Relevant Markers for Molecular Diagnosis of 46,XX SRY-Positive Azoospermic Men

Iris Pereira-Caetano[1], João Gonçalves[1,2]

[1] Human Genetics Department, National Institute of Health Dr Ricardo Jorge, Lisbon, Portugal

[2] Center forToxicogenomics and Human Health, Nova Medical School, Lisbon,Portugal

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Introduction

- **Molecular screening of Y-chromosome AZF microdeletions** and chromosome analysis - first step in the genetic diagnosis of male infertility.

- Routine in the workup of infertile patients with severe oligozoospermia or secretory azoospermia of idiopathic cause.

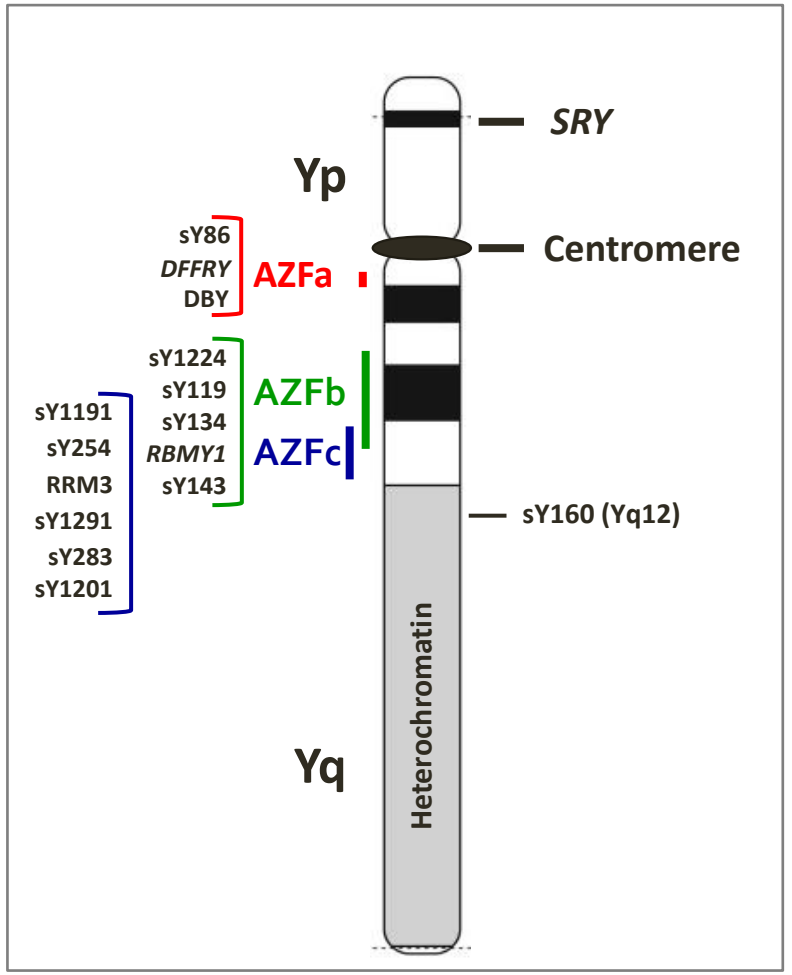
- Microdeletions can cover one or more of the three AZF regions - associates with specific testicular histology or infertile phenotype, ranging from Sertoli-cell-only syndrome (SCO) (AZFa), gamete maturation arrest (AZFb) to hypospermatogenesis (AZFc).

- **Complete AZF deletions** (AZFabc) are very rare (1–3%)
  Most likely related to **abnormal karyotypes** such as 46,XX, 46,X,del(Y)(q11.1) or 46,X,iso(Y)(p10) - **causing azoospermia with SCO**.

- In such cases, it is not appropriate to propose testicular sperm extraction due to the impossibility to retrieve testicular spermatozoa for intracytoplasmic sperm injection.

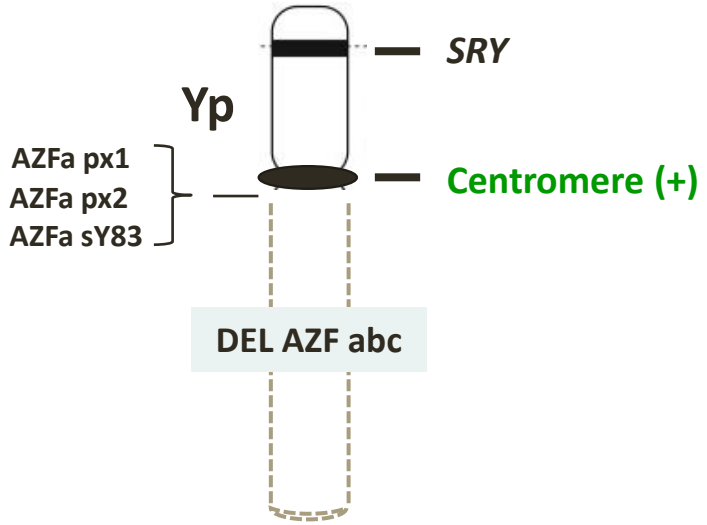
Methodology

- Since 2000 – **348** samples of **azoospermic** men were analyzed
- Compliance with the EAA/EMQN guidelines for Y-chromosomal microdeletions testing
- Annual participation in EMQN-EQA programs
- Genomic DNA was analyzed by **multiplex-PCR amplification** of **STS specific for each AZF** region – SRY and AR (in Xq12) as control markers



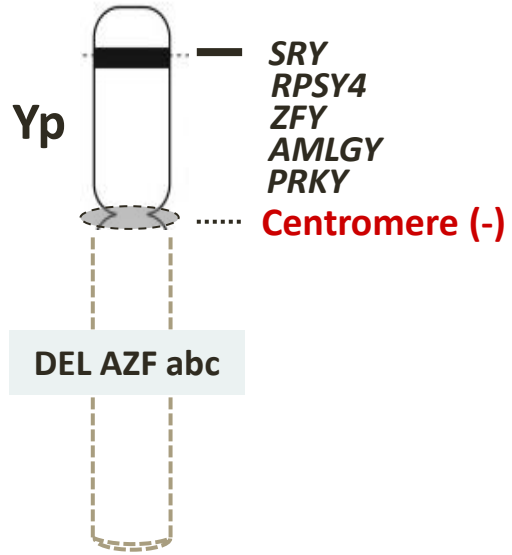
Methodology

- **AZFabc deletions – extension PCR-analysis for DYZ3-Y-centromere**:
- if **present**- screening of other Yq centromeric proximal borders
- if **absent** (most cases of 46,XX males SRY**-**positive) - screening of other Yp specific genes



Results

- We characterized **10 men with AZFabc deletions** (2,9%)
- **8** of which **46,XX SRY-positive** - **negative for the centromere** and all the AZFabc markers



Discussion

- In such cases (46,XX SRY-positive - negative for the centromere and all AZFabc markers) **screening for heterochromatin** (e.g. sY160) and **markers mapping between the centromere** and AZFa is **inappropriate.**

- Is highly unlikely that these patients have Yq material between AZFa and the centromere and terminal Yq sequences.

- Testing for the presence of **additional markers do not have any relevance** for the diagnosis nor the clinical management of these patients.

- **Karyotyping** evaluation should be **recommended.**

References: Krausz *et al* 2014 *Andrology* 2(1): 5–19