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Newborn Screening For Adrenoleukodystrophy: Genetic Testing and Counseling Considerations

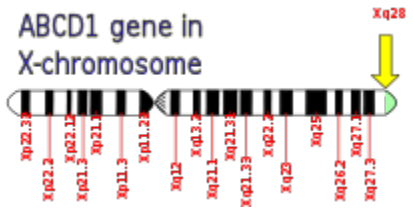
February 20, 2018

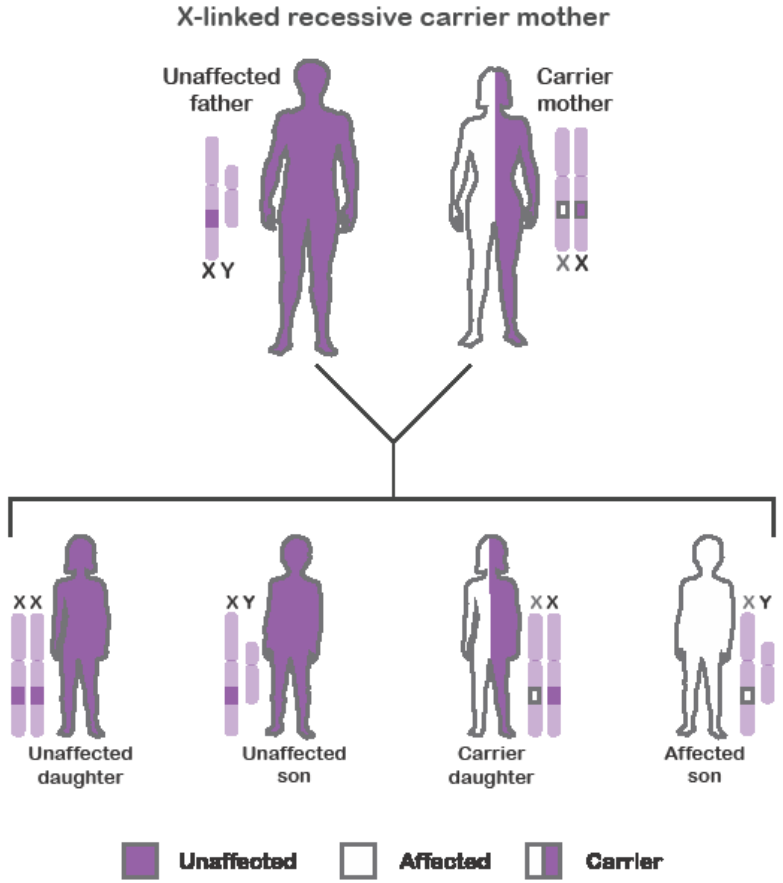
Outline

- Use of sequencing
- De Novo mutations
- Unusual possibilities
- Education and communication about mutations

Background

- ALD caused by mutations in the *ABCD1* gene
- Mutation database
  http://www.x-ald.nl/



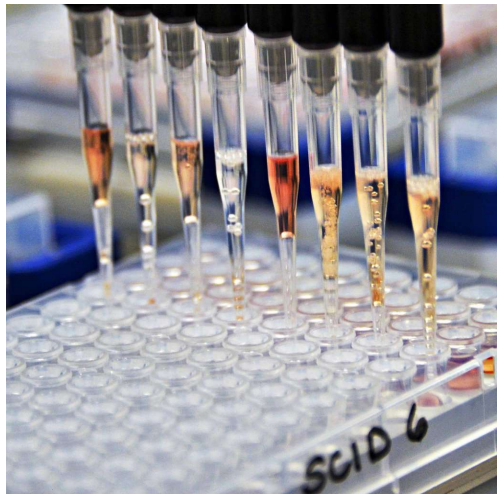


Use of Sequencing

- Varies by State
  - Performed as part of newborn screening laboratory process or ordered by clinical provider
  - Determined by each program based on staffing, cost, state policies and referring provider preferences

Use of Sequencing

- Clinically well newborns with elevated C26:0 on newborn screening
  - Newborns in the NICU with symptoms of other peroxisomal disorders may not need *ABCD1* sequencing, especially if other peroxisomal studies are abnormal (plasmalogen)

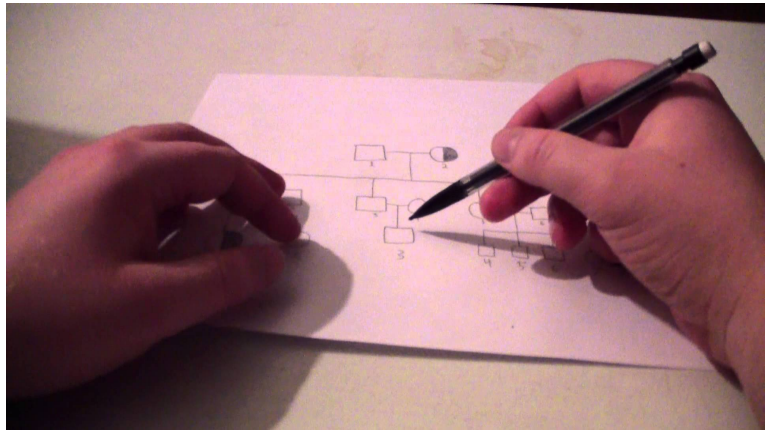


Use of Sequencing

- Parental testing
  - Maternal testing indicated for males with a mutation
  - Maternal and paternal testing indicated for females with a mutation (carriers)
- Purpose of parental testing
  - Identify carrier/disease status
  - Facilitate pedigree review and familial testing

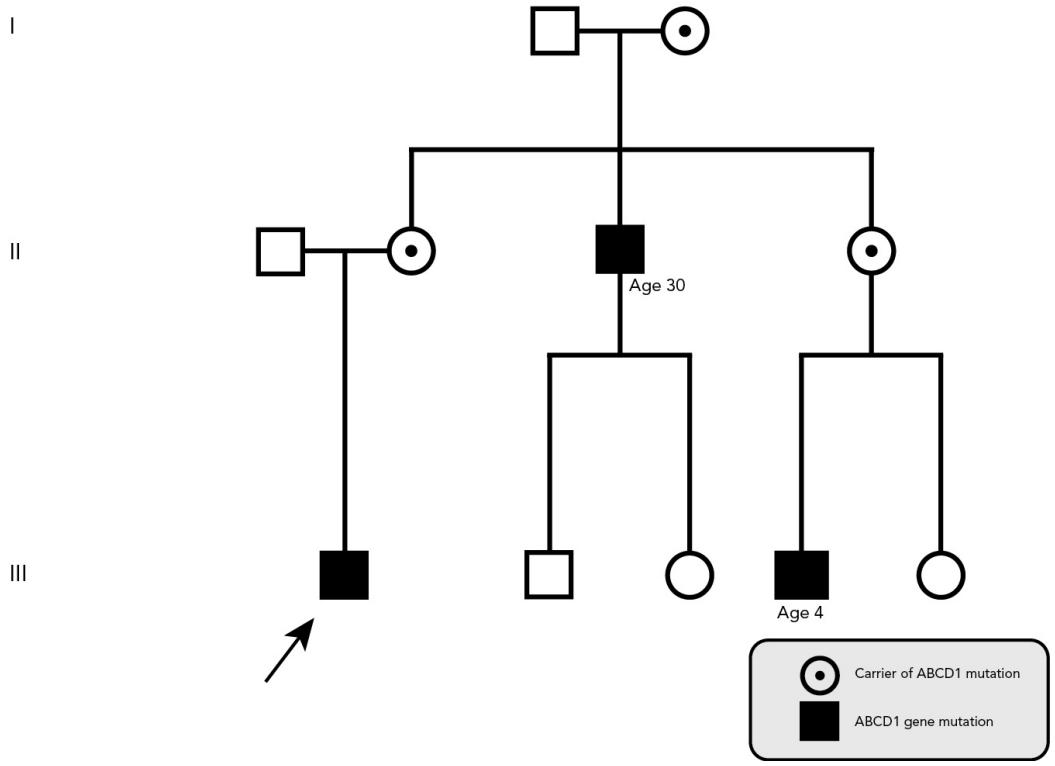
Use of Sequencing

- Pedigree review and testing
  - Identify family members that need genetic counseling and possible genetic testing

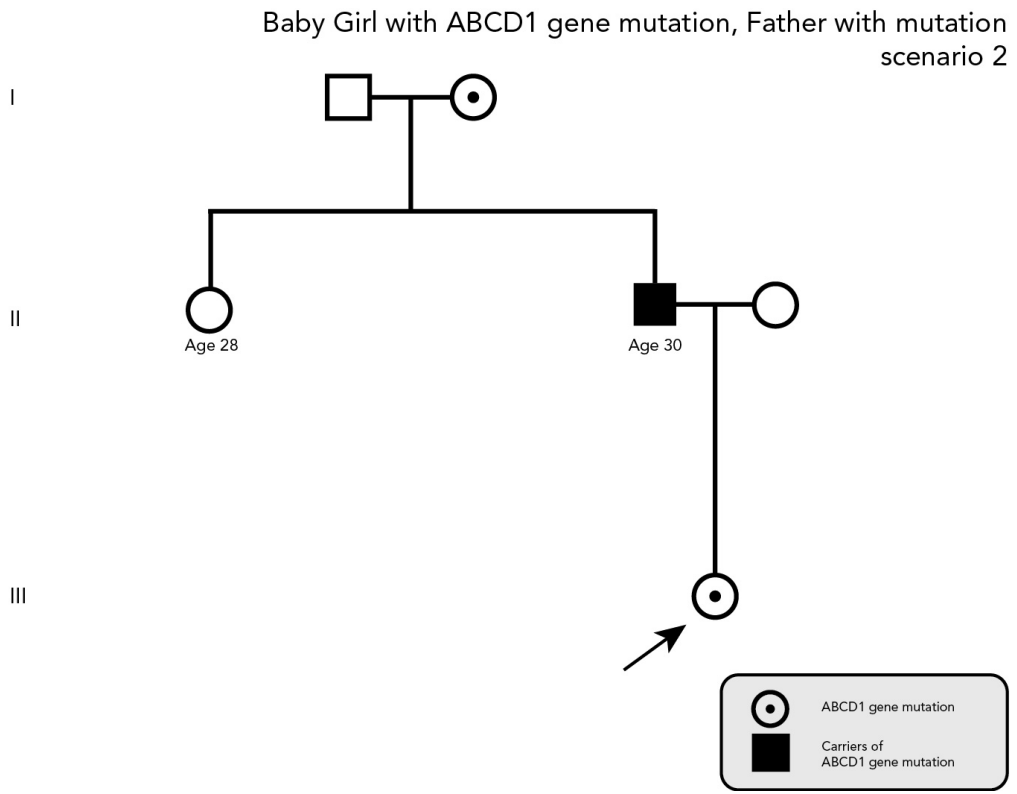


Pedigree Review
Newborn Boy with *ABCD1* Mutation

Baby Boy with ABCD1 gene mutation, carrier mother and grandmother.



Pedigree Review
Newborn Girl with *ABCD1* Mutation



De Novo Mutations

- Neither parent has the mutation identified in the child
  - De novo (9/75 in NYS - ~12%)
  - Non-paternity
  - Gonadal mosaicism
    - Two or more children with the condition

Unusual Possibilities

- Male who is a carrier due to Klinefelter syndrome (XXY)
- Female with disease due to Turner syndrome

Talking to Primary Care Providers about DNA Results

- Educate them “just in time” when giving the referral information.
- Most just want high level – “what do I need to tell my patient’s parents until they see the specialist?”
- Be careful about message

Tips for Newborn Screening Programs and Referral Sites

- Provide DNA results in writing versus reading over the phone
- Have conversations about:
  - What tools will be used for variant interpretation
  - Family testing procedures

Tips for Communicating with Parents about DNA Results

- Information is better explained in-person versus as part of a phone call
- Mothers often experience guilt if they also have a mutation (carriers)
- Resources may be needed to explain genetics to other family members

Questions?