SMART BREEDING: SELECTION WITH MARKERS AND ADVANCED REPRODUCTIVE TECHNOLOGIES.

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SUMMARY

SMART breeding: the integration of molecular marker technology and novel reproductive technologies with traditional genetic evaluation has the capacity to revolutionise genetic improvement programs. Molecular genetic analysis in cattle is identifying gene markers for production and product quality traits which will be used as predictors of the future performance of a bull or heifer, or their progeny. Since the genetic makeup of an animal remains fixed from the time of fertilisation gene marker testing can be applied to embryos. Novel reproductive technologies now make it possible to produce embryos from heifer calves. These embryos can undergo genetic diagnosis for sex, inherited disorders and gene markers for specific traits. Used in combination, these technologies have the ability to significantly enhance breeding programs. Applications include rapid gene introgression and/or trait selection, accelerated production of multi-breed composite cattle, rapid generation of progeny from parents of high genetic merit, and efficient selection amongst and within families, lines or breeds.

Keywords: Gene markers, heifer calf breeding

INTRODUCTION

SMART breeding, ***S***election with ***M***arkers and ***A***dvanced ***R***eproductive ***T***echnologies, integrates molecular marker technology and novel reproductive technologies, and has the potential to revolutionise genetic improvement.

Molecular marker technology includes the identification of gene markers which serve as indicators of an animal's genetic merit. The markers can then be used in combination with other performance measures to more accurately predict the breeding value of a bull or heifer (Davis and DeNise, 1997). Since the genetic makeup of an animal is fixed at the time of fertilisation, predictive gene marker tests can be applied to embryos. Embryo production from heifer calves is an emerging reproductive technology with considerable potential. When combined with gene markers, embryo production from heifer calves can significantly enhance genetic improvement through a variety of applications. These include rapid gene introgression and/or trait selection, accelerated production of multi-breed composite cattle, rapid generation of progeny from parents of high genetic merit, and efficient selection amongst and within families, lines or breeds. In this paper, emerging gene marker and reproductive technologies are briefly described and an example of their impact when integrated is examined by modelling a two-tiered breeding system.

GENE MARKERS

The construction of physical and linkage maps of the genome of cattle (Barendse *et al.* 1996) has greatly facilitated the mapping of genes and the development of gene marker tests allowing systematic searches for genes across the whole genome. Major genes for double muscling in cattle (Charlier *et al.* 1995), muscular hypertrophy in sheep (Cockett *et al.* 1994) and meat quality in pigs (Milan *et al.* 1995) have been mapped. Recent studies on traits considered truly quantitative have identified Quantitative Trait Loci (QTL) for growth and carcass characteristics in pigs (Andersson *et al.* 1994) and milk yield and composition in dairy cattle (Georges *et al.* 1995). In beef cattle, gene markers for QTL affecting birth weight, eye muscle area, marbling score and tenderness have recently been reported (Hetzel *et al.* 1997).

Gene markers can be diagnosed on young animals and even embryos. If the accuracy of prediction is sufficiently high, the markers can be used for selection of animals before phenotypic information is available (Meuwissen & Goddard, 1996). This is also utilised in velogenetics, the rapid introgression of major genes into a novel genetic background using markers and foetal oocytes (Georges and Massey 1994). Where markers have been evaluated and demonstrated to have utility within a family line, these markers can then be used to select amongst individuals within elite full or half-sib families that can be created using the novel reproductive technologies described below.

EMBRYO PRODUCTION FROM HEIFER CALVES

At the time of birth, the ovaries of heifer calves have in excess of 100,000 primordial follicles, each containing an oocyte. The single outstanding reproductive advantage of heifers, compared with bulls, is that viable oocytes can be recovered from heifer calves before puberty, and fertilized *in vitro* to produce embryos. In recent studies, an average of 20 to 30 good quality oocytes were recovered from Brahman heifer calves, aged from 3 to 6 months, after ovarian follicle growth was stimulated with follicle stimulating hormone (Maclellan *et al.* 1997a,b). Approximately 60% of the oocytes were fertilized *in vitro*, and 20-30% of those recovered developed to blastocysts. As indicated above, the full potential of embryo production from heifer calves will be realised when this technology is combined with pre-implantation genetic diagnosis of *in vitro* produced embryos, and gene marker-assisted selection.

INTEGRATION OF GENE MARKER AND REPRODUCTIVE TECHNOLOGIES

A deterministic herd model was used to evaluate and compare the potential impact of artificial insemination (AI), embryo production from heifer calves (HC), and embryo production from heifer calves combined with selection based on markers within full-sib families (SMART). The structure of the herd comprised a closed bull-breeding nucleus and a base-breeding group, with a total herd size of 4,000 cows. Four hundred of these females consituted the nucleus herd. The reproductive technology was only applied in the group of nucleus herd females (NHF).

Full details of procedures used to estimate the selection intensities and generation intervals, and ultimately responses, are described elsewhere (Davis *et al.* 1997). Briefly, a matrix of gene flows was defined based on the proportion of animals from each sex born in either the nucleus or base

that were used for breeding in either the nucleus or base. The selection differntial based on these proportions, and the average merit of the group and generation intervals based on the defined age structures in the nucleus and base were used to predict response in the nucleus and base and across the total structure. The effect of the markers was incorparated into the prediction of genetic merit of animals within full-sib families created in the nucleus. The response is based on a single generation of selection.

A proportion of the nucleus herd females (NHF) were utilised for application of the reproductive technology. The proportion varied with each scenario but for each technology ranged from 3-18% for AI, 1-10% for HC and 0.5-5% for SMART. These and the other key parameters used are shown in Table 1. Genetic response curves are shown in Figure 1. The responses represent the ratio of rate of genetic gain due to using the reproductive technology (R*) to a standard response based on 3% of nucleus females mated to AI (R). It is also assumed that the genetic merit of the nucleus group is one standard deviation above the base group and that the genetic marker is associated with an effect of one standard deviation.

Table 1: Key parameters for females for different reproductive technologies and proportions of NHF mated using each technology for each scenario

	AI						HC						SMART					
Females per bull	200						5						1					
Calves per female	0.7						4						10					
Years used	3						1						1					
Maiden age	2						1						1					
Scenario	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6
Proportion of NHF (%)	3	6	9	12	15	18	1	2	4	6	8	10	1/2	1	2	3	4	5

DISCUSSION

The predicted relative responses (Figure 1) suggested that integration of new genetic and reproductive technologies would result in significant increases in rates of genetic gain when coupled with conventional genetic evaluation methods. Under the parameters examined here a comparable or better rate of genetic improvement can be achieved using HC or SMART with significantly fewer females. Figure 1 shows that a program involving 3% of females (n=13) in a HC program or only 0.5% (n=1) in a SMART program results in equivalent genetic response to that of an AI program involving 18% of females (n=78). It also appeared that the optimum level of response that is reached is achieved at a lower level for AI than for SMART breeding. The response to SMART breeding is directly related to the proportion to the variance accounted for by the marker(s). Potentail improvement could be dramatic, though this is conditional on the impact of inbreeding. Further evaluation of SMART breeding is required for a variety of family structures and marker effects to examine the rate of response over time and to allow for inbreeding and it's consequent effect on the utility of the markers.

The integration of these technologies will potentially facilitate restructuring of the breeding sector of the beef industry. The use of SMART breeding enhances the use of family selection and the

construction of specialised sire and dam lines. Breeding from heifer calves also accelerates composite construction. Markers will have most utility for traits that are difficult or expensive to measure which includes a number of high value traits in the beef industry. Thus structures may evolve whereby conventional genetic evaluation is used for efficient selection amongst family lines, whilst SMART breeding is utilised for selection within family lines at an early age on traits for which conventional prediction has low accuracy and for the construction of specialist composites.

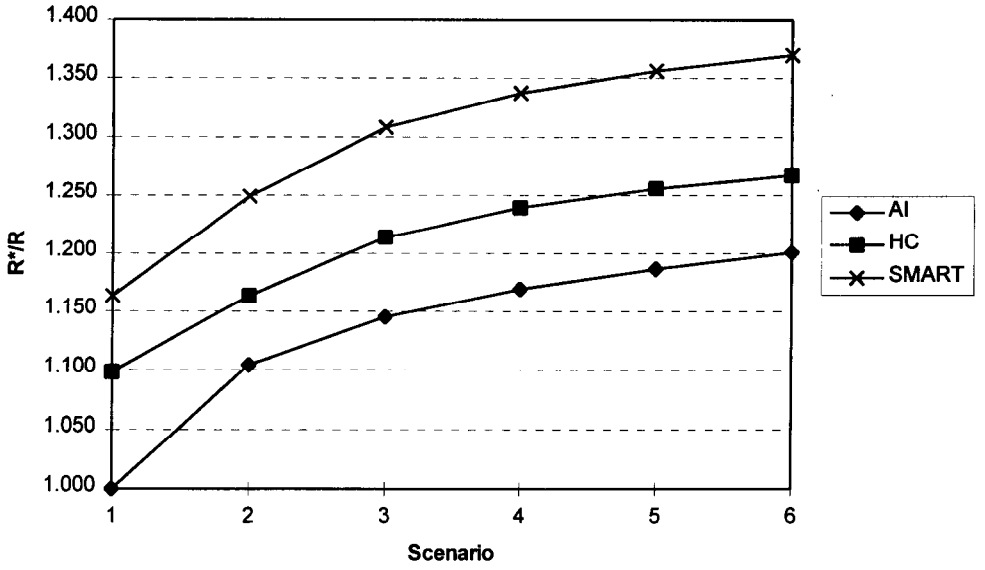

Figure 1: Relative response to selection with six different proportions of nucleus herd females for AI (3-18%), HC (2-10%) and SMART (0.5-5%)

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