Role of the X-chromosome linked, testis-specific *TAF7L* gene in gonadal function and spermatogenic failure

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Introduction

Spermatogenic failure expressed as infertility in human is likely to be caused by defect in genes involved in spermatogenesis. The precise temporal and spatial expression of specific transcription regulation factors (TRF) have long been considered essential for proper execution of spermatogenesis. Recently, mammals have been speculated to have evolved more specialised *TRF* genes. In human the X-linked, testis-specific gene *TAF7L* may be obligatory for maintenance of spermatogenesis. In this study, we attempted to investigate the possible role of *TAF7L* gene in testicular function and spermatogenic failure.

Methods

In a case-control retrospective study, sixteen carefully selected infertile males with consistent, non-obstructive azoospermia without elongated spermatids in testis biopsy (when available) and with normal serum follicle stimulating hormone levels were recruited. Twenty age-matched men with normal spermatogenesis with the same ethnic background (Caucasian) were recruited as controls. Genomic DNA extracted from peripheral blood was screened for sequence changes in the coding regions and part of the flanking introns of the *TAF7L* gene by direct sequencing. Amino acid sequence was compared to the NCBI standard sequence (BC043391). Semen analysis and hormone evaluation were performed.

Results

Six nucleotide variants, consisting of exonic changes in the nucleotide sequence of exon 9, 10, 13, and one in the flanking intron of exon 8, with concomitant changes in amino acid sequence were observed in 4 patients. Most of these alterations were also found in 8 controls with the exception of changes in exon 13. Though none of these changes were previously described in NCBI database, some are described in a recent publication (1). There was no association or relationship observed with reproductive hormones.

Tab. I Group Statistics of clinical parameters evaluated in patients and controls

Parameters	Patients N = 16	Controls N=20	" t "	P
AGE (year)	35,31± 6,45	35,15± 7,29	0.070	0.945
VOLUME (ml)	3,37± 2,09	3,39 ± 1,59	0.063	0.950
PH	7,77± 0,32	7,88 ± 0,087	1.122	0.833
GLUCOSIDASE (IU)	46,20 ± 31,95	71,23 ± 28,28	2.023	0.054
FRUTOSE (mg/dl)	56,58 ± 50,71	50,67± 28,28	0.339	0.737
ZINC (IU)	9,24 ± 13,49	5,2421 ± 2,61	1.269	0.216
LH (U/l)	4,16 ± 1,62	3,71 ± 1,08	1.269	0.216
FSH (U/l)	4,31 ± 1,75	3,59 ± 1,75	0.999	0.325
PROLACTIN (mU/l)	229,14±152,56	231,0 ± 99,10	1.222	0.230
T (nmol/l)	15,4375 ± 5,52	16,89 ± 6,31	0.043	0.966
SHBG (nmol/l)	31,54 ± 15,34	33,15 ± 11,76	0.722	0.475
E (pmol/l)	70,07 ± 20,02	90,40 ± 32,25	2.089	0.045*
PSA (µ/l)	0,63 ± 0,31	0,79 ± 0,318	1.194	0.243
FREE T (pmol/l)	336,0 ±126,09	372,65±197,36	0.594	0.557

Values expressed as mean ± standard deviation.

Results

Tab. 2. Frequency and summary of detected polymorphisms among patients & controls.

	Sequence variants	Patients No	%	Controls No	%
1	Intron 8. 15061 A > G	0	0	1	5
2	Exon 9.c.922 A > G, Glu > Lys (E61K)	0	0	1	5
3	Intron 8. + Exon 9	1	6	1	5
4	Exon 10. c. 1047-1052 (GGA TGA) Microsatellite deletion (NGA) repeats) Glu & Asp (p.D350-E351del.).	0	0	3	15
5	Intron 8. + Exon 10.	2	13	2	10
6	Exon 13. c.1373 G > A, Arg > His (R458H)	1	6	0	0
	Total	4	25	8	40

Chi-square = 5,444 (P = 0,245); characteristics not statistically related

Summary

Our observations showed that *TAF7L* gene is highly polymorphic. These polymorphisms are not associated with gonadal dysfunction. Although, our data showed that common sequence variants of *TAF7L* gene may not play an obligatory role in spermatogenic failure, several inactivating mutations might exist, not identified in the present study. In addition to specific pattern of *TAF7L* gene polymorphisms described in our Caucasian study population we documented a SNP in intron 8 which have not been described previously.

(1) Stouffs K, Willems A, Lissens W, Tournaye H, Van Steirteghem A and Liebaers I (2006). The role of the testis-specific gene *hTAF7L* in aetiology of male infertility. Molecular Human Reproduction. 12 (4) 263-267.