Chapter 14

Positional cloning, candidate genes, synteny/comparative mapping

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Introduction

This very brief chapter gives an outline of the candidate gene approach to gene detection.

Chapter 16 contains some discussion about confidence in declaring that we have found the gene that causes the QTL effect we see. It also discusses key aspects of using candidates genes in breeding and production programs.

Candidate genes

A ***candidate gene*** is a gene whose effect is known to be related to the biological systems which might affect the trait(s) of interest. This information usually comes from work in other species such as humans and mice.

A ***positional candidate gene*** which is in the region of the genome identified from a genome scan as likely to host a Quantitative Trait Locus (see Comparative Mapping, below).

Recall that a QTL locus is a place in the genome. So a *trait locus* is a place (region) which affects that trait. This could span several genes, one or more of which affects the trait. Each gene is located at a *gene locus*. These definitions are adopted here following confusion at the review itself. It has become common to take 'QTL' as equal to 'major gene', and these two terms will be used with equivalence in this review.

A candidate gene is ‘promoted’ to the status of a ***quantitative trait gene*** when we have sufficient information.

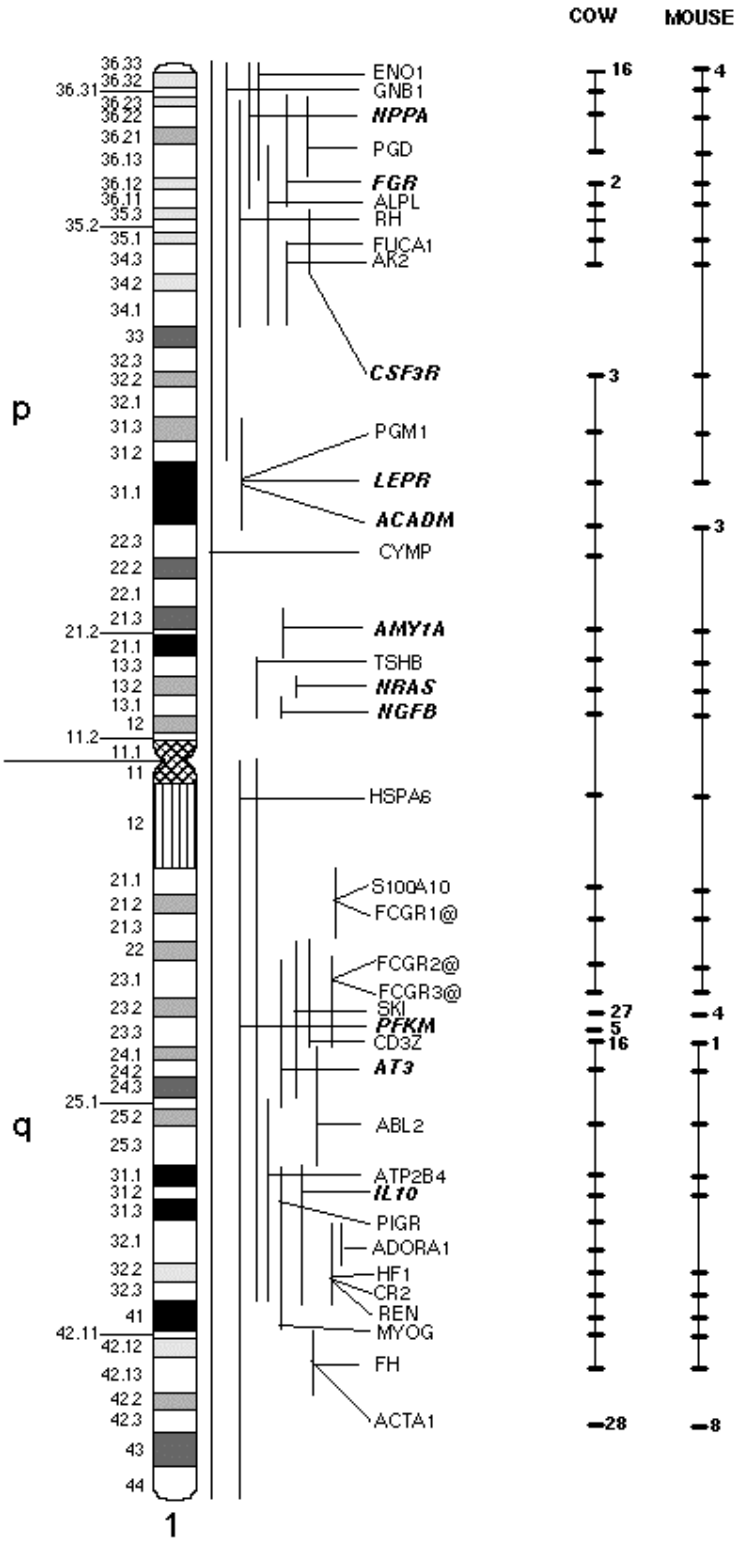
After this, we hopefully have a ***functional marker*** of ***causative marker*** to handle this gene. This is a direct marker whose DNA variations are a cause of functional differences in the host gene. This means that the marker is a causal mutation. Of course it is possible that other regions in the gene also contain functional DNA variations. The only 'foolproof' marker is a complete sequence of the full gene. We may have to resort to use of a non-functional but closely linked marker.

Comparative mapping

This is the study of the pattern of genomic locations of known genes in different species. Usually it is practiced by mapping genes in one species and then comparing the locations of the same genes in other species and drawing conclusions on genome structure and evolution. Homologous regions between the chomosome of one species and the whole genome of another are often spread quite widely though the genome of the second species.

Here is an example of human-mouse homology …
http://www3.ncbi.nlm.nih.gov/Homology/human9.html

And from http://bos.cvm.tamu.edu/htmls/HBM.html we can find “Bovine and Mouse on Human Comparative Maps”, as shown on the next page.



Human chromosome 1 is on the left. Syntenic groups for cow and mouse are shown, with numbers representing the chromosones on which the homologous regions come in these species. With thanks to the Animal Genome Server at Texas A&M University (http://bos.cvm.tamu.edu/htmls/HSA1.html)