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
- Nonsense
- Insertions
- Deletions
- Splicing

“There was an old cat who lived in a shoe”
Types of Mutations

• Silent
• Missense
• Nonsense

• Insertions
• Deletions
• Splicing

“There was an old lady who”
Types of Mutations

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

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

- Silent
- Missense
- Nonsense
- Insertions
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- Splicing

“There an old lady who lived in a shoe”
Types of Mutations

- Silent
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- Splicing

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

Recessive

Dominant
Inheritance

Recessive

Dominant

SLC3A1 and SLC7A9

SLC7A9
Recurrence Risk

Autosomal Recessive Inheritance
- Carrier parent
- Non-carrier child (25%)
- Carrier children (50%)
- Affected child (25%)

Autosomal Dominant Inheritance
- Affected parent
- Affected children (50%)
- Unaffected children (50%)
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

<table>
<thead>
<tr>
<th></th>
<th>London</th>
<th>Bristol</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients screened</td>
<td>87</td>
<td>28</td>
</tr>
<tr>
<td>SLC3A1</td>
<td>59%</td>
<td>71%</td>
</tr>
<tr>
<td>SLC7A9</td>
<td>32%</td>
<td>21.5%</td>
</tr>
<tr>
<td>SLC7A9 carrier</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>SLC3A1 carrier</td>
<td></td>
<td>7.5%</td>
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<tr>
<td>No mutation</td>
<td>3%</td>
<td></td>
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<tr>
<td>Total number of different</td>
<td>63</td>
<td>56</td>
</tr>
<tr>
<td>mutations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Future work

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