P454: GENOME-WIDE METHYLATION SIGNATURE OF RELATIVE TELOMERE LENGTH IN A COHORT OF SARCOPENIA AND FRAILTY PATIENTS OF LITHUANIAN ANCESTRY

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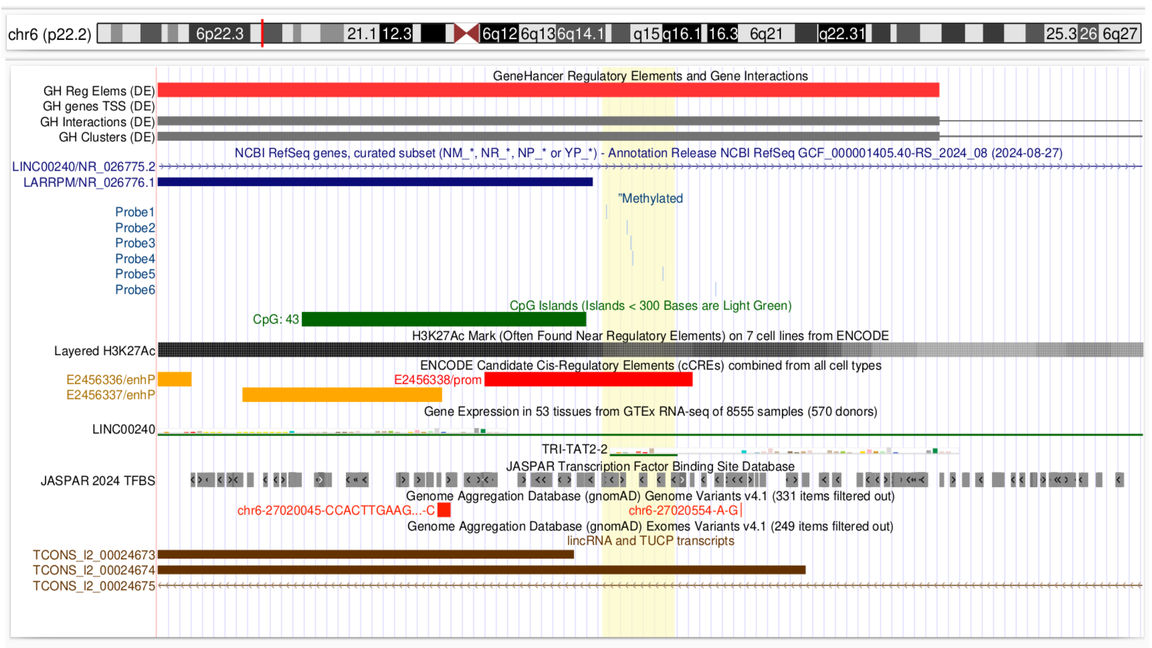
Background

Our study aimed to identify and describe genome-wide methylation signature significantly associated with the relative telomere length in a cohort of Lithuanian elderly with sarcopenia and frailty.

Materials & Methods

Methylation of a total of 62 subjects (43 females aged 85.5± 6.1 and 19 males aged 82.9 ± 8.8) diagnosed by both: sarcopenia (defined by the criteriset by EWGSOP2) and frailty (determined by Fried's criteria [weakness, low walking speed (WS), low physical activity, weight loss, exhaustion]) were profiled by Illumina Infinium EPICv2 arrays. Leucocyte relative telomere length (TL) was determined by real-time qPCR on DNA extracted from blood samples and quantified as the telomere/single-copy gene (T/S) ratio. Phenotypic data were collected via the questionnaires, scales, geriatric assessment tools (PACE, GDS and Katz ADS) and testing of anthropometric and physiological characteristics.Quality control and filtering of the raw methylation data was performed in R (4.4.2) by a package 'SeSAMe' (v1.24.0) followed by a differential methylation analysis performed with R package 'DMRcate' (v3.2.1). Genomic locations of the differentially methylated regions (DMRs) significantly associated with the TL were analyzed in UCSC Genome browser. Trait associations with the genes, harboring identified DMRs were taken from NHGRI-EBI GWAS registry.

Figure 1. Genomic context of *LNC00240* methylated region in sacopenia group.



Results

The results showed that DNA methylation levels are not related to age or gender. The TL was associated with 49 differentially methylated CpG probes at 95% confidence level of false discovery rate (fdr <0.05). The CpG sites covered 7 genetic loci overlapping *FPGT, LRRIQ3, TNFSF9, ZDHHC14, LINC00240, MPL* and *SH3F3* genes and regulatory ENCODE regions and H3K27Ac mark elements in them. These genes conjointly associated with phenotype of patients: smoking, alcohol consumption, educational attainment, mentality, depressive symptoms, body mass index (BMI), body fat mass, bone mineral density presented in Table 1. *LINC00240* associated with leucocyte TL. Genomic context of methylated *LINC00240* probes within the highlighted region is shown in Figure 1 demonstrating its proximity to the regulatory genome elements (genome build hg38).

Table 1. Gene-associated phenotypes

MPL	Learning ability, brain morphology, thrombocyte counts
FPGT	BMI, body weight, smoking, obesity, learning ability, educational attainment
SH3RF3	Curiosity, brain morphology, bone mineral density, height, BMI
LNC00240	BMI, hip circumference, mscle mass, intellect, neuroticism, life satisfaction, iron level, depression, leucocyte telomere length, ischemic heart disease, alcohol consumption, smoking
ZDHHC14	Smoking, learning ability, educational attainment, bone mineral density, iron status, depression, alcohol consumption, body fat mass
TNFSF9	Metabolism, face morphology - cleft lip and palate.

Conclusion

We found significant association between the TL and methylation levels in genes associated with lifestyle traits potentially linked to the risk of developing sarcopenia and frailty in Lithuanian elderly.

Project "Genome, epigenome ir telomere length features of sarcopenia and frailty" **GEPITEL** has received funding from the Research Council of Lithuania (LMTLT), agreement No S-MIP-22-36

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