Molecular Genetic Strategies for QTL Detection

**Genome Scan Approach**

- Anonymous genetic markers placed across genome (every 20 cM)

<table>
<thead>
<tr>
<th>$M_1$</th>
<th>$M_2$</th>
<th>$M_3$</th>
<th>$Q$</th>
<th>$M_4$</th>
<th>$M_5$</th>
<th>$M_6$</th>
</tr>
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- Look for association of markers with trait phenotype
- Requires populations segregating for QTL and markers
- Requires linkage disequilibrium between markers and QTL
  - Marker and QTL (expected to be) in population-wide equilibrium (unless tightly linked)
  - Need specific family/resource population designs that generate sufficient linkage disequilibrium

**Populations designs for marker QTL mapping**

- Crosses between inbred (preferred) or outbred lines
  - Back cross
  - F2 cross
  - Advanced intercrosses (F3, etc.)
  - Must differ in QTL frequency

- Within outbred populations
  - Half sib families
  - Full sib families
  - 3-generation families (e.g. grand daughter design)
  - Selective Genotyping
  - Selective DNA pooling (Bulk segregant analysis)
Selective Genotyping

<table>
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<th>$M$</th>
<th>$Q$</th>
<th>$m$</th>
<th>$q$</th>
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</table>

$q$ progeny

$Q$ progeny

$\mu_L$ $\mu_2$ $\mu_1$ $\mu_U$

$P_{LM}$ $P_{UQ}$ $P_{LQ}$ $P_{UQ}$

$\alpha$

M linked to QTL if $(P_{M,U} - P_{M,L}) = 0$

$(1-2r)\alpha = (\mu_M - \mu_m)/\sigma_s^2$

Power of alternative QTL mapping designs

For given number of animals genotyped

Candidate gene > F2 > BC > Fullsib > Halfsib

Strategies to reduce # genotypings

- 3-generation families (grand-daughter design)
- Selective genotyping
Selective DNA Pooling QTL mapping with flanking markers

Model for frequencies in upper tail

\[
E(p_{UM}|p_{UQ}) = (1-r_1)p_{UQ} + r_1(1-p_{UQ}) + u_{UM} + e_{UM}
\]

\[
p_{UM} = r_1 + (1-2r_1)p_{UQ} + u_{UM} + e_{UM}
\]

\[
E(p_{UM} - p_{LM}) = (1-2r_1)(p_{UQ} - p_{LQ})
\]

\[
= (1-2r_1)(2p_{UQ} - 1)
\]
((p_{UM} - p_{LM}) vs (p_{UN} - p_{LN})) provides information on QTL position and effect

\[
E(p_{UM} - p_{LM}) = (1-2r_1)(2p_{UQ} - 1)
\]

\[
E(p_{UN} - p_{LN}) = (1-2r_2)(2p_{UQ} - 1) = (1-2\Theta)(2p_{UQ} - 1)/(1-2r_1)
\]

\[
\hat{r}_1 = \frac{1}{2} - \frac{1}{2} \sqrt{[(1-2\Theta)(p_{UM} - p_{LM})/(p_{UN} - p_{LN})]}
\]

\[
\hat{p}_{UQ} = \frac{1}{2} + \frac{1}{2} \sqrt{[(1-2\Theta)(p_{UM} - p_{LM})/(p_{UN} - p_{LN})]}
\]

\[
\hat{\alpha} = (\mu_M - \mu_m)/s^2
\]

Selective Genotyping across the Population
With linkage disequilibrium between the Marker and QTL

- Total
- PLM
- PUM
- Qq
- QQ
- qq

- a
- d
- a