ALLELIC IMBALANCE OF GENES IN SPONTANEUS TUMOR AND IN TUMOR OF PERSONS EXPOING LONG-TERM OCCUPATIONAL RADIATION

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1. INTRODUCTION

The allelic imbalance and LOH cases have been shown for many genes in sporadic tumors of various organs. The allelic imbalance at radiation carcinogenesis has not been practically studied. As such, the study will assess the

distinctive features of radiation compared to spontaneous carcinogenesis and identify marker genes that can be used to identify radiation carcinogenesis. In this study the allelic imbalance in the tumor tissues on the background of low-level radiation was examined.



2. METHODS

Extracting DNA from paraffin blocks

The real-time PCR method

Genotyping SNP-markers

XPD1 rs13181, hOGG1 rs1052133, TP53 rs1042522, RB1CC1 rs2305427; PTEN rs701848; CYP2C19 rs4244285; ABCB1 rs1045642; *BAX* rs1805419, *MTHFR* rs1801133

To compare the genotype distribution of polymorphic loci in cancer patients

Two group of cancer patient were analyzed

Employees of Siberian Group of Chemical Enterprises (SGCE) which was professionally exposed to radiation (10–154 mSv). at 99 samples.

normal tissues | cancer tissues

at 157 samples.

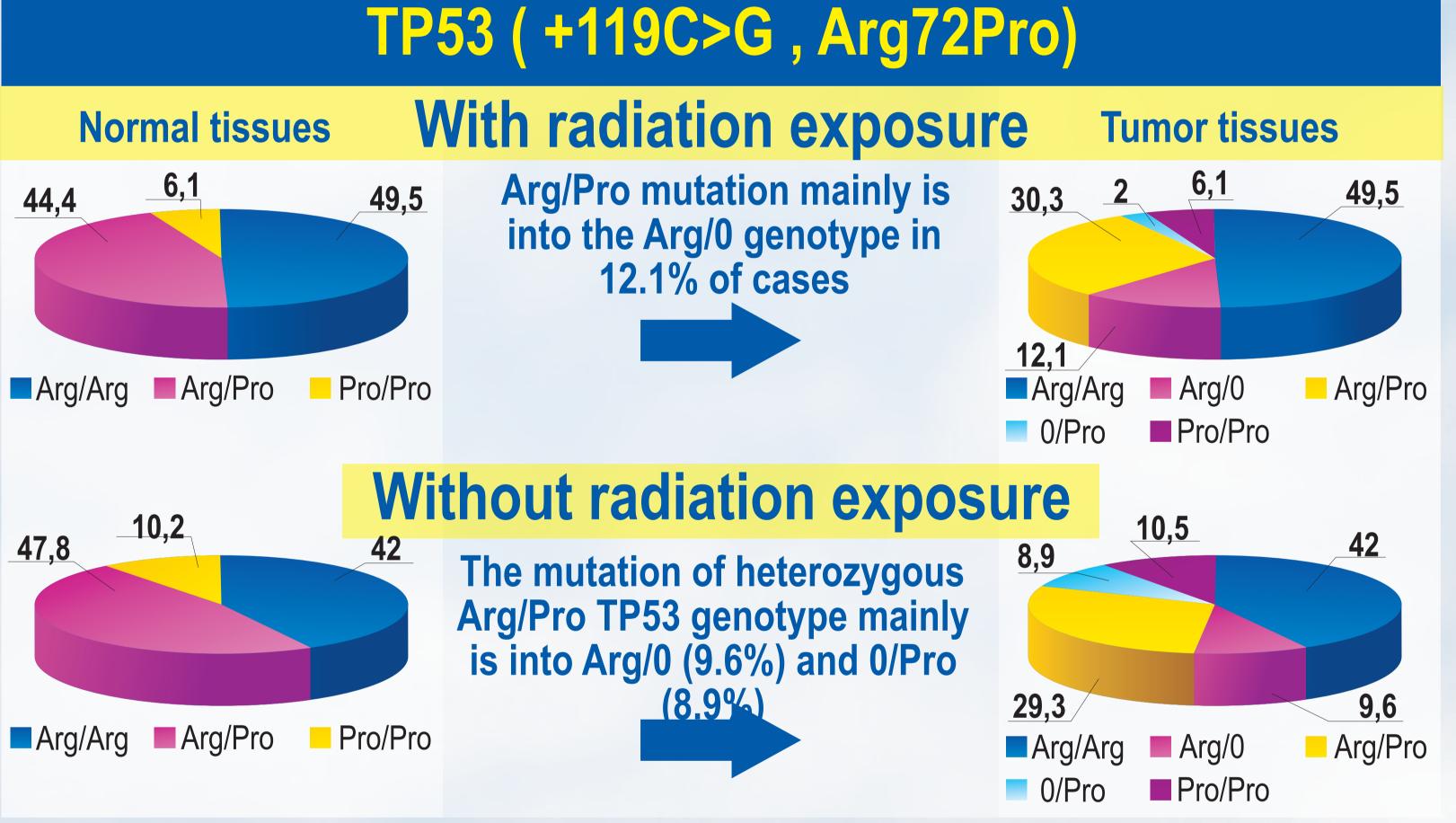
normal tissues cancer tissues

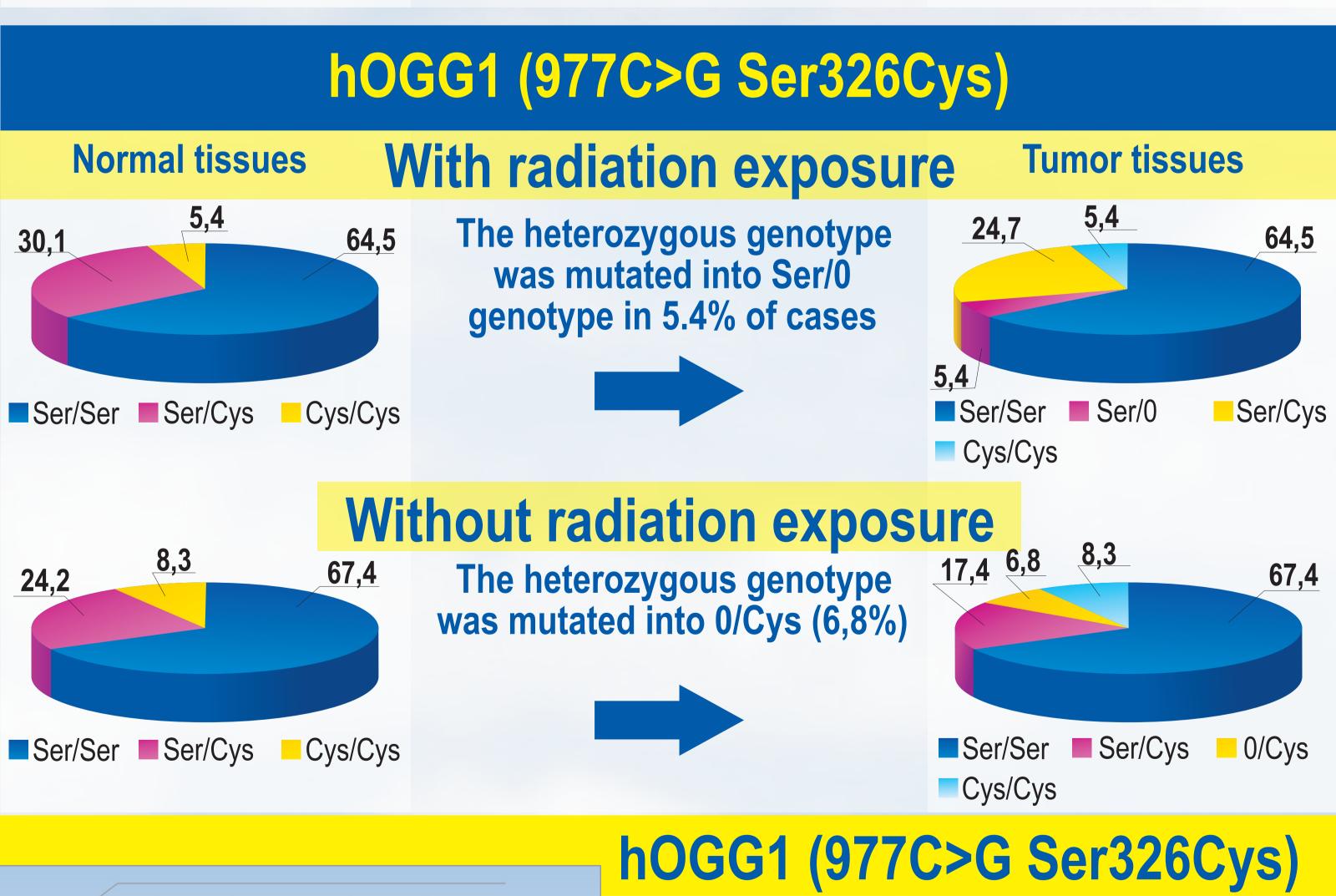
Non-exposed residents of

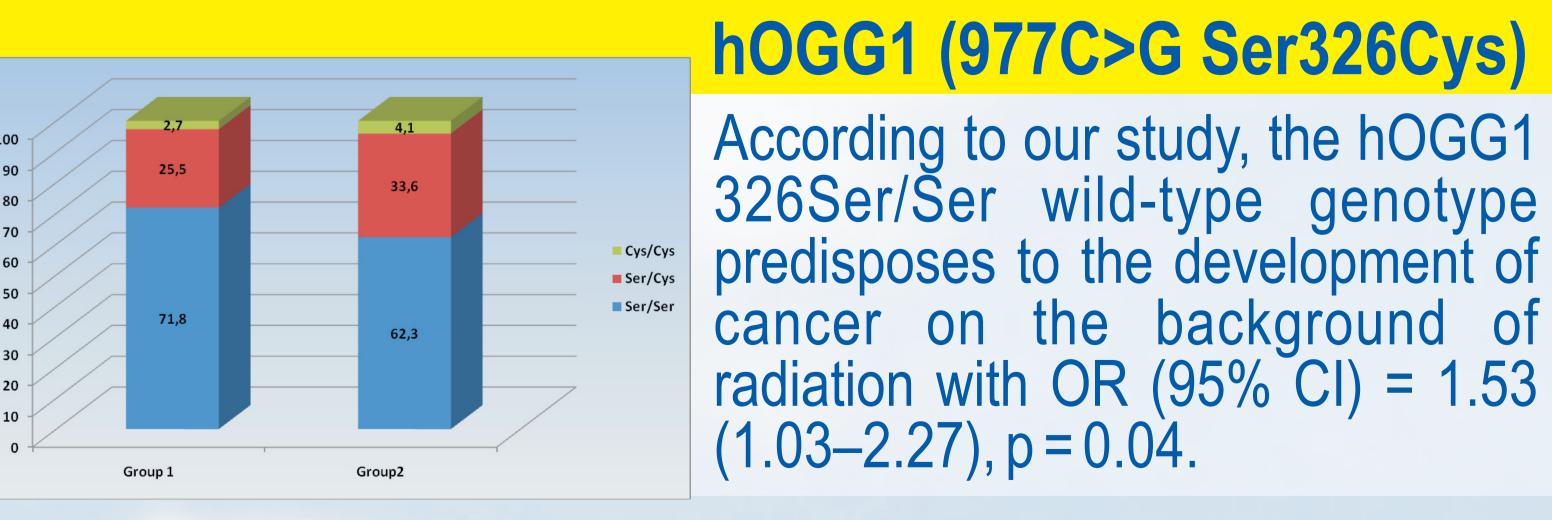
exposed SGCE employees.

Seversk as well as non-

3. RESULTS



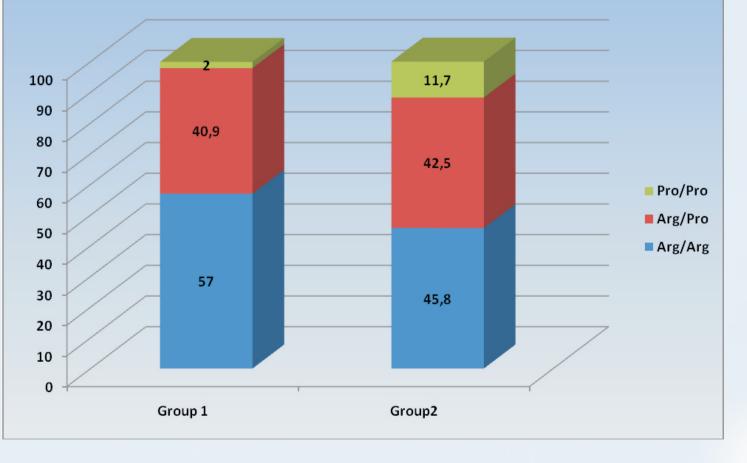




XPD1 (2251A>C Lys751Gln) With radiation exposure **Tumor tissues Normal tissues** The heterozygous genotype was 46,2 24,2 45,1 mutated into 0/Gln genotype in 16.5% of cases 16,5 13,2 Lys/Lys Lys/Gln Gln/Gln Lys/Gln Lys/Lys Lys/0 Without radiation exposure 14,8 33,9 51,3 The heterozygous genotype was 3,5 mutated into Lys/0 (7,8%) and 0/Gln (3,5%) 22,6 Lys/Lys Lys/Gln Gln/Gln Lys/Lys Lys/0 Lys/Gln

DNA Additional studies: samples blood employees with cancer (group1, 149 samples) and healthy SGCE employees' (group2, 908 samples) professionally exposed to the low-level y-radiation, were genotyped.

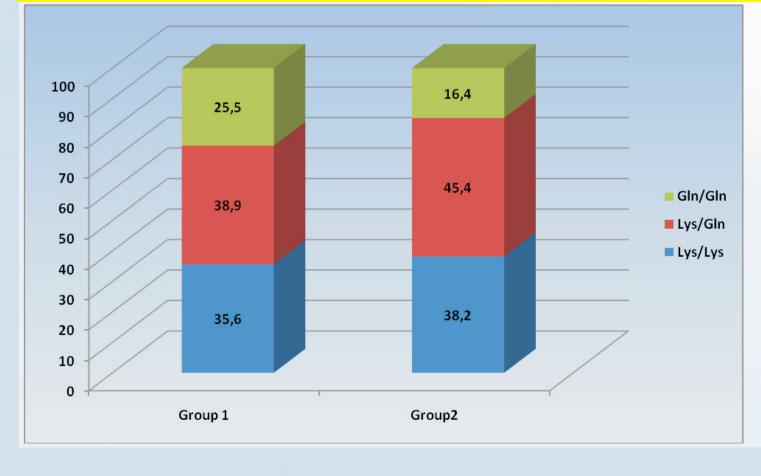
TP53 (+119C>G, Arg72Pro)



According to our data, the Arg/Arg genotype TP53+119C>G Arg72Pro is a risk marker for the development of tumors on the background of the radiation with OR = 1.51 (1.05-2.77), and Pro/Pro genotype has a protective anti-tumor effect.

■ Gln/Gln

XPD1 (2251A>C Lys751Gln)



Ehe Gln/Gln genotype of XPD1 2251A>C Lys751Gln with OR (95%) CI) = 1.76 (1.15-2.69), p = 0.03predisposes to the development of cancer on the background of radiation. This association is weak

4. CONCLUSION

- 1. Our studies have shown the phenomenon of the allelic imbalance in tumor tissues appeared on the background of low-level exposure and spontaneous tumors for the selected SNPs that indicates the universality of the mechanism
- inactivating heterozygous genotypes. 2. The directions of mutations at the heterozygous loci are different between sporadic tumors and tumors with the

irradiation background indicating that there are genetic differences between spontaneous and radiation carcinogenesis.

3. The distinct direction of the vector of mutations at the heterozygous locus in tumor tissues coincides with the associative model of data. Evaluation of allelic imbalance in tumor tissues may be used as an additional criterion to evaluate either the risk significance of polymorphic loci or the verifiability principle.