The spectrum of mutations in the *EXT1* gene among patients with Multiple Hereditary Exostoses in the Republic of Sakha (Yakutia)

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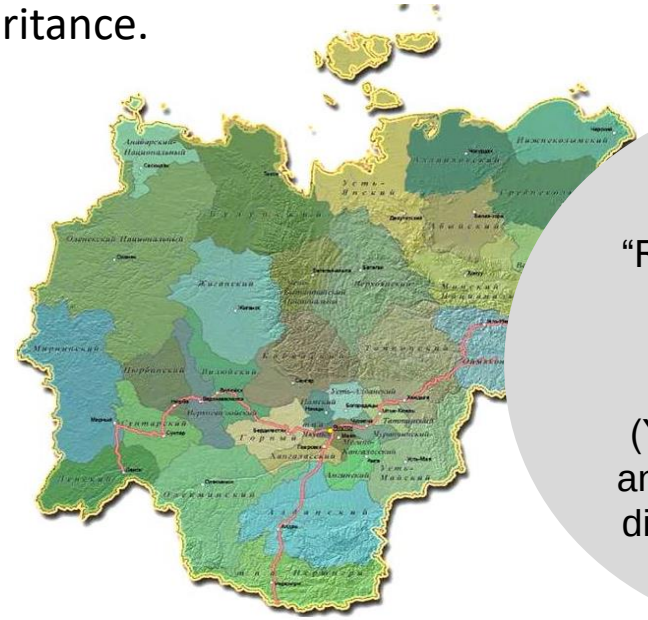
Multiple hereditary exostoses (MHE) or multiple osteochondromas (MO) (OMIM 133700, OMIM 133701) is a genetically heterogeneous disease with an autosomal dominant mode of inheritance.

The most common cause is mutations in the *EXT* genes, which are responsible for at least 70% of all cases of MHE

Genes	Location in the chromosome	Known mutations
EXT1	8q24	More than 500
EXT2	11p12	About 400
EXT3	19p	Isolated cases



Republic of Sakha (Yakutia)

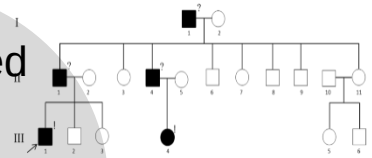
According to data obtained from the “Register of hereditary and congenital pathology of the Republic of Sakha (Yakutia)” 85 patients and their relatives from different ethnic groups were registered.

Studies of the molecular genetic cause of MHE in the Republic of Sakha (Yakutia) not been carried out. Therefore, the study of MHE in Yakutia is both a fundamental scientific problem and a medical and social task for diagnosing, preventing and predicting the course of this hereditary disease.

This paper presents the results of a molecular genetic study to search for mutations in the *EXT1* gene among patients with MHE in Yakutia.

MATERIALS AND METHODS

57 unrelated probands with the clinical diagnosis of MHE



DNA extracti on

Polymera se chain reaction

Clinical exome sequencing on a high-performance MiSeq sequencer (Illumina, USA) using a Trusight One Sequencing panel (Illumina, USA)

Sanger sequencing were used

For verification and validation of molecular genetic analyzes

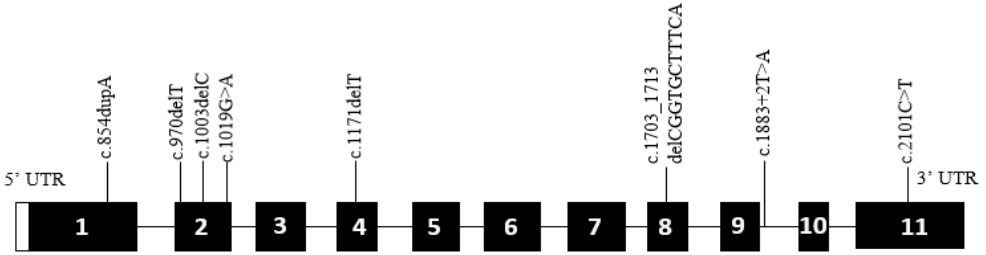
Variant Studio 3.0 programs, ExAC, 1000G and ESP6500 bases were used for bioinformatic analysis

SIFT, PolyPhen2, MutationTaster software tools were used to check the functional significance *in silico*

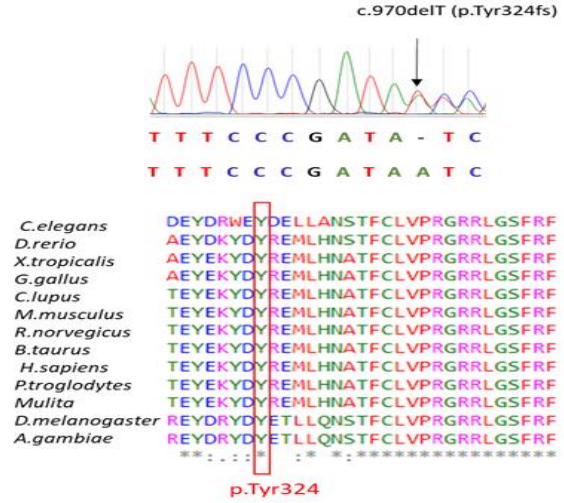
RESULTS

Only 8 mutations were found in the *EXT1* gene, of which were previously published

Genes	Location	Mutation
EXT1	Exon 1	c.854dupA (p.His285Glnfs*4)
	Intron region 9	c.1883+2T>A
	Exon 11	c.2101C>T (p.Arg701*)
	Exon 2	c.970delT (p.Tyr324Phefs*35),
		in–c.1003delC (p.Leu335Trpfs*24),
		c.1019G>A (p.Arg340His)
	Exon 4	c.1171delT (p.Ser391Leufs*12),
	Exon 8	c.1703_1713delCGGTGCTTTCA (p.Thr568Asnfs*16)



According to the results of the study, mutations in the *EXT1* gene were found in 22.8% of the examined patients.



Previously unknown mutation in exon 2 of *EXT1* gene – c.970delT (p.Tyr324Phefs*35)

Conclusion: The results of this study made it possible to expand the pathological spectrum of mutations in the *EXT1* gene and to establish the etiology of the MHE disease. New data have been obtained, which can be further used in the diagnostic program of patients with MHE.

ACKNOWLEDGEMENS

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THANK YOU FOR YOUR ATTENTION!