Androgen insensitivity syndrome (Testicular feminization)

Genetics

-AR (Androgen receptor; Xq11-q12)

-XLR

Clinical findings/Dysmorphic features

-Evidence of feminization (i.e. undermasculinization) of ext. genitalia; abnormal secondary sexual development; infertility in those with 46, XY karyotype

-Spectrum: complete androgen insensitivity syndrome (CAIS), with typical female genitalia --> partial androgen insensitivity syndrome (PAIS) with predominantly female/predominantly male/ambiguous genitalia --> mild androgen insensitivity syndrome (MAIS) with normal male genitalia

Etiology

-2:100,000 to 5:100,000 for CAIS

Pathogenesis

-Nearly all missense variants in the androgen-binding domain impair androgen binding and impair transactivation by the AR --> male sex hormone androgen cannot bind/activate

-Missense variants in the zinc fingers or α-helical portions of the DNA-binding domain impair binding to a sequence of regulatory nucleotides known as an androgen response element

Genetic testing/diagnosis

-No formal diagnostic criteria for identifying AIS have as yet been published

-Single gene sequencing of AR: 97%, Deletion/Duplication analysis: 3%