Inheritance of Dystroglycanopathies

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From Cell to Protein

Cell → Nucleus → Chromosome → DNA Strand → Gene Code → Protein
Genes & Proteins

CHROMOSOME → GENE → PROTEIN PRODUCT

Each chromosome is composed of one large DNA molecule

A gene is a segment of DNA that makes a protein product

Normal gene

Gene with a (G to T) mutation (message has changed)

Working Protein

Non-working Protein
Males have 1 X chromosome
Females have 2 X chromosomes
Autosomal Recessive Inheritance

- Most Limb-girdle muscular dystrophies
- Most congenital muscular dystrophies
- Genes associated with dystroglycanopathy
  - LARGE
  - FKRP
  - FKTN
  - POMGnT1
  - POMT1
  - POMT2
  - ISPD
Autosomal Recessive Inheritance

- Males and females are affected equally
- Both parents are carriers
- ¼ chance that carrier parents will have an affected child
- If not affected, the offspring have a 2/3 chance to be carriers
Autosomal Recessive Inheritance: One parent is affected

- All the offspring will be carriers
  - Unless the other parent is affected or a carrier (unlikely)
  - Carrier testing of the other parent is recommended for common conditions!!
    - 1:40 are SMA carriers
    - 1:110 are F-ataxia carriers
    - 1:400?? Are carriers for more rare forms of MD
Autosomal Recessive Inheritance: One parent is a carrier

- Unlikely to have affected children, unless the other parent is a carrier.
- We all are carriers of 4-6 recessive genetic conditions.

With each pregnancy---
1. Either parent can be a carrier—male or female.
2. There is a 50% chance the child will inherit the recessive gene (rN), making them a carrier.
3. A child who is a carrier can be a male or female.
4. Carriers are usually unaffected.
Prenatal Genetic Diagnosis

- Preconception
  - Genetic counseling—know the chances!
- Prenatal testing
  - Amniocentesis around 15 weeks
  - Chorionic villus sampling (CVS), 12 weeks
- Pre-implantation Genetic Diagnosis (PGD)
- Donor eggs/sperm/embryos

Newborn screening??
Prenatal Testing
Preimplantation Genetic Diagnosis

Conception achieved by *in vitro* fertilization

Mitotic cell division

Preimplantation diagnosis

Holding pipette

Microscopic pipette suctions away one cell for genetic analysis

Genetic testing of DNA within single cell

Mutation detected; embryo discarded

No mutation detected; attempted implantation of embryo

From GeneReviews glossary
Genetic Resources

Genetics Home Reference - Handbook
  - Cells and DNA
  - How genes work
  - Mutations and health
  - Inheritance

Gene Reviews – reviews LGMD & CMD
  - Characteristics, diagnostic testing, management, inheritance