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MRE11A locus rs533984 - A marker of selective survival up to the age 85+ in Croatian population

Ž. Celinšćak, M. Šetinc, L. Bočkor, A. Stojanović Marković,

M. Zajc Petranović, M. Peričić Salihović, T. Škarić-Jurić

Institute for Anthropological Research, Zagreb, Croatia

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INTRODUCTION

- Human longevity is a multifactorial characteristic, influenced by both genetic and environmental factors.
- **Aim:** to investigate whether there is any difference in the longevity genes' makeup in two extreme age cohorts originating from the same population.

MATERIALS & METHODS

- 42 SNPs, selected due to their reported association with human longevity and their involvement in different metabolic pathways, were genotyped in a Croatian study sample consisting of 411 individuals.
- Allele and genotype frequencies were compared between 314 individuals aged 85+ (Old cohort) and 97 individuals aged 20-35 years (Young cohort).

Table 1. Longevity allele and genotype frequencies that showed significant difference (p<0.05) between the Old (85+ yrs) and Young cohort (20-35 yrs) from Croatia.

GENE: SNP	Longevity alelle	"Olds" frequency	"Youngs" frequency	p	Genotype	"Olds" frequency	"Youngs" frequency	p
MRE11A rs533984	G	60.5	47.3	**0.002**	GG	35.0	22.2	**0.006**
					GA	50.6	51.5	
					AA	14.3	26.3	
APOE rs7412	T	7.6	3.2	**0.042**	CC	85.7	92.9	0.151
					CT	13.3	7.1	
					TT	1.0	0.0	

Other investigated SNP's belonging to genes: *IL6, KLOTHO, TOMM40/APOE/APOEC1, FOXO3A, TERC, CDKN2B/ANRIL, IRF4, TP53/CDKN2A, SH2B3/ATXN2, LPA, TNF-alfa, TP53, GHSR, TERCIGF1R, ERCC2, GHRHR, IGF1R, IGF2R, LINC02227 (EBF1), PAPPA, PARK, PTPN1, RAD50/IL13 region, SIRT6, TERC, TERT, TXNRD1, FOXO3A* did not reach significant difference between the investigated cohorts.

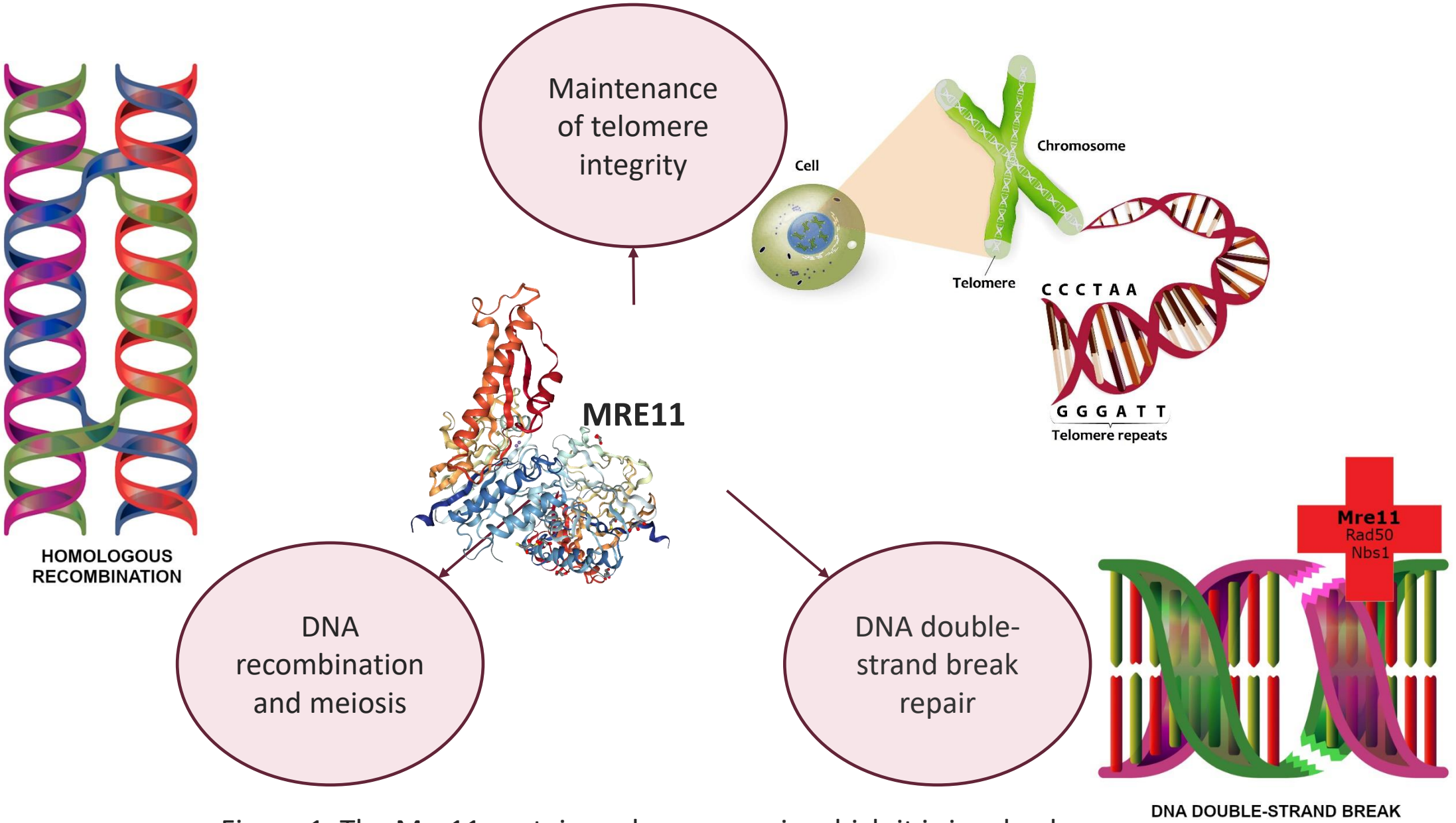

Figure 1. The Mre11 protein and processes in which it is involved.

RESULTS

- Table 1 presents allele and genotype frequencies of the *MRE11A* rs533984 and *APOE* rs7412, as these were the only ones out of 42 investigated longevity loci that showed significant differences between Old and Young Croatian cohorts.
- The allele ($p = 0.002$) and genotype ($p = 0.006$) frequencies differed only in the rs533984 of the *MRE11A* gene belonging to the DNA repair pathway (Figure 1), with the longevity allele G being more frequent in the Old cohort.
- A marginal difference is also found for the *APOE* rs7412 allele frequency ($p = 0.049$), with the longevity allele T (determining ε2 isoform) being more frequent in the Old cohort.

DISCUSSION & CONCLUSION

- G allele of rs533984 was previously confirmed as favourable for survival to the very old age in Danish females (Dato et al, 2018).
- However, to our knowledge this is the first time that the allele and genotype frequencies of rs533984 were found to differ between old and young cohorts.
- Differences in allele and genotype distribution between the two extreme age groups of the Croatian population open the possibility that the G allele of the *MRE11A* gene rs533984 locus might contribute to positive age-related selective survival.

Reference

Dato et al: The genetic component of human longevity: New insights from the analysis of pathway-based SNP-SNP interactions. Aging Cell. 2018 Jun;17(3):e12755.

Contact: zeljka.celinscak@inantro.hr