Copy-number variants in infertile men detected by array comparative genomic hybridization

I.Maleva[1], Madjunkova S.[1] , Chakalova L.[1] , Plaseski T.[2] and Plaseska-Karanfilska D.[1]

[1] *Research Centre for Genetic Engineering and Biotechnology, Macedonian Academy of Sciences and Arts, Skopje, Republic of Macedonia*

[2] *Clinic of Endocrinology and Metabolic Disorders, Faculty of Medicine, Skopje, Republic of Macedonia*

INTRODUCTION

Spermatogenesis is a dynamic and multistep process of male germ cell proliferation and differentiation by which spermatozoa are produced from primordial germ cells. The causes of spermatogenic defects in infertile men include environmental, nutritional, behavioral and genetic factors. Despite enormous progress in the understanding of human reproductive physiology, the underlying cause of male infertility (MI) remains obscure in about 50% of cases.

AIM OF THE STUDY

The aim of this study was to determine the Copy Number Variants (CNVs) that may be involved in the origin of male infertility.

MATERIALS AND METHODS

We performed Comparative Genomic Hybridization (array-CGH) on eight patients with idiopathic infertility. Four patients were azoospermic with a histopathological diagnosis of maturity arrest, and four patients had sperm counts ranging from azoospermia to normozoospermia and carried gr/gr partial AZFc deletion. We used 180K Agilent Human Genome CGH Microarrays. Scanned data were analysed using the Genomic Workbench software. We used the Database of Genomic Variants (DGV, http://projects.tcag.ca/cgi-bin/variation/) to compare our findings to previously reported CNVs.

RESULTS

A total number of 70 CNVs were detected with sizes ranging from 6 kb to 700 kb. Fifty six of them were considered as common CNV (DGV), 10 were in regions without known genes and 4 were CNVs in regions with candidate genes causing or being risk factors for spermatogenic failure: *UGT2B17* on 4q13.2 (Figure 1); *STEAP2* on 7q21.13; *TPTE* on 21p11.2-11.1 (Figure 2) and *H2BFWT* on Xq22.2 (Table 1).

Table 1. CNVs potentially associated with MI.

Patient details	Genomic region	Size	Type of CNV	Genes potentially associated with MI	Gene function
azoospermia-maturity arrest	chr4 q13.2	70 kb	del	UGT2B17	glucoronidase essential for urinary testosterone excretion
azoospermia-maturity arrest	chr4 q13.2	70 kb	dup	UGT2B17	glucoronidase essential for urinary testosterone excretion
normozoosprermia-gr/gr deletion	chr7 q21.13	69 kb	dup	STEAP2	transmembrane epithelial antigen of the prostate
oligozoospermia	chr21 p11.2-p11.1	279 kb	dup	TPTE	signal transduction pathways of the endocrine or spermatogenetic function of the testis
normozoosprermia-gr/gr deletion	chrX q22.2	117 kb	dup	H2BFWT	testis-specific histone

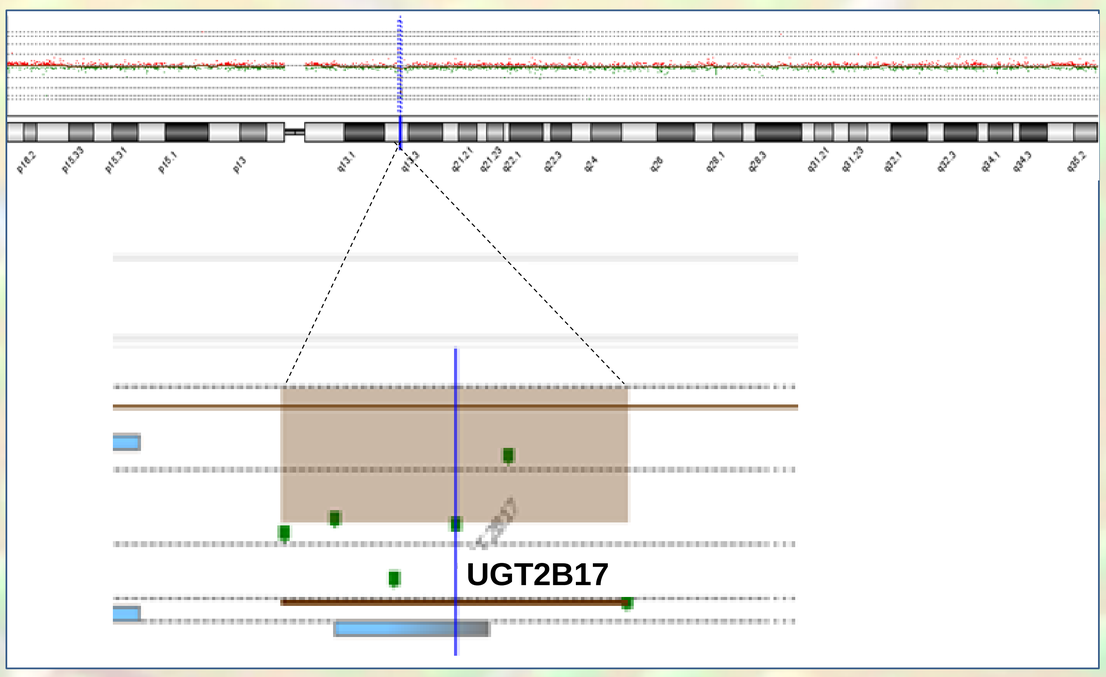

Figure 1. Genomic Workbench shapshot of chr4 q13.2 deletion.

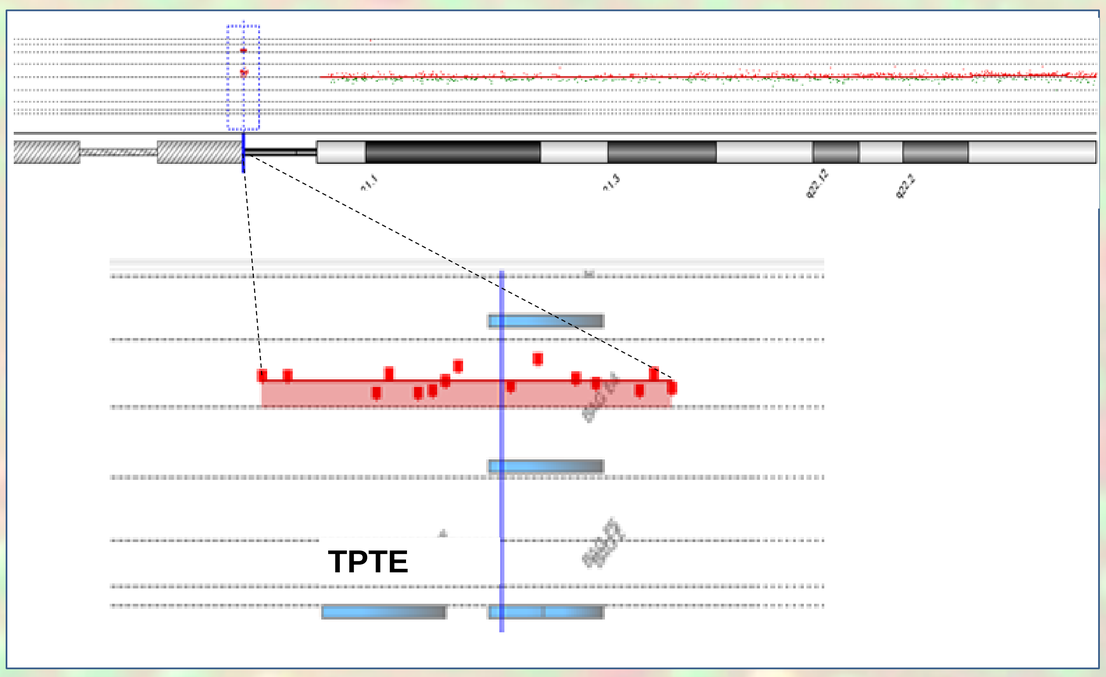

Figure 2. Genomic Workbench shapshot of chr21 p11.2-p11.1 duplication.

CONCLUSION

In conclusion, our initial results using array CGH analysis to study male infertility revealed several CNVs that may represent a risk factor for impaired spermatogenesis and male infertility.

ACKNOWLEDGMENTS

This study was supported by project CRP/MAC09-01 from ICGEB-Trieste and FP7 project No. 229458 from the European Commission (both to Dijana Plaseska-Karanfilska).