Y chromosome microdeletion analysis

Contact details:
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Sample Required:

Adult: 5mls blood in EDTA

Samples should be accompanied by a FULLY completed BGL infertility request form (page 2 of this document)
Please include details of test, clinical information, address and POSTCODE, NHS number, referring clinician, unit/hospital, billing contact and address

Consent and DNA Storage:

All genetic testing requires consent. **It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.**

DNA is stored from **ALL** patients undergoing DNA testing, unless consent for this is specifically denied.

Stored material from all referrals may be retained for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics:

- Microdeletions of the Y chromosome are the second most frequent genetic cause of spermatogenetic failure in infertile men after Klinefelter syndrome.
- 2-10% of men affected with azoospermia/severe oligospermia (sperm concentrations $<1.10^6$/mL) may have microdeletions of Yq11 classically subdivided into three regions called AZFa, AZFb and AZFc, respectively (Vogt *et al* 1996). Note that the AZFb and AZFc regions are now described as overlapping.
- Azoospermic men have a higher incidence of microdeletions than oligospermic men. Typically, routine laboratories receiving referrals without controlled patient selection have a pick-up rate of ~2-5%. The analysis undertaken in this laboratory is expected to detect approximately 90-95% of deletions in the three AZF regions.
- Y microdeletions usually result in non-obstructive azoospermia/severe oligospermia compared with male infertility due to obstructive azoospermia *(CBAVD, see CF serviced proforma).*
- The finding of a Y microdeletion provides the clinician with guidance whether sperm is retrievable on testicular sperm extraction (TESE) as only AZFc deletions are compatible with TESE.
- Genetic counselling is recommended in patients with a Y microdeletion result, especially prior to treatment with assisted reproduction techniques. This result may be of relevance to any brothers of a Y microdeletion patient due to possible germinal mosaicism for the deletion in the father. As sex chromosome mosaicism has been found in some patients with a Yq deletion, additional cytogenetic screening may be appropriate.

Service offered:

- Testing is carried out according to the EAA/EMQN best practice guidelines. This protocol is expected to detect between 90-95% of published clinically relevant deletions.
- First line screen: PCR analysis of 2 markers from each of the three *AZF* regions plus appropriate controls in a two multiplex format:
  AZFa: sY84 and sY86
  AZFb: sY127 and sY134
  AZFc: sY254 and sY255
- Further analysis: If a Y microdeletion is detected on the above screen, further analysis is carried out to confirm deletion of the above markers and analysis of appropriate markers at the borders of the AZF region(s) involved.
- It may be appropriate to request karyotyping simultaneously to exclude a chromosomal abnormality.

Referrals:

- Referrals should be made using the BGL request form for infertility referrals (for form see page 2 below).
- Referrals should be accompanied by provision of a possible reason for the patient's infertility.

Target reporting Time: TAT

First Line Screen - 42 days
Extended analysis charged on a case by case basis.

Quality Assurance:

- BGL participates in the EMQN scheme (and has UKGTN approval) for this service.

Please contact the laboratory for up to date prices

Severn Pathology
North Bristol NHS Trust

BRISTOL GENETICS LABORATORY REQUEST FORM FOR INFERTILITY REFERRALS

Sample required: ***CFTR*** **mutation and Y microdeletion testing: 3ml whole blood in EDTA tube(s)**
Chromosome analysis: 5ml whole blood in lithium heparin tube(s)

Date & time sample taken: **Inoculation Risk: Yes/No** **Please give details:**

Surname:		Sex:		**Tests Requested:**
Forename:		DOB:		*CFTR* Mutation Analysis ☐
Hospital No:		Hospital:		Chromosome Analysis ☐
NHS Number:		NHS ☐ Private ☐		Y Microdeletion Analysis ☐
Postcode:		Date of next appointment:		***Billing Contact and Address:**
Consultant:		Sample Type:		

***SAMPLES WILL NOT BE PROCESSED WITHOUT CLEAR BILLING CONTACT AND ADDRESS INFORMATION**

CLINICAL INFORMATION. **Patient being referred due to:**

A: AZOOSPERMIA

Please indicate whether:

- Patient has CBAVD ☐
- Patient definitely does NOT have CBAVD ☐
- Patient has NOT been investigated for CBAVD ☐
- Cause is unknown ☐

B: OLIGOSPERMIA / SEVERE OLIGOSPERMIA

Please indicate whether:

- Patient has CUAVD ☐
- Patient definitely does NOT have CUAVD ☐
- Patient has NOT been investigated for CUAVD ☐
- Cause is unknown ☐

Please indicate sperm count: million/ml

C: POPULATION RISK SCREENING

- Tissue share donor ☐
- Male infertility other than azoospermia/oligospermia (please provide details in section D) ☐
- Partner of patient undergoing infertility treatment ☐

D: FURTHER INFORMATION

Clinician Signature (print if illegible):

Please forward to: **BRISTOL GENETICS LABORATORY**
PATHOLOGY SCIENCES
SOUTHMEAD HOSPITAL
BRISTOL BS10 5NB

TELEPHONE: 0117 414 6168

FOR LABORATORY USE ONLY: -
EXTRACTION METHOD:
INITIALS:
DATE:

INFORMED CONSENT:
In submitting this sample the clinician confirms that consent has been obtained for testing for the disorder/test requested and for long term DNA storage.
The patient should be advised that the sample may be used anonymously for quality assurance and training purposes for requested assays.