Identification of Distant Relatives Using Linked Autosomal STRs

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Genome Sciences
DNA Identification

<table>
<thead>
<tr>
<th>Unlinked Markers</th>
<th>Linked Markers</th>
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<tbody>
<tr>
<td>• Recombination</td>
<td>• No recombination</td>
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<tr>
<td>– CODIS loci</td>
<td>– Y-STRs</td>
</tr>
<tr>
<td>• Direct matching</td>
<td>– Mitochondrial DNA</td>
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<td>• Paternity analysis</td>
<td>– X-STRs</td>
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<td></td>
<td>– Autosomal SNP haploblocks</td>
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<td>– Linked autosomal STRs</td>
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<td>• Complex kinship analysis</td>
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<td>• Historical identification</td>
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<td>• Remains identification</td>
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Remains Identification

• American soldier missing since WWII

• Remains discovered in ocean near Australia (2002)

• Identified through mtDNA sequencing
Humanitarian Identifications by the King Laboratory

- Children of the Disappeared (Argentina)
  - mtDNA sequencing
  - Kinship analysis

- Present case
  - Associate the alleged daughter with living members of the soldier’s family
  - Infer paternity of the alleged father
A Question of Kinship

- Australian woman raised as soldier’s posthumous daughter
- Baptismal certificate
- Confirm kinship for personal and legal reasons
- No autosomal DNA from remains
- No Y or mtDNA relationship
Approach

• Evaluate relatedness between alleged daughter and putative second cousins

• Likelihood ratio analysis using forensic autosomal STR loci

• Haplotype analysis using linked autosomal STR loci
Likelihood Ratio Analysis

40 autosomal STRs
- Identifiler (15)
- NIST 26plex (25)

\[ LR = \frac{\text{Probability of genotypes if 01 and putative 2\textsuperscript{nd} cousin are 2\textsuperscript{nd} cousins}}{\text{Probability of genotypes if 01 and putative 2\textsuperscript{nd} cousin are unrelated}} \]

Likelihood Ratio Analysis

40 autosomal STRs
• Identifiler (15)
• NIST 26plex (25)

Likelihood ratios for comparisons of:
• Putative 2\textsuperscript{nd} cousins ranged from 0.5 to 0.9
• Undisputed 2\textsuperscript{nd} cousins ranged from 0.5 to 3.9

Probability of sharing one allele identical by descent = 1/16
Autosomal Haplotype Strategy

Identify shared allele (D19S433)

Genotype STRs in region (~3 MB)

Determine profile frequency

Infer phase

Identify shared haplotype

N = 960 Cauc.
Profile Frequency

0 out of 960 controls could have a genotype consistent with the observed haplotype.

95% confidence limit from zero proportion

\[ = 1 - \alpha^{(1/N)} \]

where \( \alpha = 0.05 \) and \( N = 1920 \) chromosomes

\[ = 0.0016 \]
Likelihood Ratio

\[
LR = \frac{\text{Probability of profiles if 01 and 05/06 are related}}{\text{Probability of profiles if 01 and 05/06 are unrelated}}
\]

\[
LR = \frac{1}{0.0016} = 641
\]

641 times more likely to observe the shared haplotype if the woman is related to this family than unrelated
Summary

- Defined a region of linked autosomal alleles
  - Constituted a haplotype in the known brothers
  - Shared by alleged daughter and brothers (putative 2nd cousins)

- Haplotype is rare in ancestry-matched population
  - Suggestive of identity by descent and not identity by state

- Region has not been broken up by recombination in the generations separating the tested relatives

- As many independent chromosomes as necessary could be evaluated
Linked Autosomal Markers

• Relatedness of persons separated by:
  – Multiple historical generations
  – War
  – Natural disaster

• Useful for particular identification or kinship cases
  – Not for direct matching

• Use when lineage markers are uninformative
Acknowledgments

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Questions

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