A novel familial androgen receptor mutation (W752G) in complete androgen insensitivity syndrome: use of in vitro study according to the nature of amino acid substitution.

#P1-360

Paris F[1,2], Boulahtouf A[3], Kalfa N [4], Guibal MP [4], Gaspari L[1], Bourguet W [5], Sultan C[1,2], Balaguer P [3]

1- Unité d'Endocrinologie Pédiatrique, Hôpital Arnaud de Villeneuve, CHU Montpellier. 2- Département d'Hormonologie, Hôpital Lapeyronie, CHU de Montpellier.
3- Unité INSERM 1194, IRCM Montpellier 4- Département de Chirurgie Viscérale Pédiatrique, CHU de Montpellier 5- CNRS-UMR 5048 CBS Montpellier, France.

Background :

Androgen receptor (AR) gene mutations are the most frequent cause of 46,XY disorders of sex development and are associated with a variety of phenotypes, ranging from phenotypic women (complete androgen insensitivity syndrome) to milder degrees of undervirilization (partial and mild forms).

Aims and Objectives:

To specify how a phenotype-genotype correlation can be refined by in vitro study based on the nature of amino acid substitution.

Patients and Methods:

2-months-old girl who was admitted for inguinal hernia:

Clinical examination: Inguinal gonads
Ultrasonography: Absence of uterus
Family questioning : one of the mother's sisters was infertile.

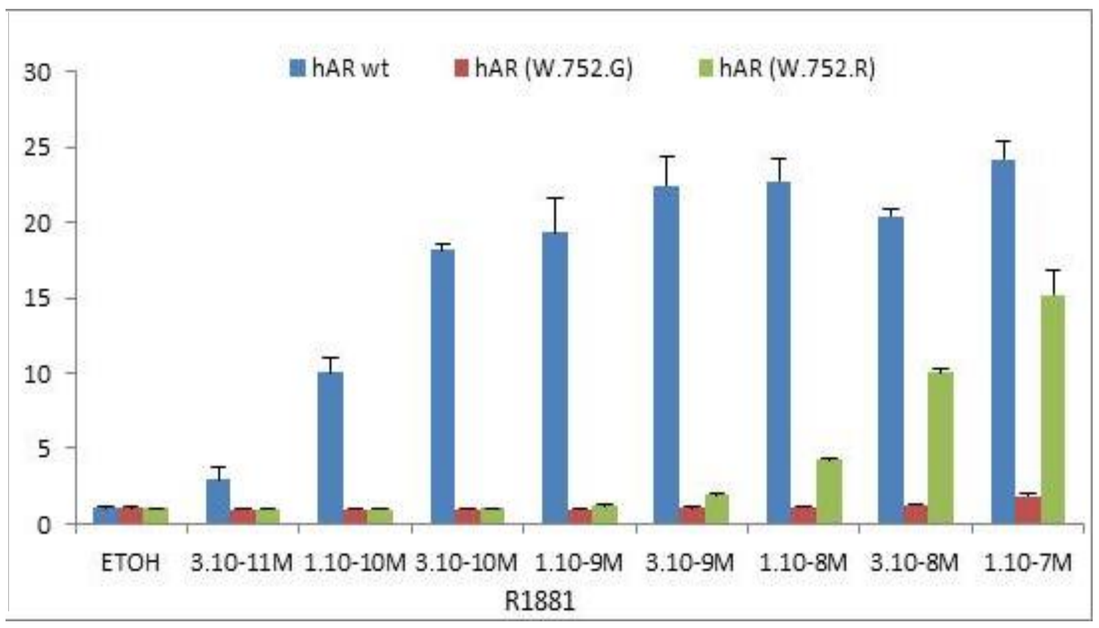
→ Surgery and reintegration of gonads in the abdominal position

→ Karyotype : 46, XY
→ AR gene analysis → new W752G mutation: CAIS

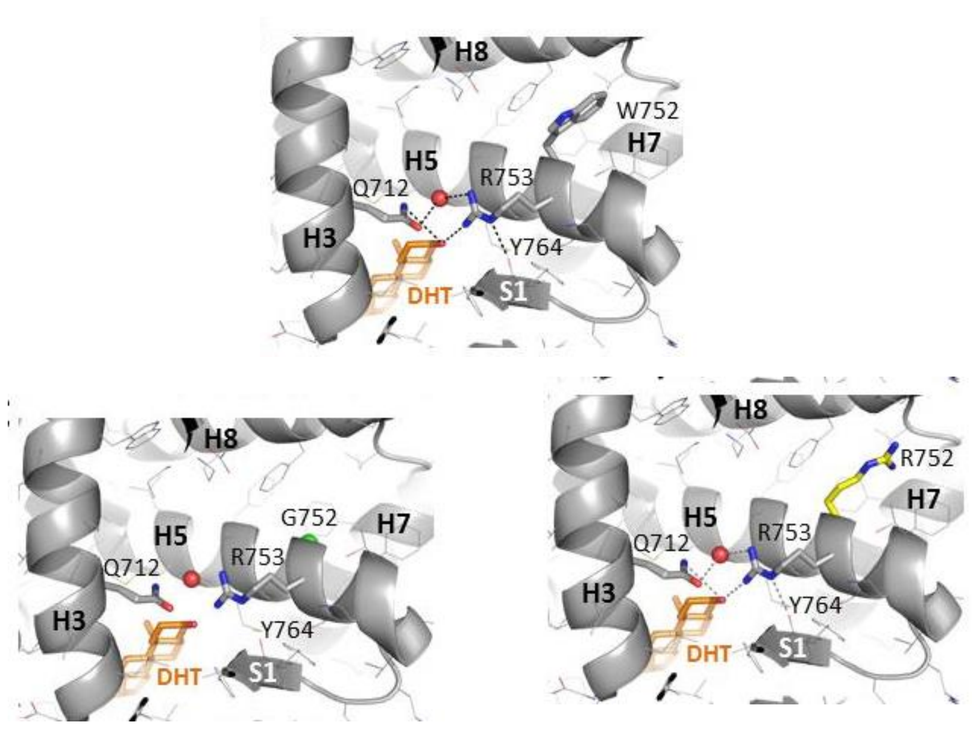
We performed in vitro study of this new mutation and the only other reported W752R mutation, previously reported in two sisters with CAIS.

Results:

Transfection studies confirmed the decrease in AR transactivation despite increased androgen concentration, whereas for the other p.W752R AR mutation transactivation increased at androgen concentrations above 10-8M. .



Structural analysis is in line with the functional data reported



Discussion and Conclusion:

Although newborns diagnosed as CAIS carriers are always raised as females, the time of gonadectomy tends to be later today than it was some years ago. This later gonadectomy timing allows spontaneous puberty, but it raises questions about potential pubertal virilization and male identity in cases of the persistence of residual AR activity. Through this report of a new W752G mutation of the AR gene in a CAIS patient, we underline the usefulness of in vitro study to better understand the virilization defect and thus better organize the follow-up of these patients based on the nature of the amino acid substitution.

55ESPE 360--P1
Gonads & DSD
franoise Paris
DOI: 10.3252/pso.eu.55ESPE.2016
Poster presented at: ESPE 2016 PARIS