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## Locating sheep genes

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Finding a gene in any mammal species is like looking for a needle in a haystack while blindfolded. The best strategies can not only mean the difference between success and failure, but can dramatically affect the resources consumed in the search. The sheep genome contains a mass of information that almost exceeds comprehension. Consider an encyclopaedia running to several hundred volumes. Then take each entry and re-sort them into a random order and finally translate the entire work into a selection of unknown languages. Now, try to find (and understand) the entry for your topic of interest ... The Human Genome Project saw the human version of the encyclopaedia transcribed ready for translation, but for sheep the current genetic map consists mostly of scattered bookmarks (markers.) Identifying or locating sheep genes is important for the industry as it will facilitate the elimination of genetic faults such as pigmented wool. Other genes may be responsible for jumps in production traits (these are called quantitative trait loci or QTL.) *Australian Piebald* is a recessive genetic condition found throughout Australian Merino flocks. Affected sheep show one or a few rounded spots located randomly on the wool-growing areas. The spots vary in size from around 5cm diameter (on adult) to covering more than half of the fleece. The Australian Sheep Industry CRC has established a pigmentation resource flock in order to locate the *Australian Piebald* gene.

Finding a gene involves good science, detective work, intuition, and a measure of luck. The best strategy in each case will depend upon the type of trait involved, how it is inherited and what genetic (animal) resources are available or can be generated. Animals can be sampled from existing industry or research flocks but this usually requires that records have been kept for pedigree and the animals' physical characteristics, and that certain family structures are present. In most cases the experimental animals must be bred as required and this represents a significant investment of time and research resources. The flock and mating design should be as efficient as possible but ensure that there will be sufficient animals available to locate the gene/s of interest, taking account of chance as a factor in reproductive rate and inheritance. Laboratory testing of DNA samples is usually the most expensive part of gene discovery. Again, human geneticists have more advanced tools (and better funds) at their disposal, while sheep geneticists have little option but to extract the best results from what they do have. Decisions about which animals are likely to be most informative and how many markers should be examined may reduce the volume of laboratory work, saving time and money. As in most of life, however, shortcuts often carry risks which must be well understood.

Data analysis is generally fast and cheap with modern computing. However, it is still important to select the analysis best suited to the data and interpret the results correctly. Computer simulation has been used to model the whole process of gene discovery for *Australian Piebald* from breeding through to analysis. This has led to recommendations about optimal breeding design and strategies for efficient laboratory testing. Most significantly however, a new method of data analysis has been devised. Variant Homozygosity Mapping (VHM) is a modification of Homozygosity Mapping (Lander and Botstein, 1987.) For the data structure, compared to HM, VHM shows equal or greater efficiency with respect to the number of animals required, the volume of laboratory work and the chance of successful gene discovery.

Lander, E. S. and Botstein, D., 1987. *Science* 236, 1567–1570.