What’s **polymorphic** about microsatellite repeats?

Person 1
- 21 repeats on chromosome 7 homolog 1
- 33 repeats on chromosome 7 homolog 2

Person 2
- 30 repeats on chromosome 7 homolog 1
- 18 repeats on chromosome 7 homolog 2

**The advantage of microsatellite repeats:**
Map construction: Identifying repeats and their genomic locations

Step 1. Make genomic library of short inserts

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Map construction:
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Step 1. Make genomic library of short inserts
Step 2. Identify repeat-containing clones

Synthesize DNA for probe: e.g., (CA)$_{20}$

probe the library

identify positives

sequence the inserts

Clone 1

...TTACACCGAACCACGCAAAGAGAAAAACACACACA CACACACACACACACACACACACACACACA CACAGTTTGATTATTGCTACTTAC...

Clone 2

...TAATTTAATTTTAATTTGGGTTTTCACACACACA CACACACACACACACACACACACACACACACACACACACACA CACAGTTTGATTATTGCTACTTAC...

e tc.
Step 3. Identify chromosomal locations of the repeat sequences
   e.g., by hybridization to metaphase chromosomes
   (somatic cell hybrids come in handy!)

Step 4. Constructing a profile: How many alleles in the population? How frequent?

Usually done by Polymerase Chain Reaction (PCR)
Determining repeat number at a polymorphic locus...

- PCR using unique sequence (flanking the repeat) as primers

Using our chromosome 7 example again:

![Diagram of gel electrophoresis with primer locations and repeat numbers]

- Primer 1
  - 21 repeats
  - 33 repeats
  - 31 repeats
  - 18 repeats
- Primer 2
  - Gel electrophoresis

- Lane 1
- Lane 2
Using polymorphisms to map disease genes

- Score disease gene allele based on overt phenotype
- Score polymorphic alleles based on PCR analysis
- Ask: can recombinants be detected?

In practice:

- Obtain DNA sample from all family members (blood ⇒ tissue culture)
- For each individual:
  - score disease phenotype, determine genotype
  - score polymorphism on each homolog (e.g., 21,33) for each of many polymorphisms
- For each polymorphism, calculate **Lod score** for various map distances

\[
\text{Lod score} = \log \left( \frac{\text{likelihood of linkage}}{\text{likelihood of not being linked}} \right)
\]

= \log_{10} \left[ \frac{\text{likelihood of linkage}}{\text{likelihood of not being linked}} \right]