SW Thames Regional Genetics Laboratory

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CPA
Accredited Medical Laboratory
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Y chromosome microdeletions

Introduction

Y chromosome microdeletions (MIM#415000) are the second most frequent genetic cause of spermatogenetic failure in men after Klinefelter syndrome, and are estimated to affect 1/2000-1/3000 males. 95% of the Y chromosome is comprised of the male-specific region (MSY), and microdeletions of this material have been classically subdivided into three azoospermia factor (AZF) regions: AZFa, AZFb and AZFc. Deletions of each region are associated with clinically different phenotypes; complete deletion of AZFa results in Sertoli-cell only syndrome (SCOS), complete deletion of AZFb causes maturation arrest of spermatogenesis, and complete deletion of AZFc shows a variable phenotype, ranging from SCOS to oligozoospermia. The Y microdeletion screen can therefore be used as a prognostic indicator when a couple is deciding whether to embark on fertility treatment.

Referrals

Individuals with non-obstructive azoospermia or severe oligozoospermia who may be candidates for TESE (testicular sperm extraction) /ICSI (intra-cytoplasmic sperm injection) treatment should be offered diagnostic testing. TESE is not recommended in the case of complete deletion of AZFa, complete deletion of AZFb with or without deletion of AZFc, or deletion of all 3 AZF regions, as there is virtually zero chance of sperm retrieval. On the other hand, sperm may be retrieved from the testes for intra-cytoplasmic sperm injection (ICSI) in two-thirds of men with complete AZFc deletions (Stahl et al, 2010 *Fertil Steril* 94:1753.)

Service offered

Multiplex Polymerase chain reaction (PCR) amplification using two markers for each of the three AZF regions in the MSY to identify microdeletions known to be associated with spermatogenic failure. When a deletion is detected, further markers are tested in order to determine the extent of the deletion. Testing is carried out according to EAA/EMQN guidelines.

Technical

Multiplex PCR amplification using primers specific to the three regions of interest; AZFa, AZFb, and AZFc. Primers for ZFY and SRY are also included to identify technical failure and male specific sequences. In order to identify each of the amplicons, the PCR products are then run on a 2.5% agarose gel, which separates the fragments by size and charge.

A normal male sample yields bands corresponding to each of the eight different primers used in the reaction; two for each AZF regions, in different multiplexes, and the two control bands (SRY and ZFY).

In patients with a deletion of a particular region, the relevant band will be missing from both multiplexes. Further markers will then be tested to determine the extent of the deletion.

Target reporting time

Diagnostic referrals are reported in 2 - 4 weeks. For urgent cases, please contact the laboratory.

Samples required
4-8mls venous blood in plastic EDTA bottles.
A completed DNA request form should accompany all samples (available on our website at http://www.southwestthamesgenetics.nhs.uk/molecular_default.asp).
Patient details/GP name and address
To facilitate accurate testing and reporting please provide patient demographic details (full name, date of birth, Address, postcode and ethnic origin), details of any relevant family history and full contact details for the referring clinician