

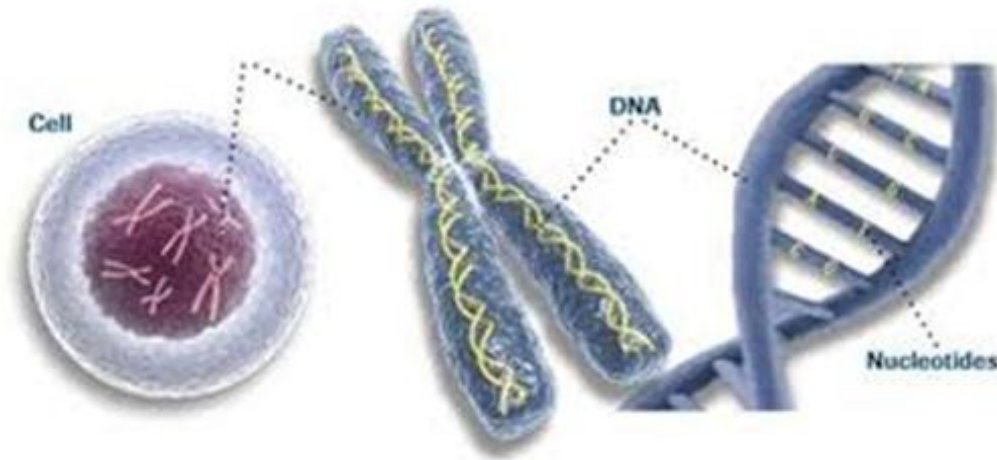
Genetics of Cystinuria

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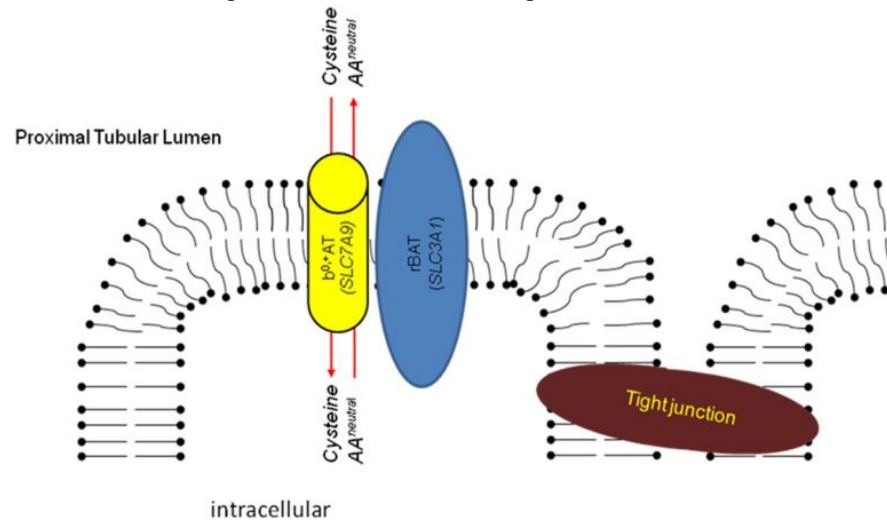
Genetics – The Basics



- DNA is contained within the cells of our body
- A gene is a small piece of DNA
- We have 2 copies (alleles) of each gene. One from our Mother and one from our Father

Cystinuria Genes

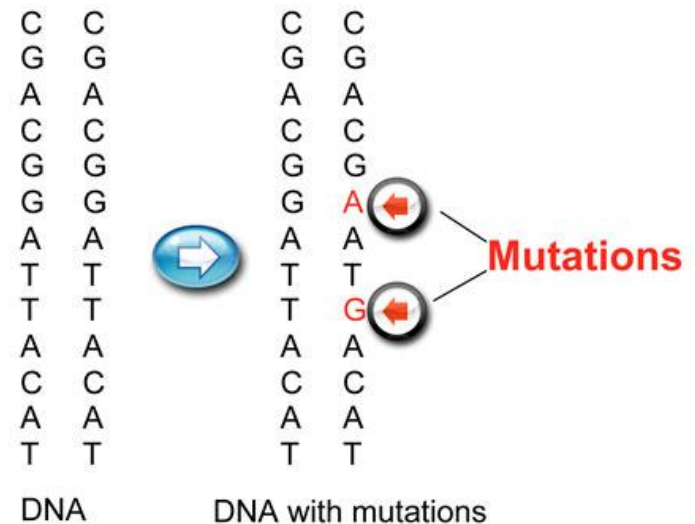
- 2 genes known – SLC3A1, SLC7A9
- Involved in transport of cystine



- Mutations in these genes result in Cystinuria

Mutations

- Errors in the DNA code
- Can be inherited
- Different types
- Can have no effect
- Disease causing



Types of Mutations

- Silent
- Missense
- Nonsense
- Insertions
- Deletions
- Splicing

“There was an old lady who lived in a shoe”

Types of Mutations

- Silent
- Missense
- Nonsense
- Insertions
- Deletions
- Splicing

“Their was an old lady who lived in a shoe”

Types of Mutations

- Silent
- Missense
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“There was an old cat who lived in a shoe”

Types of Mutations

- Silent
- Missense
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“There was an old lady who”

Types of Mutations

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“There was was an old lady who lived in a shoe”

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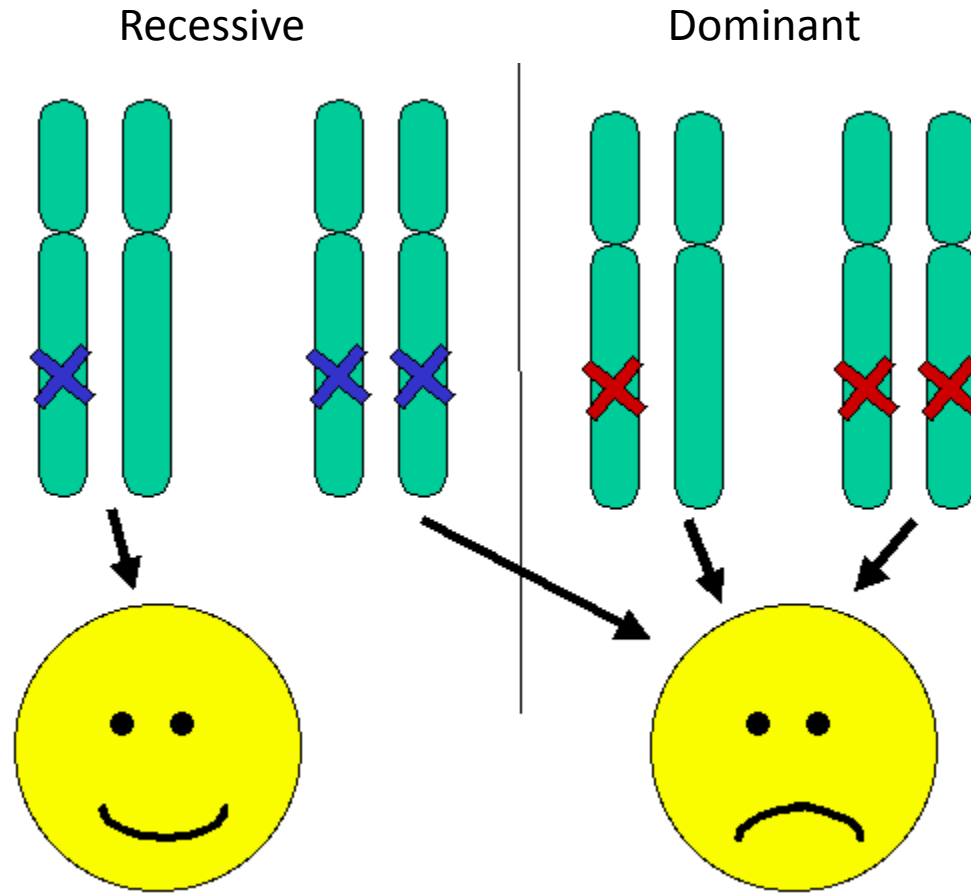
“There an old lady who lived in a shoe”

Types of Mutations

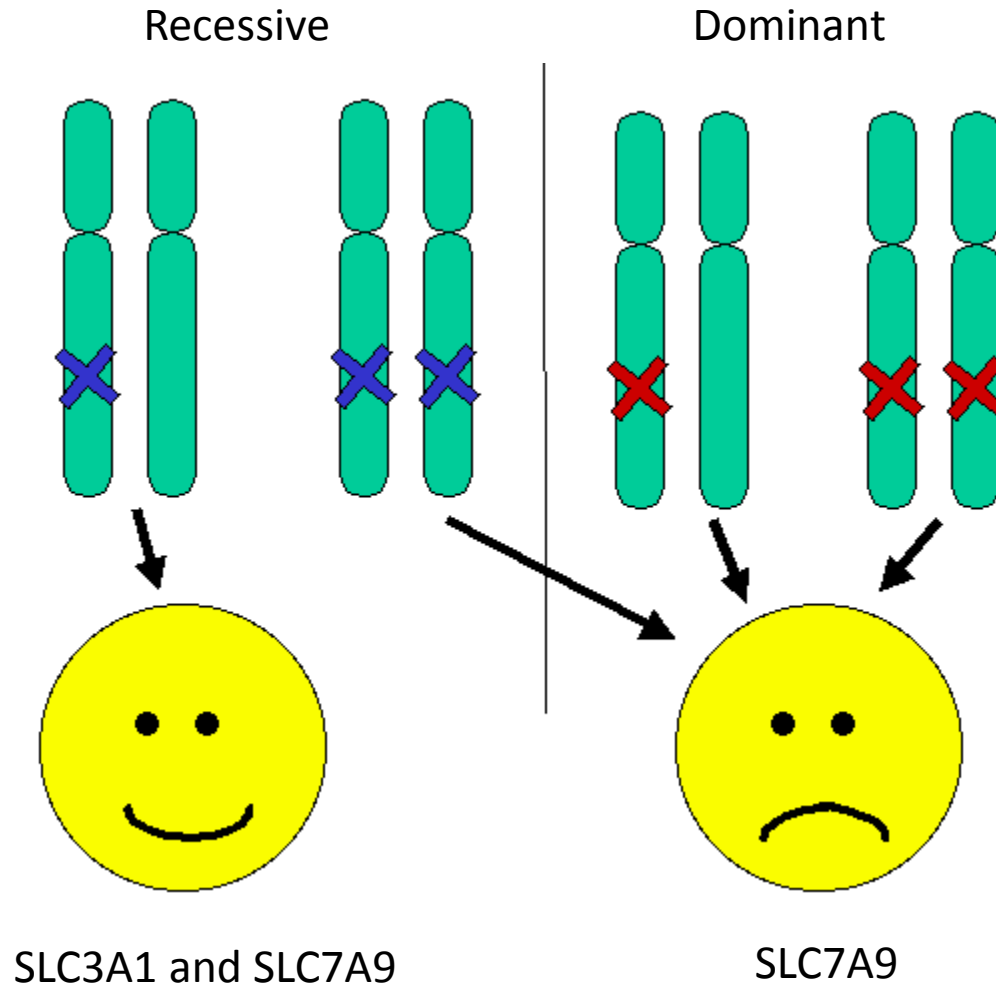
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“There was an old lawh oli vedin as h oe”

Inheritance

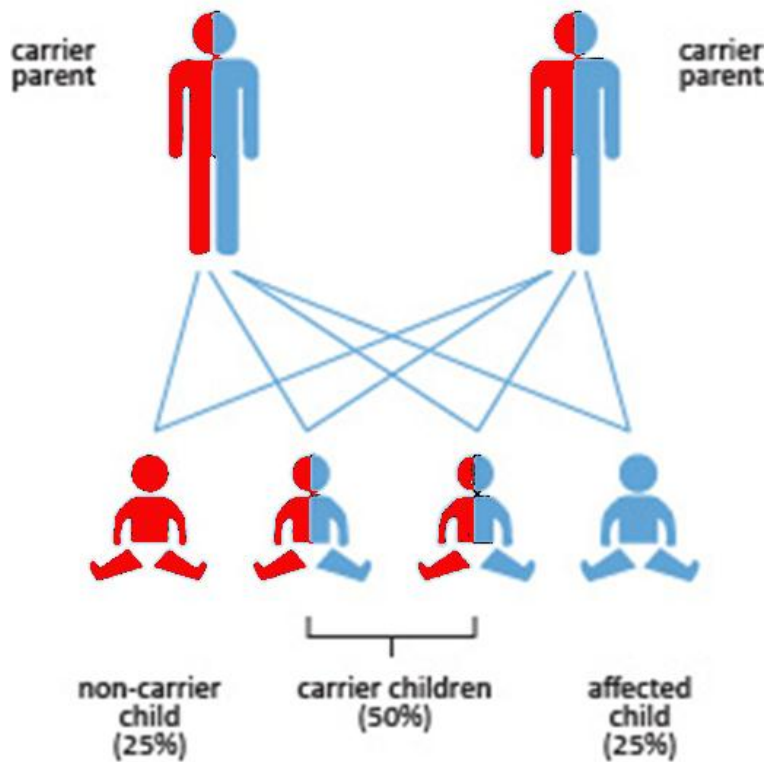


Inheritance

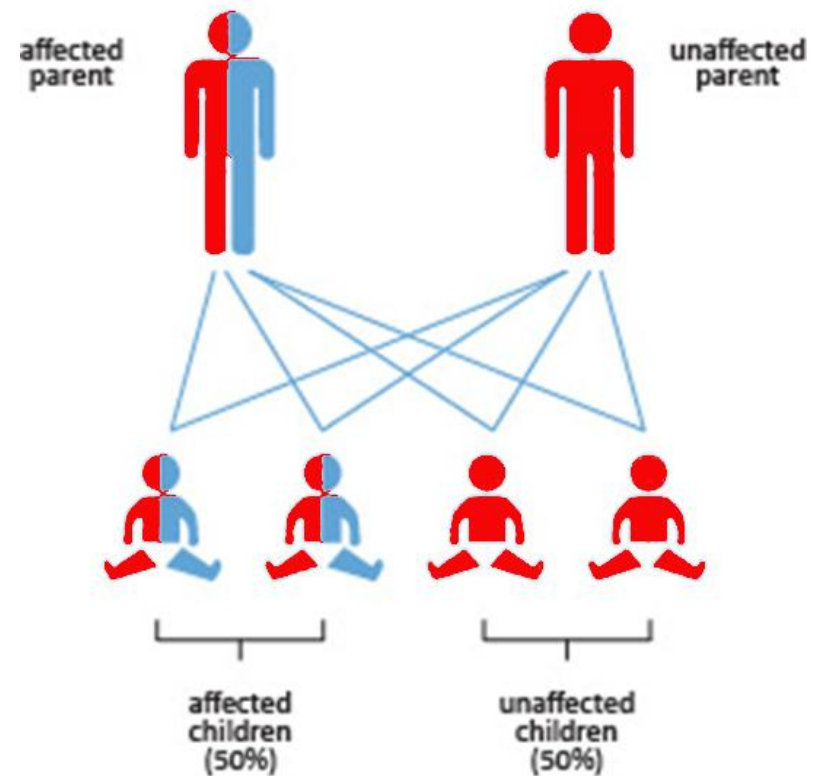


Recurrence Risk

Autosomal Recessive Inheritance

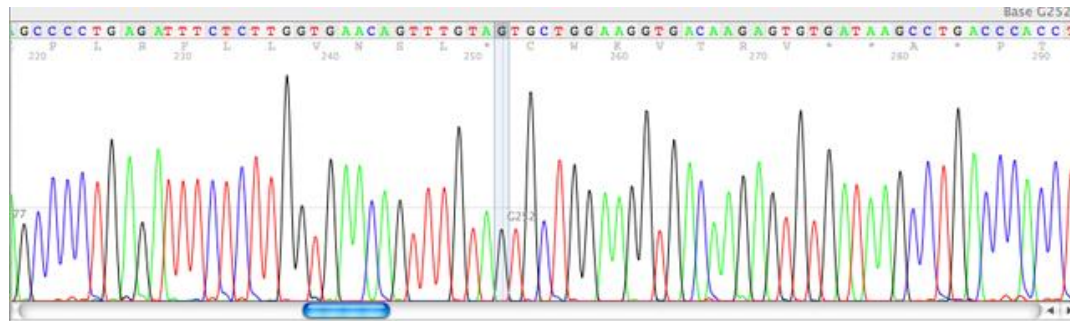


Autosomal Dominant Inheritance



Genetics Testing

- Sequence analysis of all exons (24 fragments)
 - Look at each letter for mistakes



- Quantitative assay to look for larger mutation
- Our techniques will detect >99% of mutations

Genetics Testing

- 2mls blood required
- Takes up to 8 weeks for mutation screening
- 2 weeks to test family members
- Reports;
 - Heterozygous
 - Homozygous

Results

	London	Bristol
No. patients screened	87	28
SLC3A1	59%	71%
SLC7A9	32%	21.5%
SLC7A9 carrier	6%	
SLC3A1 carrier		7.5%
No mutation	3%	
Total number of different mutations	63	56

Future work

- Look for correlation between condition and mutation
 - may lead to targeted management depending on mutation(s)
- Look for new genes