eumelanin and pheomelanin – determining skin, hair and eye colour. None of these organs leaves fossils, but there is reason to believe that human skin was white 6 million years ago, evolved darker colours for millions of years, and then became lighter in Eurasian populations after they left Africa, less than 100,000 years ago, reflecting different selective regimes. Artificial Intelligence can help associate multilocus genotypes with complex phenotypes; the available algorithms predict skin, hair and eye colour with roughly 4% error. After the discovery that five Mesolithic Europeans (13,000-5,800 years BP) had very dark skin we systematically analysed a dataset of 93 samples from Western Eurasia, spanning from Mesolithic times to the Iron Age. We confirmed previous inferences about Mesolithic samples, using an updated approach. A general trend towards light skin colours was evident, with a major turning point associated with the Neolithic demic diffusion, and with the spread of light-skin alleles at the SLC45A2 and SLC45A5 loci. However, the pattern is more complex than it initially seemed, with evidence of very pale skin in a Mesolithic hunter-gatherer from Sweden, and a very recent shift towards light pigmentations. From a Baltic perspective, the available samples of Latvian hunter-gatherers consistently showed intermediate skin colours.

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MAP OF THE LITHUANIAN POPULATION: DISTRIBUTION OF GENETIC MARKERS

Dr. Ingrida Kavaliauskienė

Laboratory for Molecular Genetics and Cytogenetics, Centre for Medical Genetics, Vilnius University Hospital Santaros Klinikos

Beginning of the Lithuanian population genetic diversity studies using Y chromosome, mtDNA, and autosomal markers were several decades ago. Research leader Acad. Prof. Habil. Dr. Vaidutis Kučinskas and scientists from the Department of Human and Medical Genetics, Faculty of Medicine, Vilnius University used the most informative markers and methods at that time. Differences in genetic diversity in the Lithuanian population were already seen in previous studies though not always statistically significant.

To confirm genetic diversity differences within the population of Lithuania that were already detected or to find new ones more comprehensive molecular genetic analyses were performed. First of all, samples from the six ethnolinguistic groups of the Lithuanian population were collected in the most representative way during the LITGEN project. Complete mtDNA (16 569 bp) was sequenced, 17 STRs and 25 SNPs of Y chromosome and genome-wide (719 666 SNPs) markers were genotyped for hundreds of samples. Statistically significant differences between ethnolinguistic groups or particular parts of Lithuania were seen based on the Y chromosome, complete mtDNA, and genome-wide data. Together with ongoing and future studies, the draft of the Lithuanian population genetic diversity map with many layers can be launched.

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PATHOGENIC AND RARE MITOCHONDRIAL DNA VARIANTS IN THE LITHUANIAN POPULATION

Kristina Grigalionienė

Department of Human and Medical Genetics, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

Mitochondria are DNA containing intracellular organelles responsible for many important cellular functions such as ATP synthesis, tricarboxylic acid cycle metabolism, fatty acid oxidation, apoptosis and others. Mitochondrial dysfunction due to defects in oxidative phosphorylation or other essential mitochondrial functions result in mitochondrial diseases. The research of these diseases is challenging due to the high clinical and genetic heterogeneity, both mitochondrial and nuclear genome involvement, diversity of mtDNA mutations (point variants, deletions / duplications, decrease of mtDNA copy number) and heteroplasmy. In addition, the pathogenicity of identified mtDNA variants is difficult to assess and interpret due to ethnically or geographically related haplogroup variants and high mtDNA sequence diversity in the population. 85 individuals with suspected mitochondrial disease were included in the study (TAP LLT-02/2015). Whole mtDNA sequence was analysed using mtDNA Sanger sequencing and deletion/duplication analysis methods.

Mitochondrial disease was confirmed in nine patients (10.6%), pathogenic mtDNA variants causing MELAS, MERRF, Leigh, Kearns-Sayre syndromes were identified. The diversity and frequencies of haplogroups were compared to the distribution of haplogroups in the general Lithuanian population (LITGEN; VP1-3.1-ŠMM-07-K-01-013), rare variants of uncertain clinical significance are discussed in the study.
Investigation of mitochondrial DNA changes is important in diagnosing mitochondrial diseases, unraveling underlying molecular mechanisms, and improving disease management. However, the interpretation of pathogenicity of rare mtDNA variants is challenging, and should be made in the context of mtDNA haplogroup and population data analysis as well as nuclear genome analysis.

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PALEOGENETICS IN LITHUANIA: SYNOPSIS OF DATA AND PERSPECTIVES FOR FUTURE

Prof. Rimantas Jankauskas

Faculty of Medicine, Vilnius University

Summary of results on human ancient DNA research will be presented (continuity of Mesolithic and Neolithic foragers of the Eastern Baltic, no genetic contribution from Neolithic farmers of Central Europe during Early and Middle Neolithic and demic diffusion of people bringing new genetic components with Corded Ware complex and remaining high proportion of hunter-gatherer ancestry in modern Balts). The talk will also cover recent findings of ancient DNA of pathogens and diseases (such as Y.pestis, treponematosis, smallpox), tentative scenarios of their spreading and evolution, and possible impact on human populations in the past.

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THE GENETIC MAKING OF THE (NORTHERN) BALTICS

Assoc. prof. Alena Kushniarevich

Estonian Biocentre, Institute of Genomics, University of Tartu

Today's Eastern Europe unites people with diverse cultural backgrounds, whose genetic heritage, however, seem to be quite similar. In this overview we first will zoom-in in today's genetic landscape of the Eastern coast of the Baltic Sea and examine the fine-scale structure of Estonians and demographic processes behind it using modern genome sequences. Then we dive in the genetic history of the region by adding the ancient DNA data spanning roughly ten thousand years. We will explore the dynamics of the ancestral components typical for European hunter gatherers, early farmers and those who lived in the Bronze Age focusing on the local details of the demographic processes in the Baltics. Then we discuss the appearance of Siberian-like genetic component in Early Iron Age people and interpret the genetic evidence within the framework of archaeological and linguistic context on cultural changes in this time period in Eastern Baltics. And finally, we give a brief overview of the ongoing research on the medieval period of the region.

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FIRST INSIGHT IN LATVIAN GENOME DIVERSITY FROM THE WHOLE-GENOME SEQUENCING DATA

Prof. Jānis Kloviņš

Latvian Biomedical Research and Study Centre

Establishing a population-specific genome variation reference is an obvious step needed to implement genome-based applicability into personalized medicine. As a pilot, to achieve this goal, we have performed whole-genome sequencing of 230 individuals from a population-based cohort included in the Genome Database of Latvian Population (LGDB). We provide the first information on the quality and composition of variants obtained from this experiment. Next-generation sequencing was performed using the DNBSEQ-T10 instrument, and the resulting data were cross-validates with genotypes obtained by an Illumina GWAS chip from the same individuals with high concordance between both platforms. We also included a larger set of genotyped samples from the LGDB to evaluate the genetic structure and ancestry admixture in the Latvian population. We observed a distinct population stratification of the Latvian sample based on ethnic and regional origin. Self-reported ethnicity to a high degree correlated with the composition of ancestral populations in admixture analysis when compared with data from neighboring countries. This study provides the most extensive to-date analysis of genetic variation in Latvia, providing a background for a public reference resource. Our results show that the genetic composition of the Latvian population is uniquely formed and should be considered as an essential factor in future genetic and biomedical studies.

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THE TURNOVER OF THE RELATIVE FITNESS FOR THE WHOLE-GENOME VARIANTS IN THE LITHUANIAN POPULATION

Dr. Laura Pranckėnienė

Department of Human and Medical Genetics, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University

Lithuania is a country that separates Central and Western Europe from Asian countries. During the wars of 1200-1990, the territorial boundaries of Lithuania have changed significantly, as well has the composition and structure of the Lithuanian population. In this respect, genetic research of the Lithuanian population is important in order to identify the individuality and uniqueness of the gene pool of true Lithuanians by origin.

The concept of epistasis has since long been used to denote non-additive fitness effects of genetic changes and has played a central role in understanding the evolution of biological systems. Owing to an array of novel experimental methodologies, it has become possible to experimentally determine epistatic interactions, as well as to generate more elaborate genotype-fitness maps. This data has opened up an opportunity to investigate the ruggedness of fitness landscapes.

Here we present the primary analysis of turnover for the landscapes of the relative fitness of the more than 12 million whole-genome Lithuanians variants over three generations using high-coverage (an average of 36.27×) whole genome sequencing for 25 trios of the Lithuanian population. We uncover that the general Lithuanian population is characterized by unique genome variants across the whole genome, highlighting the importance of characterizing genetic diversity of the local populations.

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INFERRING WHOLE-GENOME SEQUENCING STRUCTURAL VARIATION DATA IN THE LITHUANIAN POPULATION

Dr. Ingrida Domarkienė

Department of Human and Medical Genetics, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University

This study is dedicated to analyse and present one more type of human genome variation – structural variants (SVs). Together with single nucleotide variation, small indels, SVs were demonstrated to contribute to many phenotypic traits and diseases. Despite technological advances, the research on structural variation still encounters many difficulties. Nevertheless, SV studies is gaining momentum while at the same time addressing challenges of analysis.

Populations are similar and differ from each other at the same time. Each population holds its uniqueness in the genomic variation form. Before analysing the dynamics of variation, it is important to determine it at an end-points. For the first time, whole-genome sequencing short read SV data of the Lithuanian population is presented in this work. To understand main characteristics of SVs and their potential contribution to the phenotype is fundamental for further research.

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GENOMIC SIGNATURES OF ADAPTATION IN THE COHORT OF CHERNOBYL CATASTROPHE CLEAN-UP WORKERS FROM LITHUANIA

Gabrielė Žukauskaitė

Department of Human and Medical Genetics, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University

Ionizing radiation (IR) is one of the environmental factors that is known to affect genomes and, therefore, challenge organisms to adapt. Until recently, there were few studies analysing genomes of individuals that experienced unusual levels of IR at a DNA sequence level. Lithuanian Chernobyl catastrophe clean-up workers (LCWC) are an exclusive object of research, because not only they survived extreme conditions, but also adapted to the life-lasting effects of IR.

Genome-wide genotyping and genome sequencing were performed for 93 and 40 LCWC, respectively. Association analysis showed statistically significant genome variants in LOXL1, CX3CR1, ZMIZ1, TSC22D1, BMP8A genes, which potentially protects against exfoliation syndrome, coronary artery disease, mental disorders or oral health problems. A novel approach using analysis of positive selection signatures in potentially protective genomic loci was used in order to justify their protective effect. The LOXL1 gene locus (chr15:73926462-73952136) falls into a region of positive natural selection with a significant effect ($\mu = 7.30$, $p<0.05$). This confirms the hypothesis of the protective role of the LOXL1gene and the investigated rs3825942 variant in the etiopathogenesis of exfoliation syndrome. Further analysis of positive selection signatures using whole genome sequencing data helped to identify 22 genomic loci in autosomes with highest positive selection scores which have been shown to affect genomic loci that are important for cell survival (cell aging, cell cycle regulation, apoptosis) and genome reparation. These loci are subject to positive selection and form unique adaptive properties of LCWC.

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THE OMNIGENIC MODEL OF THE BEHAVIOUR TRAITS IN THE LITHUANIAN AND OTHER POPULATIONS

Dr. Tautvydas Rančelis

Department of Human and Medical Genetics, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University

Studying the genetic basis of traits that have multifactorial inheritance, such as behaviour, is very challenging as it is determined by both genetic and environmental factors. Even regardless of the environmental impact, the identification of genetic factors is difficult as a complex trait is determined by a polygenic combination of genome variants.

One of the most important leaps forward in the identification of complex traits has been genome-wide association studies (GWAS), which have helped to identify thousands of genomic variants associated with a particular trait. However, the research showed that in many cases of GWAS it was difficult to replicate results and genomic data retrieved from GWAS could have contradictory results. Most importantly, having thousands of variants for one trait is complicating aspect of the phenotypic prediction.

For the prediction of complex traits from genome data, an omnigenic model could be applied, which expands the view of complex traits from polygenic to omnigenic. The main basis of this model is that some gene products have a direct effect on the phenotype. These genes can be referred to as core genes. Genes that have a small impact on a particular trait and that far outnumber the core genes could be called peripheral genes. Finding core genes of complex traits and focusing on them could simplify the phenotypic prediction from the genome data. To review the usefulness of the omnigenic model for the prediction of complex traits, behaviour traits are being used as an example and shown in the Lithuanian and global population.

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