Fig. 11.17

(a) Original markers to obtain rough position

Extending the map position of the disease locus found to be linked to M1 and M2

New markers used for higher-resolution linkage analysis

(c) Identify candidate genes

(d) Compare candidate genes from two groups of people

- Normal individuals
- Individuals with mutant phenotype

Difference correlates with phenotype
<table>
<thead>
<tr>
<th>Vector</th>
<th>Insert size</th>
<th>Host</th>
</tr>
</thead>
<tbody>
<tr>
<td>YAC:</td>
<td>100-1000kb</td>
<td>yeast</td>
</tr>
<tr>
<td>BAC:</td>
<td>80-300kb</td>
<td>bacterium</td>
</tr>
<tr>
<td>Cosmid:</td>
<td>20-50 kb</td>
<td>bacterium</td>
</tr>
<tr>
<td>Lamda:</td>
<td>10-20kb</td>
<td>bacterium</td>
</tr>
<tr>
<td>Plasmid:</td>
<td>0.2-15kb</td>
<td>bacterium</td>
</tr>
</tbody>
</table>
In Arabidopsis: $1 \text{ cM} = \text{about } 200 \text{ kb (50 genes)}$

In human $1\text{cM} = \text{1000 kb (~17 genes)}$
Fig. 11.19

![Diagram of genomic sequence with homology to mouse sequence, good open reading frame, present in an EST clone, and evidence for a gene.](image)
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(a) 1. Tissue 1 (ovary)  Tissue 2 (testes)  Tissue 3 (lung)  Tissue 4 (blood)  
    Purify RNA
    Ovary RNA  Testes RNA  Lung RNA  Blood RNA

2. Load RNA samples in wells of a gel.


(b)  

Testes-determining factor (TDF)
Transgenic analysis

Fig. 11.21

Foreign DNA injected into male pronucleus of newly fertilized egg.

Injected eggs surgically implanted into uterus of "foster" mother and allowed to develop.

Mice are born with foreign DNA in every cell nucleus.
Cloning cystic fibrosis transmembrane conductance regulator (CFTR)

Fig. 11.22a
Northern blots help eliminate other 3 candidate genes

Fig. 11.22b
(c) Exons

Mutations

(d) Corresponding wild-type polypeptide structure

Folded protein inserted into membrane