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PROSPECTS OF BIOTECHNOLOGY APPLICATIONS IN ANIMAL GENETICS AND NUTRITION

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SUMMARY

Biotechnology is viewed as the growth point for many agricultural research systems and is well established in many of the developed countries of Europe and America. The corporate marketing systems, established markets and the commercial nature of the agricultural sectors lend themselves to the use of biotechnology. The successful application of biotechnology in South Africa rests on our ability to create wealth from its application and to make this technology accessible and affordable to all sectors of the population.

Aspects of animal biotechnology discussed :

* **Diagnostics** (defects, susceptibility), **identification** (individual), **characterization** and **detection** (favourable genes, novel mutations) (using i.e. PCR) and **bioinformatics**
* **Bioprocessing** - Recombinant production of proteins (vaccines, hormones, pharmaceuticals for animal and human use (in animals as well as in plants)
* **Genetic modification** (cloning (genes, cells and organisms), cell fusion (creating novel genomes, assisted reproduction) and remediation (genetic therapy)) and **genetic reorganization** (increase variation?)
* **Bioadaptation** - Adaptation of organisms to its environment (micro-organisms, animals)
* **Bioremediation** -, environmental quality enhancement and waste remediation (in animals and dealing with animal wastes)

Keywords: biotechnology, DNA profiling, animal genetics, bioprocessing, resource-limited entrepreneur.

INTRODUCTION

Africa is a continent with immense agricultural potential. Under commercial farming conditions, the continent has the potential and natural resources to be the major food supplier of the world. Africa also has a wealth of well-adapted animals and plants of which the genetic merit is still largely unknown and untapped. On the downside, the continent faces the loss of biodiversity at an ever increasing pace despite valiant efforts by many African scientists to protect against this trend. The agricultural resources are under extreme pressure by the increasing populations of many nations mainly due to insufficient knowledge and training. Very limited financial resources and underdeveloped infrastructure, both physical and economical, are major factors limiting agricultural potential. The drought/famine cycles in many marginal regions also has a draining effect on the continent's resources.

Biotechnology can have a major impact on solving these problems.
Prospect: L. *pro*, forward, + *specio*, look; A consideration of the future
Application: L. *applico*; > *ad*, to; *aplico*, fold; The act of applying
The shortage of food is an ever present problem and a solution is agricultural biotechnology – literally making agriculture more efficient.
What is biotechnology? There are several definitions of which the following are two examples:

* The integrated use of biochemistry, microbiology and engineering sciences in order to achieve technological applications of the capabilities of living organisms, including micro-organisms, tissue culture cells and parts thereof.
* Any technique in which living organisms are used to make or modify living organisms or products to improve plants or animals or to develop micro-organisms for specific purposes.

For the purpose of this talk (see definition of "application") biotechnology must be limited to:

The manipulation and exploitation of single biological processes, in isolation or in combination, to create and / or improve goods or services.

Biotechnology has had a major impact on the world and, in South Africa, we have experienced many of the benefits of this technology. In human health care there are new drugs, diagnostic systems and an expansion of knowledge that has advanced the frontiers of medicine. Agriculture has also felt the benefits of this technology.

Animal biotechnology would thus incorporate:

* **Diagnostics** (defects, susceptibility), **identification** (individual), **characterization** and **detection** (favourable genes, novel mutations) (using i.e. PCR) and **bioinformatics**
* **Bioprocessing** - Recombinant production of proteins (vaccines, hormones, pharmaceuticals for animal and human use (in animals as well as in plants)
* **Genetic modification** (cloning (genes, cells and organisms), cell fusion (creating novel genomes, assisted reproduction) and remediation (genetic therapy)) and **genetic reorganization** (increase variation?)
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Against the background of:

How far have we come/what is already available and applied?

What is possible vs. what is feasible vs. what will make money for investors vs. what is needed (developed vs. developing nations)?

If the technology is developed and readily available, will it be embraced/used

What are the technical limits?

To what extent can South Africa be a part of it?

DISCUSSION

Diagnostics, genetic profiling and characterization, gene detection and bioinformatics:

To "know" the genetic blueprint of a species has long been the dream of geneticists. In the beginning of the new millennium this dream has finally realized for a few species. The human genome project has created huge expectations and opened up many opportunities which include, amongst others, the public awareness of the value of genomics in disease detection and eradication. Coupled with new PCR technology, the opportunity to detect single point mutations accurately and to rapidly design diagnostic tests, sometimes tailor-made for a specific individual, has revolutionized the way that the average person perceives genetics.

Sometimes, within days after the genome of a particular species has been deciphered, a myriad of PCR-based tests to detect genetic sequences for every gene product in the species' genome is made available commercially. Organisms of which the genomes have already been sequenced are the fruit fly (*Drosophila melanogaster)*, the nematode *Caenorhabditis elegans* and bakers yeast (*Saccharaomyces cerevisea)*. The degree of similarity between genes of these organisms and humans permits the use of these organisms as model organisms for human gene expression and modulation, e.g. the p53 tumor suppressor gene in the fruit fly. Almost 60 percent of the 289 known human disease genes have equivalents in flies and about 7 000 (50%) of all fly proteins show similarities to known mammalian proteins. More than 6 000 nematode proteins (33%) and 2 300 yeast proteins (38%) are similar to those of mammals. This holds great promise for animal scientists as, although the way forward is definitely linked to deciphering the genome of economically important livestock species, some of the information in the human genome will definitely be extrapolatable to livestock. (Some poetic justice – after consuming livestock for centuries, the human may now serve as a guinea pig for livestock!)

Specific, rapid and inexpensive tests for a particular allele of a gene will enable breeders to purpose-design breeding plans based on exact genomic information. When genes directly linked to adaptability and additive environmental effects can be detected and actively propagated, they will be used in assisted reproductive techniques.

However, the downside is that this information can be a very sharp axe in the hand of a blind woodcutter and indiscriminate and inaccurate use may propagate unwanted and detrimental characteristics extremely quickly.

One of the first widespread applications of biotechnology was artificial insemination (AI). This has had a vast impact on the cattle industry as the genetic make-up of a prime bull can be widely distributed on a worldwide basis in a very short period of time or the semen can be kept frozen almost indefinitely. AI is not only practised by stud and commercial breeders but is now used in many of the rural areas of South Africa with good effect on the standard of living of the population.

Unfortunately this practice can also have a negative effect as undesired genes or characteristics can also be distributed rapidly. One such example was the spread of the 1/29 Robertsonian translocation from an AI bull. This anomaly was first reported by Gustavsson in 1969 and results in a reduction of fertility with subsequent economic implications. It has been found in many breeds worldwide and is not detectable phenotypically. After the hard lesson learnt, in South Africa, many AI bulls are now routinely screened for all cytogenetic anomalies before they are put into service.

DNA technology was revolutionized by the advent of the polymerase chain reaction (PCR) where as little as the DNA contents of one cell can be amplified and minute amounts of tissue can be used. The applications are not only many and varied but are continually expanding.

When DNA fingerprints were discovered in the early 1980's and the bands were found to be individual-specific, the technique was used in cases of disputed parentage in humans. It soon became widely accepted especially as a legal tool in paternity suits and cases of violent crimes such as murder and rape. A study of DNA fingerprints in mammals soon followed and here it was found that, as in humans, the bands are individual-specific. With this discovery came the realization that different aspects of genetics could be studied with these DNA fingerprints or profiles as they are now called.

With the worldwide demise of blood typing of cattle, in South Africa DNA profiling is replacing this system for the registration of livestock. This includes cattle and some breeds of horses. Parentage can now also be established beyond reasonable doubt in sheep, goats and dogs using this technology.

In South Africa, the increasing incidence of stock theft is a shocking reality with the accompanying cruelty to animals and the all too frequent murder of farmers. Stock theft affects all sectors of the farming community from the large commercial organizations to the stud breeders and extends to the rural farmers who may own one or two cattle only. The effect is devastating. Several farmers have even changed from animal husbandry to forestry with far reaching implications especially for food security. DNA technology is now used to an ever increasing extent in solving these crimes. This has led to numerous court cases where the criminals have been convicted on the strength of the forensic DNA evidence. The South African Police Stock Theft Units collect blood, meat, hair or other tissues from the scene of the crime and meat in a house or blood on the suspect's clothes. The samples are sent to the laboratory where the DNA is extracted and the profiles are analyzed to determine whether the tissues originate from the same animal. In cases of disputed ownership, DNA profiles are used to establish parentage and these are also used in legal wrangles.
Animal forensics followed the same route as human forensics in terms of detecting polymorphic sequences in non-coding DNA. Fortunately, animals are not bound by the same constraints as for humans, and a future prospect is that, in animal forensics, coding DNA could be used, not only to generate a DNA identity profile or "fingerprint", but also to yield a "phenotypic profile" that would help the police in tracing animals involved in disputes.

Animal biotechnology need not always be "high-tech". A direct application of this technology has been developed in our laboratory as an attempt to curb this heinous crime of stock theft. This has been named the Lidcat™ system - Livestock Identification Catalogue. Here the owner plucks hairs with the roots from the animals and these are sent to the laboratory where they are stored and, if an animal is stolen, the original DNA from the hair is available for comparison purposes. Positive feedback has been received from participants in this scheme.

The objective of breeding and selection programmes is to improve the genetic potential of livestock and subsequently phenotypic production traits. The problems faced by conventional breeding programmes are, firstly, an accurate evaluation of the genotype on which the phenotype is based and, secondly, the fact that, although the entire genome of an animal is always assessed, only half of the genome of the selected animal is passed on to its offspring. The possibility of detecting a specific gene or group of genes directly, including the homozygous or heterozygous state, is an option of great interest to animal breeders.
Recent advances in molecular genetics have led to the development of diagnostic tests. These include the tests for two genetic disorders found in Holstein Friesian cattle. These disorders, Bovine Leucocyte

Adhesion Deficiency (BLAD) and Deficiency of Uridine Monophosphate Synthase lead to the premature death of calves and the abortion of embryos respectively. The results of these tests allow for the effective selection against these disorders and the obvious economic benefits.

Malignant Hyperthermia (MH) is an inherited disease in pigs. MH pigs are extremely sensitive to stress and under such conditions their body temperature rises very rapidly leading to death. MH is closely linked to heavy muscling and a low fat ratio and selection for these characteristics has led to the high incidence of this condition. The meat is unacceptable to the consumer as it is pale, soft and exudative (PSE) and thus has serious financial implications. The DNA test for this defect is performed under licence to Canada and, in the past decade since the test was introduced, the incidence of the defect has fallen dramatically as breeders now have a selection tool for improved management. This is a very positive example of the use of biotechnology in the past and its continued use in the future.

The development of DNA technology and especially of the PCR has provided the animal breeder with a useful tool to assist in the process of selection. One great advantage of the technology is that selection for specific characteristics can be done on a genotypic level that allows the breeder to differentiate between dominant homozygotes and heterozygotes. It can also be used for the determination of the status of a gene that is not expressed in an individual, for example milk proteins in bulls. The interest in these milk protein alleles lies in the fact that they differ in their suitability for different milk products. For example, B kappa-casein has far better cheese making properties than A kappa-casein.

Research into the linkage of DNA markers to different milk proteins and the use of these proteins in the manufacture of fermented milk products is important in South Africa. This research also has specific relevance in the study of allergies and lactose intolerance – a problem in a large proportion of the population and will have great beneficial implications in the rural areas of South Africa in particular.

It is well known that certain livestock breeds are more resistant to certain diseases than others and there are several investigations to establish gene maps and genetic markers to aid in the selection for disease resistance. This has great applicability in South Africa and the selection of these animals will be of great advantage in the sustainability of livestock farming especially in resource-poor areas where the price of chemicals for the control of parasites are beyond the financial capacity of the community.

Research in reproduction physiology and molecular technology has focused on several aspects of consequence to practical animal breeding with the ultimate goal being the rapid genetic improvement of livestock.

DNA technology in general and DNA profiling in particular are relatively new but are part of the fastest expanding fields of biotechnology and even greater strides will be made in the next five years. Agriculture is facing new challenges from the pressures of urbanization, sustainability and the extension of global and regional markets.

It is essential that we in South Africa keep pace with the rest of the world by the adaptation of new trends to our specific circumstances as this will lead to greater prosperity in the livestock industry as a whole and the resource poor farmers specifically.

An important aspect is the improvement of the biological and economic efficiency of animals through scientific research, evaluation, development and technology transfer, thereby enhancing the quality of life of all peoples of South Africa.

Major growth in this sector will come from improved computer hardware to detect and characterize particular DNA sequences in microarrays on silicon chips. Although the investment in the development of the technology is immense, the widespread use will ensure that these mini laboratories will be extremely affordable, easy to use and will give accurate results even in untrained hands.

Along with the genome revolution comes the bioinformatics "gold rush". Centres of excellence will strive to "mine" the data generated in the genome projects. In the developed world the field of bioinformatics is set to become a major player with regard to the generation of money. The developing world must find affordable practical solutions to pressing problems.

The explosion in genomic information has created an unprecedented need for scientists with a deep working knowledge of the biological sciences and computational methods. The change has been so rapid that universities have been caught unprepared. Interdisciplinary training programmes must provide training that bridges departments and integrates computational methodologies into biological education and must focus on the molecular biology and physics of the cell. The use of advanced mathematics and computation must be emphasized as an integral part of the armament of the twenty first century biologist.

Bioprocessing

The first large-scale application of biotechnology in the form of a genetically modified organism (GMO) was the use of BST (Bovine Somatotropin). This has a significant impact on productivity and, consequently, the profit per cow increases without a loss of quality. The increase in milk production amounts to four to six kg per cow per day. In 1993 the FDA reported that there was no evidence that BST poses a threat to man or beast. This could lead to slightly smaller herds of dairy cows, less pollution as there would be a decrease in the use of fertilizers for feed production and, subsequently, less manure and therefore less methane production. The implication for improved management systems cannot be over-emphasized.

We are set to see a tremendous growth in the biopharmaceutical industry in the next five to ten years. Recombinantly produced human vaccines, e.g. vaccine against Hepatitis B, are some of the safest vaccines on the market today. As microorganisms cannot be used for the recombinant production of glycosylated proteins, transgenic yeasts, animals and plants will play a major role in the production of these proteins. For instance, Bio-farms can replace the income for many tobacco farmers feeling the pinch following a crackdown on the US tobacco industry.

Vaccines that target specific diseases very precisely will be engineered and produced against most animal diseases in future, making animal production possible in regions where infectious diseases are limiting and livestock production more efficient in other areas.

Genetic Modification

When biotechnology is discussed, the subject of cloning and "Dolly" in particular is invariably raised. Work on cloning started as long as 30 years ago on frogs but was never completely successful. However, Dolly's success story has indicated that adult nuclei can become totipotent.

Ethical issues usually go hand in hand with cloning but, as this work is extremely expensive and the viability of artificial embryos is significantly less than normal embryos, it is envisaged that this will not be a problem for many years. Under ideal conditions, only 20% of manipulated embryos are successfully implanted.

The production of transgenic animals, although generally expensive, opens a world of opportunities for the production of therapeutic substances with great advantages for both man and animals. One of the first of these to be produced was insulin and this has proved to be extremely cost effective. The use of transgenics will no doubt become more efficient and cost effective in the future.

The improvement of the quality or composition of animal products through the transfer of respective gene constructs could provide new prospects for animal production.

The challenge for gene transfer applications in domestic animals is to influence traits that are based on multiple genes. Until recently it has been possible to influence only traits that are based on a single gene or on a very limited number of genes. There is only a limited number of traits of interest to breeders, that are based on a single gene. However, growth, one of the classical quantitative traits in animal breeding, was changed to become a quasi-qualitative trait through the transfer of a single growth hormone gene that was related to a feedback independent regulation mechanism. In cattle it seems preferable to concentrate the very expensive and complex technique of gene transfer to fields which until now could only be improved with limited success through conventional breeding programmes, such as breeding for increased disease resistance.

A model proposed by Mercier (1987) has the reduction of the lactose content of milk as its objective. In the milk of transgenic sheep and cattle carrying a lactose gene, combined with an udder specific promoter, lactose is split into galactose and glucose. Such milk could then also be consumed by the large percentage of the world's population suffering from lactose intolerance. Through gene transfer, researchers have tried to promote the synthesis of cysteine in the mammal organism and to influence wool growth positively (Ward, Murray and Nancarrow, 1986; Ward *et al.*, 1986).

Gene farming. A suitable combination of tissue-specific promoters and the transfer of these genes into domestic animals may lead to the efficient and biologically reliable production of proteins (Lathe *et al.*, 1987). In particular, efforts have been made to use animals as bioconversion systems (Clark *et al.*, 1987). Gordon *et al.* (1987) and Simons, McClenaghan and Clark (1987) have also achieved the expression of human T-PA and sheep beta-lactoglobulin respectively in the milk of transgenic mice.

DNA vaccines are already in an advanced stage of testing. Tests of two types of measles DNA vaccine have been carried out in primates, using DNA that codes for surface proteins of the measles virus.

Bioadaptation

Bioadaptation need not be "high tech". The application of current knowledge provides small farmers and landless livestock owners with simpler, cheaper and easier means of maintaining their animals e.g. molasses/urea blocks that distribute vital nutrients or the use of pelletized Newcastle disease vaccines to protect the birds of poultry owners with limited resources.
On a broader scale, research currently underway may open up the use of hitherto unsuitable environments on the continent. An example is the development of probiotics for improving the digestion in ruminants. Another aspect of this research is the development of micro-organisms in ruminants that can digest or neutralize unpalatable or poisonous plants. The impact on communities in certain areas of South Africa will be significant.

Bioremediation

BIOREMEDIATION: The process by which living organisms act to degrade or transform hazardous organic contaminants. It is important to note that life-forms can be found in the most inhospitable and contaminated environments on earth. Nature's own adaptation to rapidly changing environments is one of the most fascinating processes to study and is only exploited to a very limited extent. The development, use and regulation of biological systems for the remediation of contaminated environments (land, air, water), and for environmentally friendly processes (green manufacturing technologies and sustainable development) is a very important aspect of biotechnology today. In terms of environmental cleanup the use of biotechnology to clean oil polluted land, chlorinated aliphatic hydrocarbons at wastewater treatment facilities, aromatic hydrocarbons from contaminated aquifers, biological waste from abattoir effluent, microbial denitrification of soils, etc. come to mind. It can be foreseen that bioremediation will play an increasingly important role as more pressure is exerted on the environment as a result of population growth. When this is achieved, the prospect of farming with livestock on previously polluted areas, is vastly improved. The nutritive advantages are obvious and the animals will thrive where previously they suffered from malnutrition or were unable to survive.

Biotechnology in Africa

A major role for biotechnology (developed elsewhere) in Africa is to increase efficiency under the current sociological and agricultural system, in order for the agricultural sectors to increase food production to cope with the needs of the growing human population. Although many developed nations can toy with the idea whether to apply a particular technology, including biotechnology, Africa is in desperate need for this biotechnology to survive. Crops genetically modified to have resistance to disease and pests (viral disease, fungi, insects), drought resistant animals and corps, disease and parasite resistant animals and livestock that is more energy efficient is desperately needed to feed the continent.

CONCLUSION

Biotechnology is viewed as the growth point for many agricultural research systems and is well established in many of the developed countries of Europe and America. The corporate marketing systems, established markets and the commercial nature of the agricultural sectors lend themselves to the use of biotechnology. This is true for part of the South African economy but the application of biotechnology will have to be adapted to encompass the range of needs that exists in South Africa. This includes both the large commercial sector and the resource-limited entrepreneur. It is this latter group who would benefit greatly from the use of appropriate biotechnology. The successful application of biotechnology in South Africa rests on our ability to create wealth from its application and to make this technology accessible and affordable to all sectors of the population.