

Screening for Y-micro deletions in male infertility

An internationally recommended test for Azoospermia and Oligospermia

Physician information material

Approximately 15% of all couples worldwide experience some form of infertility and half of them attribute to male infertility. Micro deletions of Y chromosome are the second most frequent genetic cause of spermatogenic failure in infertile men after the Klinefelter syndrome. European academy of Andrology (EAA) and American society of Human genetics (ASHG) recommend routine molecular analysis of Y-micro deletions during the workup of male infertility in men with Azoospermia or Oligospermia.

Identification and analysis of pathology associated with Y-chromosome deletions is an important tool in the management of male infertility. It permits the cause of the patient's Azoospermia/Oligospermia to be established and to formulate a prognosis and planned management.

Micro deletions that are clinically relevant and are found in men with oligo- or Azoospermia are: **1) AZFa** **2) AZFb** (proximal P1 and P5) **3) AZFbc** (distal P1/distal P1 and P4/P5) **4) AZFc** (b2/b4) on Y chromosome. PCR amplification of using Sequence tag sites (STSs), nested in and around the spermatogenesis genes is used for the deletion detection.

Genotype/Phenotype correlation

1. AZFa deletions

Deletions of the entire AZFa region invariably results in complete Sertoli Cells Only (SCO) syndrome and/or Azoospermia. The diagnosis of a complete deletion of AZFa region implies the virtual impossibility to retrieve testicular sperm for ICSI.

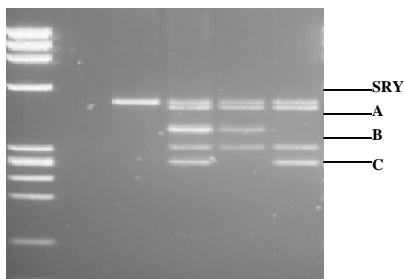
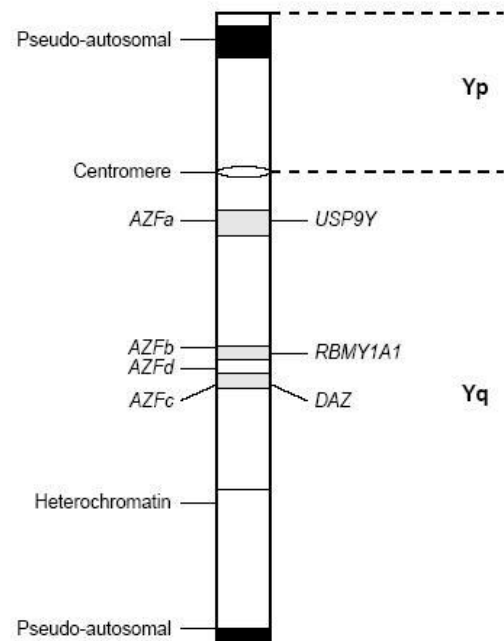
2. AZFb deletions

Diagnosis of complete deletions of AZFb or AZFb+c is also incompatible with sperm retrieval and ICSI is not recommended to these patients.

3. AZFc deletions

Deletions of AZFc region are associated with a variable clinical and histological phenotype. AZFc deletions are compatible with residual spermatogenesis. AZFc deletions can be found in men with Azoospermia or severe Oligospermia and also in men with history of natural conception.

In men with Azoospermia and AZFc deletion there is a fairly good chance of retrieving sperm from TESE and children can be conceived by ICSI. However such patients can transmit the deletion to male offspring. Therefore, there is a need to provide information by prenatal diagnosis in such conditions.



GeneTech protocol

GeneTech's protocol is a well standardized, robust and reproducible method for Y chromosome deletions with detection of non-polymorphic, pathology related sequence tag sites (STSs) from all AZF regions. It is developed based on the 'laboratory guidelines for molecular diagnosis of Y-chromosomal micro deletions' stated jointly by the European Academy of Andrology (EAA) and the European Molecular Genetics Quality Network (EMQN). Reports are written in standardized format with picture and clear interpretation that is understandable to the physician.

Summary

Patients with Azoospermia and severe Oligospermia who may be candidate for ICSI, TESE/ICSI or other artificial reproductive technologies should be offered deletion screening because TESE should not be recommended in cases of complete deletion of AZFa region, or complete deletion of AZFb or deletions of the AZFb+c regions. Moreover, micro deletions of the AZFc region are transmitted to the male offspring if assisted reproduction is performed and prenatal diagnosis such be offered. Genetic counseling is helpful in providing such information to families.

