Rare Genetic Variants Associated with Lung Cancer in a Romanian Population

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Introduction

•For more than a decade, the genome-wide associations studies (GWAS) represented a step forward in the identification of genetic risk factors involved in the pathogenesis of cancer. Today, the GWAS continue to reveal new single nucleotide polymorphisms (SNPs) associated with lung cancer.

•Lung cancer is a major public health problem in Romania and other Eastern European countries, with incidence and mortality rates among the highest worldwide.

Methods and Materials

•The study included a cohort of genotyped Romanian subjects. 1835 lung cancer cases and 1437 cancer-free controls passed a data filtration process and were included in an association test between lung cancer and 95205 markers.

Results

•Nine tested variants reached GWAS significance (p-value < 5×10^{-8}) and 82 SNPs had a p-value under 5×10^{-6}.

•The SNPs mentioned in Table 1 have not been previously associated with lung cancer. They are protective variants and have a lower allele frequency in cases than in controls. Also, their allelic frequency in cases is lower than in global and European populations.

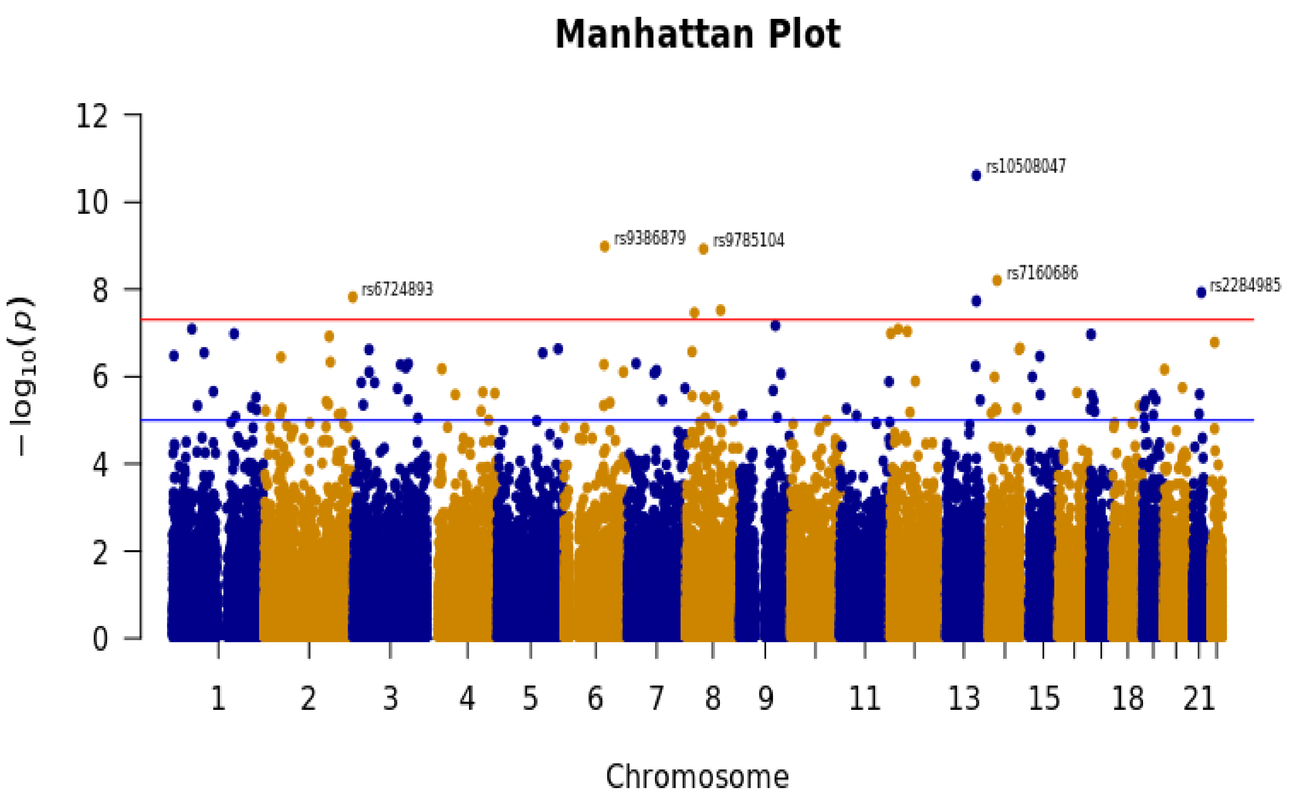
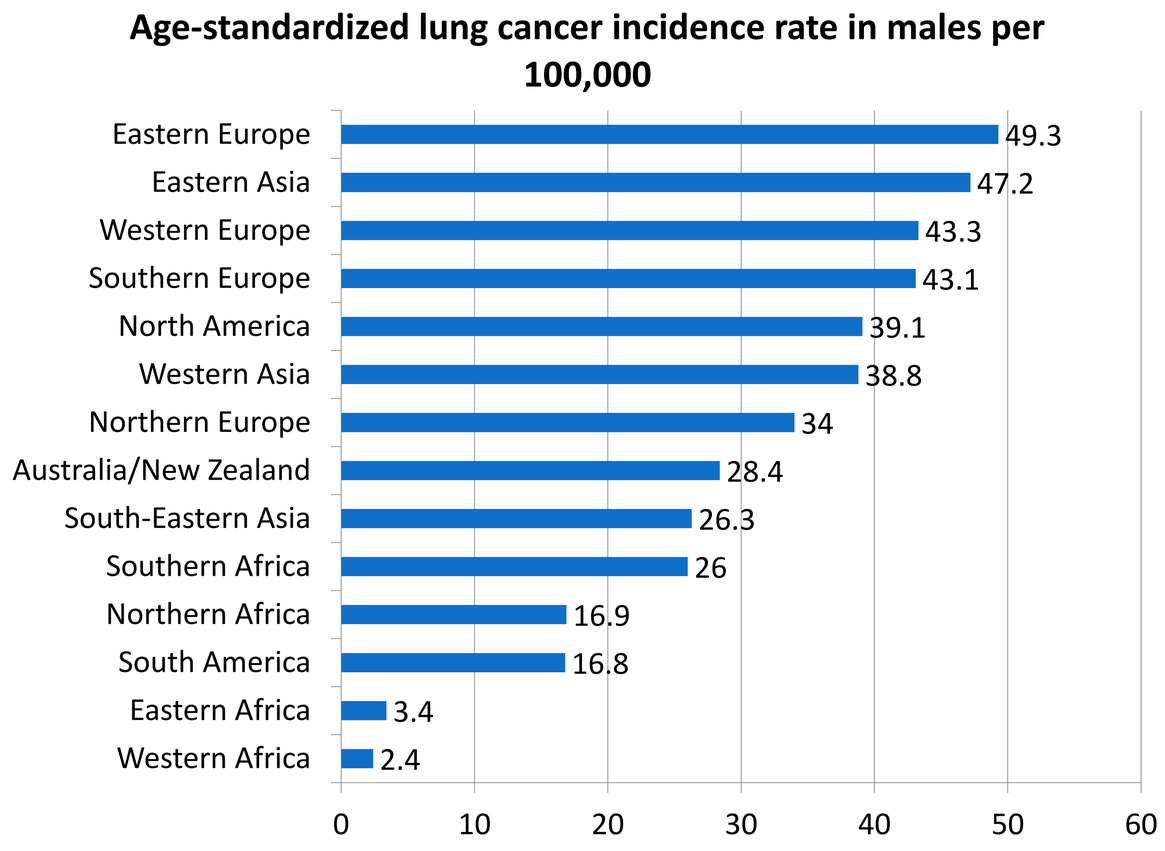


Figure 1. Manhattan Plot. The annotated SNPs are the variants with a p-value lower than the threshold of 5×10^{-8}, which are further detailed in Table 1.



Chromosome	SNP	MA	p-value	OR	Gene	FA	FU
13	rs10508047	G	2.44×10^{-11}	0.26	NALCN-AS1	0.01	0.03
13	rs4445762	G	1.85×10^{-8}	0.58	NALCN-AS1	0.06	0.11
8	rs6558165	C	3.42×10^{-8}	0.47	CCAR2	0.02	0.06
21	rs2284985	T	1.19×10^{-8}	0.57	SIM2	0.06	0.1

Table 1. The most statistically significant SNPs in our study. MA – minor allele; OR - odds ratio; FA – minor allele frequency in cases; FU – minor allele frequency in controls;

Conclusions

•Our study, the first GWAS of lung cancer patients in Romania, shows a convincing correlation between this pathology and genetic variants that have not been previously known to have any clinical significance. These findings are important, given the high incidence and mortality rates of lung cancer in Romania.

References

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