

# Y chromosome haplogroup R1a1 is associated with prostate cancer risk among Macedonian males

D. Plaseska-Karanfilska<sup>1</sup>, P. Noveski<sup>1</sup>, N. Matevska<sup>2</sup>, A. Dimovski<sup>2</sup> and G.D. Efremov<sup>1</sup>

<sup>1</sup>Macedonian Academy of Sciences and Arts, Research Center for Genetic Engineering and Biotechnology, Skopje, Republic of Macedonia,

<sup>2</sup>Faculty of Pharmacy, Center for Biomolecular Sciences, Skopje, Republic of Macedonia

## INTRODUCTION

Prostate cancer (PC) is one of the most common male-specific cancers. Its incidence varies considerably between populations. Recent surveys suggest that PC is influenced by both genetic and environmental factors, although the etiology of the disease remains unknown in the majority of cases. Certain Y chromosomal lineages have been suggested to predispose individuals to prostate cancer in Japanese population, but no association has been found among Korean and Swedish patients.

## AIM OF THE STUDY

The aim of this study was to investigate the association between Y chromosomal haplogroups and a predisposition to prostate cancer in Macedonian men.

## MATERIALS AND METHODS

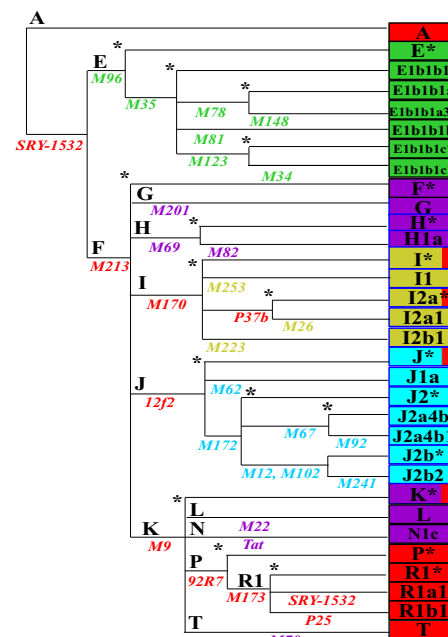
We studied 84 PC patients of Macedonian ethnic origin. Of them, 25 were younger than 65 years, while 59 were 65 years of age or older. Gleason grade was  $\geq 8$  in 24 of them and  $<8$  in 60 of them.

Control group consisted of 126 males of Macedonian ethnic origin from the general population.

The Y chromosome haplogroups were determined by 32 Y-chromosome SNP markers, which were typed following a hierarchical method, in five multiplex PCR/SNaPshot reactions (Figure 1). A representative electrophoreogram from a sample assigned to haplogroup R1a1 with multiplex SNaPshot 1 is given in Figure 2.

## RESULTS

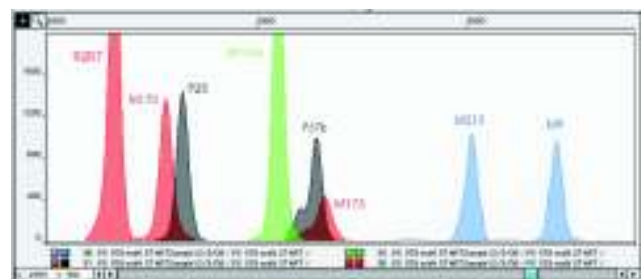
Nineteen different Y haplogroups were determined; the most frequent being I2a-P37b, E1b1b1a-M78, R1a1-SRY1532, R1b1-P25 and J2b2-M241 (Figure 3). Carriers of haplogroup R1a1 had an almost 2,5-fold increased risk of developing prostate cancer risk [OR=2,41 (1,09-5,36); p=0,027; Table 1]. When stratified according to age, even stronger association was observed between haplogroup R1a and prostate cancer in patients of  $>65$  years of age [OR=3,24; 95% CI, 1,41-7,46; p=0,004]. The frequency of R1a1 was also higher in patients with milder disease (Gleason grade  $<8$ ) in comparison to the controls, but the difference was not statistically significant (Table 2).



**Figure 1.** Phylogenetic tree defined with the binary Y-chromosomal polymorphisms analyzed. Marker names are shown above the lines. Colors represent multiplex groups.

**Table 1.** Association between Y chromosome haplogroups and prostate cancer risk.

Y haplogroup	Prostate cancer		Controls		OR	95% CI	p value
	No.	%	No.	%			
E1b1b1a	16	19	25	19,8	0,95	0,47 - 1,91	0,887
Other Hgrs	68	81	101	80,2			
I2a	17	20,2	36	28,6	0,63	0,33 - 1,22	0,173
Other Hgrs	67	79,8	90	71,4			
J2b2	6	7,1	8	6,3	1,13	0,38 - 3,40	0,821
Other Hgrs	78	92,9	118	93,7			
R1a1	17	20,2	12	9,5	2,41	1,09 - 5,36	0,027
Other Hgrs	67	79,8	114	90,5			
R1b1	9	10,7	12	9,5	1,14	0,46 - 2,84	0,778
Other Hgrs	75	89,3	114	90,5			



**Figure 2.** SNaPshot multiplex from a sample assigned to haplogroup R1a1-SRY1532.

**Table 2.** Association between R1a1 haplogroup and prostate cancer risk in PC patients according to their age and severity of the disease (Gleason grade).

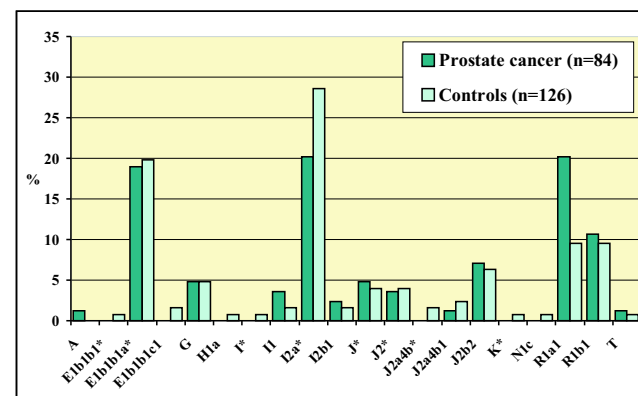
Study group	Hgr R1a1		Other Hgrs		Total No	OR	95% CI	p value
	No.	%	No.	%				
Prostate cancer								
< 65	2	8,0	23	92,0	25	0,83	0,17 - 3,94	0,807
$\geq 65$	15	25,4	44	74,6	59	3,24	1,41 - 7,46	0,004
Gleason grade $< 8$	11	20,0	44	80,0	55	2,38	0,98 - 5,78	0,060
Gleason grade $\geq 8$	3	13,0	20	87,0	23	1,43	0,37 - 5,50	0,617
Controls	12	9,5	114	90,5	126			

## CONCLUSION

Our results suggest that Y chromosome haplogroup R1a1 is associated with an increased prostate cancer risk in Macedonian men.

## ACKNOWLEDGMENTS

This study was supported in part by project No.13-1000/3-05 from the Ministry of Education and Science, R. Macedonia and FP7 project No. 229458 from the European Commission.



**Figure 3.** The distribution of Y haplogroups among patients with prostate cancer and controls.