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DAIRY TECHNOLOGY CONTRACT SESSION

INTRODUCTION

Currently, several very significant research projects are being undertaken in New Zealand that will impact the pastoral industry, and the dairy industry in particular, during the next ten years. This session highlights some of the technologies in the R&D pipeline, examines the impact these technologies will have on the industry, and explores what this means for the way scientists conduct animal production research.

Professor John McRae, Deputy Director of Research at the Rowett Institute, UK, is the Landcorp Lecturer who opens the session by giving a world view of some of the new technologies and opportunities for pastoral industries. Undoubtedly one of the largest advances expected in the next ten years will be in animal genetics. John McEwan (Agresearch) describes the bovine genome project and what the project means for New Zealand, Richard Spelman (Livestock Improvement Corporation) provides an update on the search for bovine QTL, and Bill Montgomery (LIC) describes the future genetic progress of dairy cattle and the implications for the industry.

Exciting progress is also being made in forage production. Dr Kieran Elborough (ViaLactia Biosciences) relates the advances being made in forage production and the implications for pastoral industries, and Ian Williams (Genetic Technologies, Pioneer) presents recent advances in maize hybrid technology. The session concludes with Stuart Gordon (LIC) describing customer focused technology, and John Caradus (Dexcel) presenting how these technologies may be integrated into future farm systems.

LANDCORP FARMING LECTURE

Nutritional opportunities for longer-term, sustainable, ruminant production

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ABSTRACT

In the present era of 'sustainability' our ability to deliver longer-term, environmentally-friendly ruminant production systems, based on forage feeding with only limited (strategic) use of concentrates, might well depend on the ability of animal scientists to embrace multi-disciplinary approaches that can capitalise on the power of the modern technologies. Whilst environmental issues tend to dominate present thinking on sustainable systems, the longer-term viability of these systems may depend on economic aspects such as an ability to improve the efficiency of converting forage protein into animal product and an ability to sell these products to the health-conscious consumer. Communication between animal and plant scientists has already led to encouraging reports from collaborations in which forage breeders, utilising genomics-based marker-assisted selection techniques, have developed forages with higher water-soluble carbohydrate content which can promote increased milk production in dairy cows and live weight gain in lambs and beef steers. Similar communications between animal and biomedical scientists may provide opportunities for enhancing the 'healthy-eating' image of ruminant products. Several examples (e.g. n-3 polyunsaturated fatty acids, conjugated linoleic acids, selenium, specific milk proteins and the protein-linked delivery of calcium and phosphorus in milk and iron in meat) are used to indicate how current knowledge on the relationships between nutrient intake and the development of non-communicable diseases such as heart disease and cancer might be badged to help promote animal products as 'healthy eating' options.

Keywords: ruminants; productive efficiency; high-sugar forage; healthy-eating.

INTRODUCTION

At the time when I first came to New Zealand to take up a post with DSIR in the late 1960s few animal scientists could have perceived the future power of molecular biology. Gurdon (1958) had cloned frogs from differentiated cells (demonstrating that all the information required to encode for an entire animal was present in the nucleus of a cell), but Morrow *et al.* (1974) were still to create the first recombinant DNA molecules and, arguably, it was not until Southern (1975) developed the hybridisation technique, allowing the identification of specific sequences in a complex array of genomic sequence, that the current microarray technologies were achievable. The development of polymerase chain reaction (PCR) technology in 1983 was important in terms of facilitating the amplification of gene sequences from a single copy of a gene to microgram quantities of sequence. Using homology based approaches, this PCR technology made possible the discovery of new genes previously unidentified due to expression levels and insufficient similarity between sequences for standard cloning techniques of the time.

Of course, the fact that a gene is transcribed into mRNA does not necessarily lead to the translation of that gene product into a biologically active protein. Yet it is the protein which regulates the functioning of the cellular process. Identification of which proteins in a cell change in order to achieve the biological response under consideration is nowadays achieved using proteomics, but, again, proteomics didn't really start before the development of two-dimensional (2-D) electrophoresis using pH gradients to separate proteins by isoelectrofocussing (O'Farrell, 1975) and the later advent of more stable film-back polyacrylamide-based pH gradients (Gorg *et al.,* 1988). The ability to identify individual proteins was revolutionised with the advent of mass spectrometry (MS), allied to the accumulation of databases through the genome projects. Nowadays, using Matrix Assisted Laser Desorption Ionisation time of flight (MALDI-tof) MS a peptide mass fingerprint can be prepared of all the proteins separated on a gel for comparison with known or theoretical matches in a range of public domain databases. Alternatively, secondary fragmentation can be used to generate sequence ladders (MALDI tof/tof) for 'unknown' proteins.

There is little doubt that these 'omics' technologies are already providing information that was not available even 10-15 years ago and certain sectors of agricultural research have embraced them with enthusiasm. Thus, in the plant sciences, physiologists and breeders have been quick to exploit the power of genomics in identifying QTLs for important traits and in developing marker-assisted selection techniques to speed-up the development of these attributes. Equally few animal geneticists could envisage life without the power of DNA technologies and most microbiology groups (rumen, human and soil) are heavily dependent now on molecular profiling, using 16S riboprobes. Yet there is growing evidence that, for the translation of knowledge gained from these programmes into practical solutions (be that in agricultural, or bio-medical science), other skills sets are required also, to examine the responses in metabolic physiology which result from the changes in gene/protein expression.

There is a long history of applying metabolic physiology to the understanding of animal science. From the early studies on VFA metabolism in the 1940s, and later the development of tracer kinetic techniques which started to elucidate the quantitative aspects of complex biological mechanisms (such as the protein and fatty acid turnover cycles) to the mathematical modelling and system research approaches applied to analyse complex biological situations in the 1980s and 1990s, animal scientists have contributed to knowledge in this area. Indeed this has been the basis for considerable improvement in production efficiency and product quality in the animal industries over the last 50 years. In this respect it could be argued that the animal industry is well placed to capitalise on present day technologies, but with one proviso - that we have a vision of where we want the industry to be in the next 10-20 years.

FUTURE OPPORTUNITIES

It would seem to me that it is possible to draw certain parallels between the challenges facing animal agriculture in New Zealand and in the UK. In both, the future for the ruminant industries is highly dependant on home-grown forages and an awareness of the need to reduce the environmental burden of animal agriculture. Certainly, the present drive towards 'sustainable agriculture' in the UK seems heavily geared to environmental and land-use issues. Yet, in the longer-term it is likely to be the economics of the enterprises which dictate 'sustainability' and in this respect, productive efficiency of the animals and future markets for the products leaving the farm gate will surely represent major challenges.

Most consumers nowadays are looking to purchase high protein: low fat ruminant products because human nutritionists and clinicians have been warning for some time against the over-consumption of saturated fats of the type which characterise most ruminant products. UK consumers took up this message with a will in the late 1980s and early 1990s as can be seen from statistics on the decline in full-fat liquid milk sales and the rise in semi-skimmed milk consumption over the last 20 years (in the mid 1980s, 90% of liquid milk sales were as full-fat, but by the late 1990s that figure had dropped to less than 25%).

Thus, one of the main drivers of consumer purchase of dairy and meat products is now the high quality protein that they provide. Unfortunately, whilst these proteins do have a higher nutritive value than most plant proteins, they are also more expensive, mainly because of the inefficiencies associated with the digestive and metabolic processes involved in converting plant protein into milk or muscle proteins in the ruminant animal. Thus, in terms of enhancing the economic sustainability of delivering these products, one first needs to consider if there are ways of improving the efficiency of conversion of plant to animal protein (meat and milk). As much of the inefficiently used plant protein (up to 75% in the dairy cow and up to 85% in growing steers and sheep) ends up as excreted waste nitrogen, any such improvements would also help towards reducing the environmental burden of grazing animals.

INCREASING PRODUCTIVE EFFICIENCY OF GRAZING RUMINANTS

Ruminant nutritionists have known for some time of the fundamental problems associated with the microbial fermentation of dietary components in the ruminant fore-stomach. Indeed, where production systems have been traditionally based on use of high levels of concentrates many ways have been devised for enhancing the conversion of dietary proteins into microbial proteins (or the by-passing of this fermentation) in order to increase delivery of amino acids for absorption in the small intestine and hence for growth and/or milk production. However, as was shown many years ago here in New Zealand (MacRae & Ulyatt, 1974) and in the UK (Ulyatt *et al.,* 1988), where grazed forage is the basis of production, the inefficiencies associated with the conversion of forage protein into microbial protein can be severe. Protein supplementation can enhance the availability of amino acids for metabolism, but, paradoxically, because of intrinsic conversion inefficiencies, animals can often be oversupplied with protein, leading to even greater levels of environmental pollution, making some ruminant feeding strategies unattractive and distinctly unsustainable.

In the wetter (western) regions of the UK, ruminant agriculture is heavily dependent upon grazed and conserved forage. On these farms, sustainable agriculture is encouraging the use of only minimal (strategic) amounts of concentrates and so the challenge will be to consider ways in which the basic forage can be altered in order to increase the efficiency of microbial capture of forage proteins in the rumen. Two possible ways of increasing the capture of forage protein during microbial fermentation have been examined.

One way is to increase the amount of readily available energy during the early part of the fermentation and here an inter-disciplinary approach between the plant and animal scientists at IGER, Aberystwyth has started to yield interesting data. IGER's forage physiologists and breeders were quick to embrace the genomics technologies. QTLs for important traits and marker-assisted selection of genes coding for these attributes have been integral parts of their breeding programmes for some time. However, until fairly recently their breeding objectives were directed predominantly at agronomically-important traits such as yield per hectare, pest and disease resistance and extending the growing season. Attributes that might improve the utilisation of the forages by ruminants were not considered, because these were not important criteria in terms of seed certification. Recently however, cross-disciplinary communication has opened up a new horizon, where animal performance has become an important breeding objective. Promising increases in milk production and nitrogen partition in zero-grazed dairy cows (Miller *et al.,* 2001) and live weight gain of grazing lambs (Lee *et al*., 2001) have been achieved where these forage breeding selection techniques have been applied to increasing the water soluble carbohydrate (WSC) content of ryegrass varieties (see Table 1 and Figure 1 respectively). These gains have been shown to come via greater capture of microbial nitrogen in the rumen and a greater passage of microbial protein to, and absorption of amino acid from, the small intestine. The dairy studies also indicated that the increase in productive efficiency was achieved partly through an alteration of the partition of forage nitrogen towards saleable product (and away from waste excreta), but partly because the cows ate considerably more of the higher WSC forage.

An alternative strategy for improving microbial efficiency in animals given forages would be to protect proteins in order to reduce the rate at which they become degraded to ammonia. The benefits of this approach have been easy to demonstrate experimentally, but the translation of the principles into commercial practice has so far proved to be more intractable. Thus, the freezing of forage (which reduces plant protein solubility by as much as 50% (MacRae *et al*., 1975)) leads to increased synthesis of microbial protein (25%) and increased absorption of amino acids from the small intestine (15%; see MacRae, 1976). Similar increases in duodenal nitrogen flows per unit nitrogen intake can be obtained with tannin-containing forages (Barry & McNabb, 1999) where the tannin is thought to cross-link with the forage protein making this less rapidly released during microbial fermentation. Indeed, this protection can be reduced if polyethylene glycol (PEG) is infused into the rumen, when the PEG competitively binds to the tannin thus making it less effective in terms of 'protecting' the forage protein. However, attempts to manipulate the plant chemistry of the main forages in order to introduce polyphenolics into commercial varieties has proved difficult and the application of this approach has been restricted to the strategic use of 'alternative crops', such as lotus sp. and sainfoin which naturally contain tannins (see Barry *et al*., 2001).

PRODUCT QUALITY, CONSUMER CONFIDENCE AND THE HEALTH BENEFITS OF PASTURE-FED ANIMALS

One of the overriding requirements of any agricultural enterprise is the economics of the system and the security of markets for the products that leave the farm gate. In this respect the consumer's perception of the quality and health enhancing benefits of the products may be crucial to longer-term sustainability. Over recent years, in the UK and Europe, the food chain and particularly its animal produce suppliers have been frequently challenged by clinicians and public health authorities with health scares, such as salmonella in eggs, E.coli in meats, Bovine Spongiform Encephalopathy (BSE) and Foot & Mouth Disease (FMD). These have, in some cases, had dramatic effects on consumer choice, leading to major economic losses in the sectors supplying the produce.

Since 1999 the Rowett Institute, which has a long history of nutrition research on farm animals, has re-focused its research into the area of diet and (human) health, with programmes that are attempting to elucidate how specific nutrients can help to off-set the incidence of human non-communicable diseases, such as coronary heart disease (CHD), colon cancer and obesity. It would seem that some important information is beginning to emerge from these biomedical programmes that could be used by the animal sector of the food chain as specific

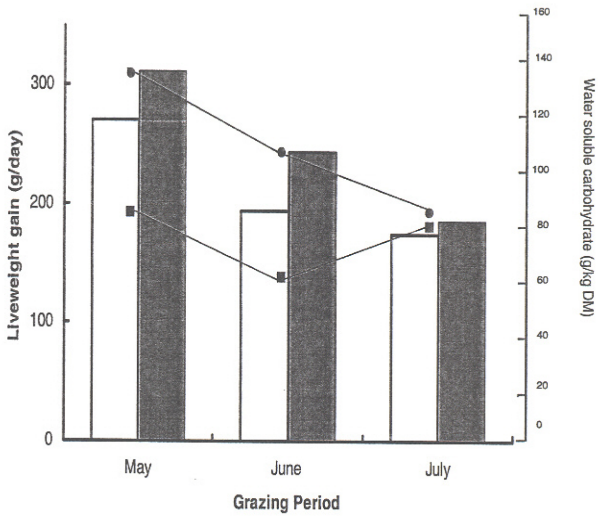
TABLE 1: Nitrogen intake and partitioning in dairy cows offered normal and high water soluble carbohydrate (WSC) containing grasses (from Miller *et al.,* 2001).

	Treatment			
	High WSC	Control	s.e.d.	Significance[1]
Nitrogen intake (g/day)				
Grass	171	181	7.3	NS
Concentrate	109	109	-	-
Total nitrogen intake (g/day)	280	290	15.1	NS
Nitrogen output (g/day)				
Urine	73.1	100	5.0	***
Proportion of N intake	0.25	0.35	0.020	**
Faeces	110	121	10.7	NS
Proportion of N intake	0.40	0.42	0.023	NS
Milk	83.3	67.5	4.12	**
Proportion of N intake)	0.30	0.23	0.012	**
Nitrogen balance (g/day)	15.1	1.3	8.83	NS
Proportion of N intake)	0.05	0.00	0.033	NS

[1]NS, not significant; ** $P < 0.01$; *** $P < 0.001$.

'health benefit' messages in promoting animal products in terms of their ability to help prevent some of the non-communicable diseases.

FIGURE 1: Lamb performance on paddocks of normal (non-shaded) and high (shaded) water soluble carbohydrate (WSC) containing grasses during three experimental periods. The insert lines represent changes in WSC levels in the normal (■) and high (●) WSC containing grass paddocks (from Lee *et al.,* 2001).



Omega-3 polyunsaturated fatty acids

There has been a history of concern about the lipid components of foodstuffs, with 'animal (ruminant) fats' being viewed with particular suspicion, because of the influence of saturated fat on the development of high levels of cholesterol in the circulating serum lipoproteins. Polyunsaturated fats (PUFA) modulate these rises in risk factor (Hegsted *et al.*, 1965) and this led to recommendations for a reduction of saturated fat in the diet. More recently however, research showing that the different PUFA are not all equally beneficial in terms of preventing the onset of the non-communicable disease is perhaps providing a better message, at least for products from pasture-fed animals. Inflammatory responses are important components of the development of CHD and cancer and in the last 10 years immunologists have found that the omega-6 PUFA (n-6 FA; e.g. linoleic acid, C18:2) are less beneficial than the omega-3 PUFA (n-3 FA; e.g. linolenic acid, C18:3 ; eicosapentaenoic acid, C20:5 (EPA) ; docosahexanoic acid, C22:6 (DHA)), because of the pro-inflammatory ecosanoids which are generated during the post-absorptive human metabolism of the n-6 fatty acids. The n-3 FA have the ability to modulate this inflammation, by competing with the n-6 metabolites for incorporation into the membranes of immune cells membrane phospholipids (Gibney & Hunter, 1993).

Present recommendations are to increase the intake of n-3 FA towards a dietary optimum n-3:n-6 FA ratio of 0.4-0.5. However, most human foodstuffs have a ratio nearer to 0.1-0.2, hence the health benefits of fish oil products (Leaf *et al.*, 2003), which contain high levels of n-3 FA. The reason why fish oils are an abundant source of the longer-chain n-3 FAs relates to the high linolenic content of chloroplast lipids. The presence of chloroplasts in marine phytoplankton is the basic building block of the Marine Food Web, but so also are they the crucial component of fresh forages and so, not surprisingly, recent research has started to identify substantial increases in the n-3:n-6 PUFA ratio in the lipids of animals fed fresh forages rather than concentrates (see Dewhurst *et al.,* 2003). This can surely be used as a positive (and specific) 'health' message to help promote the sales of pasture-reared beef and sheep and the milk from forage-fed dairy cows.

Conjugated linoleic acids

Over the last 5 years data coming from laboratory animal studies has indicated potential health benefits from the consumption of the conjugated linoleic acids (CLA). These have included, reducing the severity of cholesterol-induced aortic lesions in rabbits (Lee *et al.*, 1994), reducing the incidence of carcinogen-induced mammary tumours in mice (Ip *et al*., 2001) and even altering the composition of body weight gain (higher protein:lower fat) in mice (Park *et al*., 1997). One of the main mechanistic attributes of the CLA is their ability to modulate the inflammatory mechanisms at the level of adhesion molecule transcript in endothelial cells. Transcription of these adhesion molecules, which lead on to plaque formation, is thought to be stimulated by cytokines generated from the oxidation of low-density lipoproteins in the tissues which underlie the endothelial cells. The CLA seem to modulate these cytokine signals and so reduce the inflammatory response (Cook *et al*., 2002) in a not dissimilar way to the n-3 PUFAs.

The CLA are very much an attribute of ruminant products, being formed as an intermediary metabolite in the biohydrogenation of C18:2 (unsaturated) linoleic acid to 18:0 (saturated) stearic acid during rumen fermentation. Hence, levels of CLA in milk, cheese, butter, lamb and beef (4-7 mg/g total FA) are considerably higher than in non-ruminant products (chicken, pork, fish, olives; <1mg/g). Unfortunately, based on the data from the animal experiments, these levels could never provide sufficient CLA intake per day to make any meaningful contribution in terms of off-setting inflammation in humans. Currently, attention is being focussed on the regulation of biohydrogenation in rumen microbes, either by dietary manipulations (Loch & Bauman, 2003), or by examination of those microbes that regulate the latter steps in this process and whether these could be manipulated to boost the CLA content of muscle and milk products (John Wallace, personal communications). If this could be achieved, then it may represent another specific health benefit with which to make ruminant products more attractive to the consumer.

Selenium

Other potential health messages relate to the delivery of bioavailable minerals and trace elements into the human diet. One of the underlying mechanisms associated with the onset of CHD and cancer is disruption of the normal cellular processes. In this respect, lipid oxidation is a major stressor, because the cytotoxic hydroperoxides formed can cause membrane damage. Intra-cellular free radical generation, accelerated in exercise, infection and even the stress of high performance, is another stressor. To modulate these processes cells depend on antioxidants such as vitamin E and a number of glutathione peroxidases (GPX). The GPX are selenoproteins and to date 25 have been identified in the human genome. It is not surprising therefore that early epidemiology studies indicated clear links between the availability of selenium (Se) in the human diet (Se levels in blood) and the incidence of CHD (Salonen *et al.,* 1982) and cancer (Clark, 1985).

One concern for clinicians in the UK and other parts of Europe over the last 10-15 years has been the substantial reduction in daily Se intake that has occurred as a result of the switch from selenium-rich high-protein North American wheat to lower-Se UK and European wheat for flour making in the mid 1980's. The volcanic and sandy soils across major sectors of the UK have had a lot of their Se washed out, leading to low levels of Se in cereals, fruit and vegetables, and as a result, the daily intake of Se in the UK population (approx. 35μ/d) is less than half of that in the USA (80-100μ/d). The question of whether the UK should follow the example of Finland and add sodium selenate to fertilisers was raised in the late 1990s (Rayman 1997), but as yet nothing has been done. Here in New Zealand, human Se intake is also only marginally sufficient and several experimental studies have identified the advantages of supplementing human diets with Se-enriched yeast or selenate mixed with brewer's yeast (see Thomson *et al.,* 1993).

Se deficiency in farm animals has been well recognised for many years. In cattle, severe deficiency will result in myodegenerative problems such as white muscle disease whilst marginal deficiencies have been linked to elevated levels of mastitis, scours, cystic ovaries and retained placenta (Villar *et al.,* 2002). As a result Se has been included in most mineral supplements for farm livestock in the UK since 1978 and therefore the Se contents of animal products are considerably higher than those of the plant components of the UK diet. Indeed, it has been estimated that >60% of the Se intake of UK consumers is derived from meats, fish, eggs, milk and dairy products (see FSA 2002). The present reluctance of governments to implement supplementation policies lies in the potential toxicity problems associated with over-consumption of selenium (>800μg per day). However, there seems no danger of reaching these dangerous levels by advocating even greater consumption of 'health-enhancing' animal products, (alongside the odd Brazil nut!) to help replete the marginal selenium intake which have developed over the last twenty years.

Adding value to milk proteins

Animal proteins have a higher biological value than plant proteins, but they are generally more expensive because of the inefficiencies inherent in their production (as discussed earlier). So, it would seem important to try to identify 'added value', associated with the consumption of these products.

The ability of milk to deliver calcium and phosphorus into the human diet was recognised many years ago and was the basis on which John Boyd Orr, the first Director of the Rowett Institute, persuaded the UK government to introduce the Free School Milk policy to help reduce rickets and promote growth in UK children in the 1930s. These minerals are delivered as part of casein micelles and nowadays much more is understood about the complex nature of the individual caseins and whey proteins which make up milk protein. Several of the whey proteins, that comprise approximately 20% of total cow's milk protein, seem to have intrinsic nutritional properties. For example beta-lactoglobulin (50% of total whey protein) has a similar structure to retinol binding protein, and is thought to be important in facilitating vitamin A absorption. Lactoferrin, another of the whey proteins, is thought to have strong bacteriocidal properties and an important role in immume system responses against infection, perhaps through its iron-binding capacity, which can deprive the invading pathogen of iron needed for growth. Normally only a minor (1-2%) component of whey protein in cow's milk, its concentration in human breast milk is 5-10 times this concentration but in colostrum it can comprise up to 20% of total milk protein. Since the human lactoferrin gene was cloned in the early 1990s lactoferrin has been produced via recombinant DNA technologies for fortifying infant formula in some countries.

Much research has been conducted into the properties of individual casein proteins (which make up 80% of cow's milk protein) because of their importance in cheese making, but more recently, molecular geneticists have started to identify that certain polymorphisms in the beta-casein gene (35% of total casein) might be producing milk with altered risk factor for this protein in terms of CHD and diabetes (Laugeson & Elliott, 2003). Indeed, screening programmes are now being advertised for selecting cows that only produce milk with A2-type beta casein, as a health-enhancing product.

Adding value to meat proteins

In the same way that milk casein can deliver calcium and phosphorus, the ability of meat protein to provide iron is another interesting phenomenon worthy of consideration within the context of the health benefits of sustainable ruminant products. Clinical records from across the EU suggest that as many as 1 in 5 pregnant women are clinically anaemic, with many more having marginal iron deficiency. Recent studies at the Rowett (Gambling *et al.,* 2003) have indicated that iron-deficient pregnant rats produce smaller pups, who subsequently exhibit marked hypertension. One of the reasons for the prevalence of iron deficiency is that the bioavailability of iron in plant products is very low (no more than 5-15%) and so at time of heavy demand for iron it is difficult to derive sufficient iron from these dietary sources. However, in animal products, where iron is an important component of haemoglobin (in blood) and myoglobin (in muscle), the bioavailability of haem iron is considerably greater than the non-haem iron in plant products. Again, this might constitute another 'health benefit' message for the marketplace, particularly for the 'quality beef breeds' such as Aberdeen Angus that seem to have higher myoglobin levels in their muscle.

Milk and meat are also major dietary sources of other micronutrients such as zinc, selenium and copper and the vitamins, folic acid and B_{12} (indeed B_{12} is only found in animal and fish products). Each of these nutrients has been linked to the prevention of non-communicable diseases and to the maintenance of a healthy immune system. Perhaps therefore, as part of its future strategy, the animal industry should start to include considerations of the products that it delivers to market not just in terms of consumer (organoleptic) preference, but also in terms of specific health benefits.

CONCLUSIONS

This paper has attempted to identify how cross-disciplinary approaches can help to enhance the opportunities for the ruminant industry over the next 10-20 years. It could be argued that we animal scientists, with the exception of the geneticists, have been slow to embrace the power of the newer technologies. However, the integrative approaches which are inherent to our discipline would seem to place us in a good position to apply knowledge from fields such as the plant, microbial and biomedical sciences (where there has been an enthusiasm to embrace such technologies) in promoting the future of sustainable agriculture over the first half of the 21st Century.

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BRIEF COMMUNICATION

The process and technologies of gene discovery to application in dairy cattle

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The heady days of biotechnology that were driven by the assumption that biotechnology would solve all biological problems with simple solutions, are over. The 'biotech' investment in the mid to late 1990's was driven predominantly by commercial and scientific enthusiasm, ignoring biological, commercial and regulatory realities. In the post-bubble environment, the dairy industry, including ViaLactia Biosciences and our research partner Livestock Improvement Corporation are undertaking a research program endeavoring to align the expectations of the market, the investors and the limits of technology. In general, the thrust has been to utilize existing or develop new biological resources and where they are required and not available, tools for discovery. Much of the on-going challenge is in defining the opportunity (desired phenotype), predicting technological developments, large scale investment in the public domain and matching the approach to the problem within time and budgetary constraints. Our approach will be presented with some examples of successes.

Background

The assumption made in the early to mid 1990's by investors was that biotechnology was sufficiently mature to enable the development of high value products principally, but not limited to, in the pharmaceutical area. Obviously, a considerable part of this investment was driven from the limited knowledge of the financial