TSPY1 copy number variation and male infertility

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INTRODUCTION

Testis-specific protein, Y-linked 1 (TSPY1) gene is located on the short arm on the Y chromosome (Yp11.2) and is present as an array of approximately 18-76 gene copies. *TSPY1* is a member of a protein superfamily that includes SET and NAP, which are activating factors of the replication process, as binding-partners of cyclin B. Full-length *TSPY1* is expressed in the normal testis, predominantly in spermatogonia and at a low level in primary spermatocytes, indicating a major role in the mitotic division of early germ cells.

MATERIALS AND METHODS

The study group included 60 azoospermic men, 66 men with oligozoospermia and 119 fertile controls with similar ethnic origin. Relative *TSPY1* copy number was determined by quantitative PCR, in comparison to a single copy *HPRT1* gene as a control locus, on a 7500 Fast reat-time PCR (Applied Biosystems) (Figure 1). Y chromosome haplogroups were determined by analysis of 28 single nucleotide polymorphisms (SNPs) using SNaPshot multiplex kit (Applied Biosystems). Statistical analysis was performed using the statistical package SPSS for Windows (SPSS Inc., Chicago, IL). A *P* value of 0,05 was considered statistically significant for each test.

RESULTS

All samples came from population with normal distribution (Figure 2). Infertile patients showed higher mean dCt values in comparison to the fertile control men with a borderline statistical significance (p=0,0785). The oligozoospermic men showed statistically higher mean dCt value when compared to the fertile controls (p=0,0170). This difference was even higher when Macedonians with oligozoospermia were compared with the Macedonian fertile controls (p=0,0098) (Table 1). The dCt mean differed between different Y chromosome haplogroups (p=0,0027) (Figure 3), but no difference was observed between infertile and fertile men with the most common Y chromosome haplogroups.

Table 1. Comparison of dCt mean between different studied groups.

Cases	N	Mean	Std. Deviation	Std. Error Mean	P value
Infertile Total					
Infertile	126	3.9169	0.7284	0.0649	
Controls	119	3.7492	0.7554	0.0692	0.0785
Infertile Macedonians					
Infertile	84	3.9142	0.7389	0.0806	
Controls	89	3.7334	0.7958	0.0844	0.1238
Infertile Albanians					
Infertile	32	3.8215	0.7394	0.1307	
Controls	30	3.7962	0.6302	0.1151	0.8859
Azoospermia Total					
Azoospermia	60	3.8004	0.7364	0.0951	
Controls	119	3.7492	0.7554	0.0692	0.6663
Azoospermia Macedonians					
Azoospermia	39	3.6980	0.7217	0.1156	
Controls	89	3.7334	0.7958	0.0844	0.8122
Azoospermia Albanians					
Azoospermia	17	3.9346	0.8006	0.1942	
Controls	30	3.7962	0.6302	0.1151	0.5156
Oligozoospermia Total					
Oligozoospermia	66	4.0227	0.7100	0.0874	
Controls	119	3.7492	0.7554	0.0692	**0.0170**
Oligozoospermia Macedonians					
Oligozoospermia	45	4.1016	0.7091	0.1057	
Controls	89	3.7334	0.7958	0.0844	**0.0098**
Oligozoospermia Albanians					
Oligozoospermia	15	3.6932	0.6670	0.1722	
Controls	30	3.7962	0.6302	0.1151	0.6147

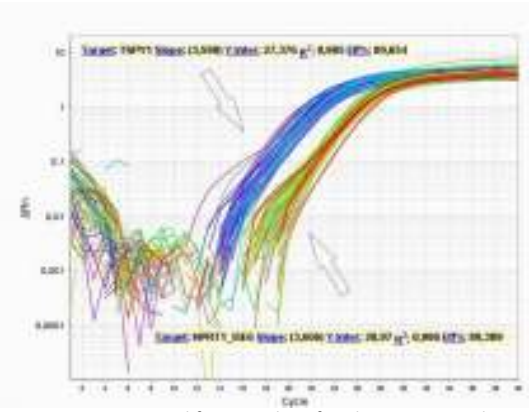

Figure 1. Amplification plot of real-time PCR analysis of multicopy TSPY1 gene and control single copy HPRT1 gene.

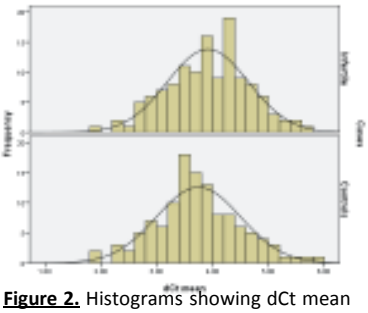

Figure 2. Histograms showing dCt mean distribution among infertile patients and control fertile men.

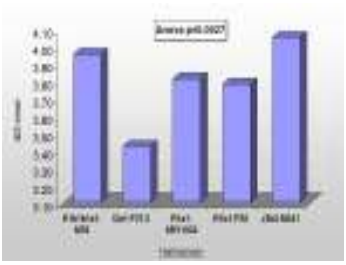

Figure 3. dCt mean in men with different Y chromosome haplogroups.

CONCLUSION

Our initial results of the study investigating relative *TSPY1* copy number in infertile men showed an association of *TSPY1* copy number with oligozoospermia. It also showed that the *TSPY1* copy number differs between different Y chromosome lineages.

ACKNOWLEDGMENTS

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