The aurora kinase C gene mutations in Tunisian infertile men

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INTRODUCTION

Macrozoospermia is a rare sperm morphological abnormality associated with male infertility and is characterized by a high percentage of sperm with large irregular head. It has been shown that spermatozoa with aurora kinase C (AURKC) deficiency are tetraploid, indicating that meiosis cannot be completed without a functional *AURKC* protein (1).

Here, we investigate the frequency of the genetic defect of *AURKC* gene that has been described as frequent in the North African population by analyzing patients from the Tunisian population.

RESULTS

We identified 18 patients presenting in our Cytogenetic Department, with macrozoospermia. All consulted for primary infertility.

An extraction of the genomic DNA is carried out by Kit Qiagen from peripheral blood leukocytes.

We initially looked for recurrent mutations of the *AURKC* gene (c.144delC, p.Y248*) after amplification by polymerase chain reaction and direct Sanger sequencing. If negative, we sequence the rest of the gene.

Aurora kinase C exon 3 was sequenced for all 18 patients. A homozygous c.144delC mutation was found in 12/18 patients (67%)(Fig.1). Exon 6 was sequenced also for all patients, 2 patients (11%) carried a p.Y248* mutation (Fig.2). Amplification of the rest of gene showed 4 novel variants which are predicted as a non deleterious polymorphisms. No other mutation was identified.

In total, *AURKC* recurrent mutation was implicated in 75% of Tunisian infertile patients with macrozoospermia (Fig.3).

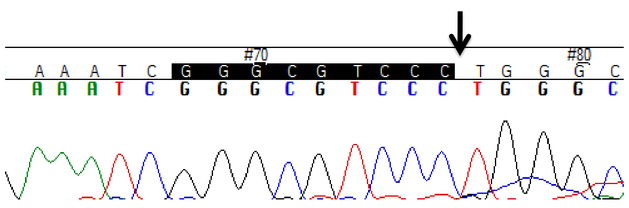

Figure1: Electrophoregram showing the c.144delC

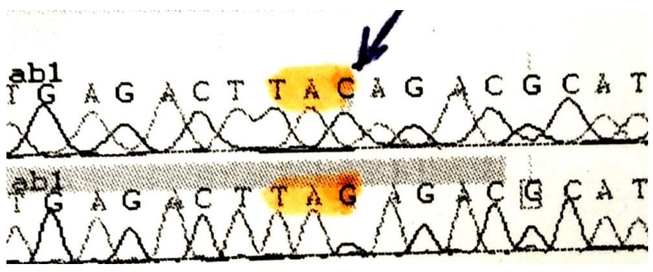

Figure 2: Electrophoregram shwonig the p.Y248 C>G

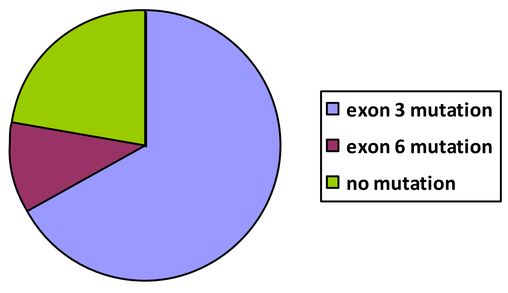

Figure 3: *AURKC* gene mutations found in our series

CONCLUSION

Our findings indicate that AURKC mutations are very frequent/recurrent and constitute the leading genetic cause of infertility in Tunisian men with macrozoospermia.

A positive genetic diagnosis provides a contraindication for *in vitro* fertilization by intracytoplasmic sperm injection (ICSI)

This highlights the importance of the molecular analysis of *AURKC* mutations for infertile men with high percentage of large headed multiflagellar spermatozoa in order to limit unnecessary in vitro fertilization attempts for them.

REFERENCE

(1) Dieterich, K., Zouari, R., Harbuz, R., Vialard, F., Martinez, D., Bellayou, H., ... & Ray, P. F. (2009). The Aurora Kinase C c. 144delC mutation causes meiosis I arrest in men and is frequent in the North African population. *Human Molecular Genetics*, *18*(7), 1301-1309.

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