STRATEGIES FOR UTILISING MOLECULAR MARKER DATA FOR LIVESTOCK GENETIC IMPROVEMENT IN THE DEVELOPING WORLD

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Abstract

In the developing world, despite the potential benefits, investment has been low for QTL detection and QTL selection has rarely been applied. A global approach to use of molecular genetic information might provide greater incentives for investment. There is theory and evidence that populations that are isolated from each other will evolve different genetic adaptations in response to a given selection pressure. If such populations (breeds) can be identified and brought together, synthetic or crossbred populations could be created with substantially better trait expression than currently exists in any one breed. A global strategy would first use molecular genetic information to determine genetic distance among breeds. Such estimates can contribute to conservation decisions. The most distantly related breeds with desirable characteristics can also be identified for use in genetic improvement. Crosses between such breeds would be created and the hypothesis that they carry different genes controlling the desirable traits tested using QTL mapping. An optimised genetic improvement program, which might or might not use QTL information in selection decisions, would then follow from the crossbred population. The global survey of molecular diversity need be completed only once, and the QTL mapping provides information that is essential for the design of the genetic improvement program, even if the optimum design turns out not to use QTL information in selection decisions. This approach assures value of the molecular genetic information whether or not it proves useful in selection, a feature that should prove attractive to funding and executing agencies.

Keywords

genetic diversity, livestock, genetic markers

Introduction

Other authors at this workshop cover the principles of use of molecular genetic markers to detect and map QTL (quantitative trait loci) and the use such loci in genetic improvement of livestock. It is clear from an extensive existing literature that use of QTL is predicted to be most beneficial for traits that have low heritability or are difficult, expensive or impossible to record in a normal breeding program. Use of QTL should therefore be particularly beneficial in the low to medium input systems of the developing world where disease resistance and adaptation traits are particularly important. Such traits are generally very difficult to record and often have low heritability. As yet, however, there only example of selection on QTL for genetic improvement in the developing world id for selection against susceptibility for Dermatophilosis in Martinique [1, 2]

In large part the failure to use QTL information reflects the lack of investment in QTL mapping in the developing world. Such investment is needed not only to detect QTL that could be useful in genetic improvement programs, but also to design improvement programs utilising QTL information that would be sustainable under developing world conditions. A limitation to obtaining the necessary investment is the lack of a cost-effective and sustainable strategy for use of molecular genetic information for genetic improvement in the developing world. A strategy for use of molecular markers that is hypothesis driven and also has clear goals and routes to impact for poor farmers would potentially be attractive to both research and to development oriented funding agencies. Such a strategy is summarised here and will be developed more fully elsewhere. The strategy described below is summarised in Figure 1.

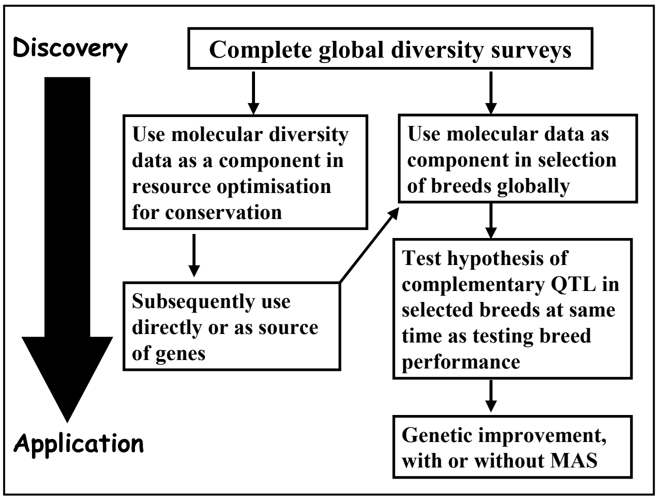

Figure 1
Schematic of an integrated strategy for use of molecular marker information in conservation and utilisation of livestock genetic resources

Mapping livestock genetic diversity

Molecular genetic markers can be used to estimate the genetic diversity within and between a set of breeds. Such information has been collected in a number of projects, and used to map the geographic distribution of livestock genetic diversity and to infer movements of livestock following domestication (eg [3, 4]). Such information is of great scientific interest. But until recently it has not been clear how information on molecular genetic marker genotypes can contribute to utilisation of livestock genetic diversity.

If we knew the distribution of potentially useful genetic polymorphisms within and between the world's livestock breeds, objective decisions on conservation and utilisation of genetic diversity would be relatively straightforward. In the absence of such genetic information, detailed phenotypic information could provide a very approximate guide to the underlying genetic polymorphism. In practice, there is very little information on the production, reproduction, adaptation and disease resistance potential of most livestock breeds. In this situation, information on genotypes at anonymous molecular genetic markers can provide valuable estimates of genetic diversity within and between populations, and this information can be used in decision taking for both conservation and utilisation of livestock genetic resources, as described below.

One goal of conservation will be to conserve the maximum amount of diversity for potential future use. In the absence of information on the distribution of potentially useful genetic polymorphisms among breeds, and with only very limited information on phenotypes of developing world breeds, molecular marker information provides the most easily obtainable estimates of the genetic diversity within and between a given set of breeds. Weitzman proposed a method for optimal allocation of finite resources for conservation to maximise future between population diversity of wildlife species [5, 6]. This method has recently been adapted to conservation of livestock breeds [7] and extended to incorporate predictions of extinction probabilities [8] and to utilise combinations of molecular marker and phenotypic data [9]. An alternative approach, designed to maximise the sum of within and between population genetic diversity, has also been developed [10]. These methods will require further development to deal with the complex reality of decision taking in conservation, but already provide a sound justification for collection of molecular marker data mapping the global diversity of livestock species.

Use of molecular marker diversity in decisions on utilisation

Population genetics theory predicts that evolution will pick up different genetic solutions to a given selection pressure in populations that are isolated from each other. Essentially, selection acts on the variation available, which will vary between populations. The more genetically distinct are two populations, the greater the likelihood they will contain distinct genetic polymorphisms and the greater the chance that selection will lead to fixation of different genetic solutions to the same problem in the two populations. Experimental support for this theory exists in model species [11, 12] and most recently also for the case of trypanosomosis tolerance in livestock [13].

While there is enormous functional diversity in the characteristics of livestock breeds, there are many cases where no breed has achieved a perfect solution to a given problem. Trypanotolerance in cattle and gastrointestinal helminth resistance in sheep are good examples, where breeds exist that are able to survive and produce under disease challenge, but such breeds still perform better in the absence of the disease. It would be desirable to produce animals with even higher resistance to disease, which would be able to thrive under the highest challenge in the absence of other disease control measures. There are well documented examples of several distinct breeds of a given species having evolved partial resistance to a given disease (eg 8 breeds of sheep have been documented with varying degrees of resistance to gastrointestinal helminths). Given the general lack of information on the characteristics of livestock breeds there are probably many more undocumented examples.

The ideal situation would be to test all breeds and all their crosses with potentially useful characteristics in each production environment in which genetic improvement is desired. Such testing is not feasible, due to economic and logistic limitations and increasingly also the difficulties related to sovereignty over livestock germplasm. What would often be feasible would be to test just two breeds from different countries. Many countries would see the advantage of a reciprocal exchange of germplasm with another country, which could overcome sovereignty concerns. Given that cost and time taken in the testing, a critical question is which two breeds would maximise the probability of being able to develop a better genotype than currently exists? Obviously the choice of breeds will involve careful examination of existing data on breed characteristics and the environments under which they evolved. But where it is desired that a particular trait such as helminth resistance be further improved one consideration will be the likelihood that two breeds have evolved different mechanisms of resistance, such that a higher level of resistance could readily be developed from a cross between them. In this case one would seek breeds with suitable phenotypes that are as genetically distant from each other as possible.

Use of molecular markers to confirm the hypothesis of different mechanisms of genetic control

Having brought two breeds together for testing in given environment based on the hypothesis that they carry different mechanisms of genetic control of a desirable trait such as helminth resistance, it will be important to test that hypothesis before proceeding with a breeding program. A suitable method for testing that hypothesis is to perform a genome-wide QTL interval mapping based on anonymous genetic markers in the F2 and/or backcrosses between the two breeds. Based on whether or not the hypothesis is confirmed, the size of the QTL detected, the performance of the pure breeds and the F2 or backcrosses, an informed decision can then be taken on a suitable genetic improvement program. The outcome might be to utilise one of the purebreds, or to develop a crossbreeding program, or to develop a new breed through selection from crossbred or backcross populations, or to introgress QTL from one breed to the other. An informed decision can also be taken on whether or not the genetic improvement program would incorporate marker-based selection. This decision will depend not just on the potential value of the marker information, but also the cost and logistics of collecting and using the marker information in the genetic improvement program.

Discussion

The important point of the proposed strategy (Figure 1) is that molecular marker information is used as a key component of the decision making process at all stages, including the decision on whether or not further marker information will be collected within the final genetic improvement program. A particular value of the approach outlined is that the QTL mapping is performed in the F2 or backcross populations that will almost certainly provide the foundation stock for the genetic improvement program. Thus the whole process can be designed such that phenotypic data and QTL mapping results are obtained almost simultaneously and the QTL mapping population can immediately be used to initiate the genetic improvement program. This minimises the costs of QTL mapping compared to undertaking an independent QTL mapping experiment and ensures minimal delay between obtaining experiment results and achieving application in terms of improved breeding stock being available for farmers.

Critical assumptions in the proposed approach are that independently evolved genetic mechanisms controlling a key trait will not display large negative epistatic interactions and that the selected breeds are not so divergent evolutionarily that there is serious recombination loss in crossbred animals [14].

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