# Transgenic Milk

P.K.Magnus, F.A. Lali *

Veterinary Surgeon
District Animal Husbandry Office, Thrissur, Kerala, India.

## Introduction

Over centuries animal breeding practices were performed to improve the genetic potential of animals and to introduce new traits, through genetic selection. But the number of gene combinations achieved through this process has limitations, since breeding is only possible between animals of same or closely related species. Transgenesis is a revolutionary technology which introduces new genes to a species, which belong to an entirely different species. The chemical combination of DNA is same in all eukaryotic species. Theoretically genes can be transferred between any species. So the resulting species will be having the desired characteristics of another species. Result of human genome project and other similar projects to reveal the genetic code has opened new arenas in medical research in combination with transgenics.

## Gene Pharming

By genetic engineering, the gene for a protein drug of interest can be transferred into another organism that will produce large amounts of the drug. Transgenic technology led to the emergence of a new kind of farming from research and development labs of several universities and small biotechnology companies- they even changed the spelling to "pharming". "Pharming" is the production of human pharmaceuticals in farm animals.

Gene "Pharming" enables production of recombinant biologically active proteins in the mammary glands of transgenic animals. This technology overcomes the limitations of conventional and recombinant production system for pharmaceutical proteins. Mammary gland is the preferred production site, mainly because the qualities of protein that can be produced in this organ using mammary gland specific promoter elements and established methods for extraction and purification of that proteins.

Numerous monoclonal antibodies are being produced in the mammary gland of transgenic goats. Cloned transgenic cattle can produce a recombinant bispecific antibody in their blood. Purified from serum, the antibody is stable, mediates target cell restricted T cell stimulation and tumor cell killing. An interesting new development is the generation of Trans-chromosomal animals. A human artificial chromosome containing the complete sequence of human immunoglobulin heavy and light chain loci was introduced into bovine fibroblasts, which were then used in nuclear transfer cloning. Trans-chromosomal bovine offsprings were obtained, that expressed human immunoglobulin in their blood. This system could be a significant step forward in the production of human therapeutic polyclonal antibodies.

## Different steps in transgenic animal production

1. Gene of interest is isolated in a strand of DNA.
2. DNA is cut specific points by restriction enzymes. The enzymes recognize certain sequences of bases on the DNA strand and cut where the sequences appear.
3. The cut DNA is jointed with a vector, which may be a virus (e.g.Retro viral vector) or a plasmid. The vector carries the gene of interest into organisms that will produce the protein.
4. When the genes are transferred in this way they get expressed in the desired organ of animals.

In addition to vector method, direct microinjection of nuclear material into *invitro* fertilized (IVF) embryos, and genetically modified embryonic stem cell transfer are effective techniques for transgenic animal production. Among these methods, transgenic animal production through stem cell transfer is very specific in locating the organ of desired action.

Transgenic milk can be prepared by two ways. One way is by inserting an extra gene into cow embryos, modifying their genetic make-up. Another method is to mate 'normal' cows with genetically modified bulls so that the next generation of calves will produce the desired protein.

Although the genetic code is essentially the same

* M.V.Sc. Scholar, College of Veterinary and Animal Science, Mannuthy, Kerala

for all organisms, the fine details of gene control differ. A gene from a bacterium will not often work correctly if it is introduced unmodified into a eukaryotic animal cell. The genetic engineer first of all constructs a transgene containing the gene of interest plus some extra DNA that correctly controls the function of the gene in the new animal. This transgene has then to be inserted into a new animal. Many genes are only expressed in particular tissues and are controlled by special segment of DNA next to the gene called promoter sequence. When constructing a transgene, scientists generally substitute the donor's promoter sequence with one that is specially designed to ensure that the gene will function in the correct tissues of the recipient animal. This is crucial when, for example the gene need to be expressed in milk of animal.

**Transgenic Animals and Milk**

Milk-producing transgenic animals are especially useful for production of medicines, nutritional supplements and pharmaceuticals. Products such as insulin, growth hormone, and blood anti-clotting factors have already been obtained from the milk of transgenic cows, sheep, or goats. Research is also underway to manufacture milk through transgenesis for treatment of debilitating diseases such as phenylketonuria (PKU), hereditary emphysema, and cystic fibrosis.

Milk composition can be altered in several ways - changing the concentration of unsaturated fatty acids, reducing the lactose content, removing ß- lactoglobulin and combining nutraceuticals in milk. By combining nutritional and genetic interventions, researchers are now hoping to develop 'medicine milk' rich in specific milk components that have implications in health as well as treatment. Cows, goats and sheep are utilized for the production of more than 60 therapeutic proteins, including plasma proteins, monoclonal antibodies and vaccines. In 1997, the first transgenic cow, Rosie, produced human alpha-lactalbumin -enriched milk at 2.4 grams per litre. This transgenic milk is a more nutritionally balanced product than natural bovine milk and could be given to babies or the elderly with special nutritional or digestive needs.

Lactoferrin, the iron-binding protein plays an important role in stimulating the immune system and acting as a first line of defence against infection. Its level in human milk is about 1 g/l (in human colostrum about 7 g/l) and that in cow's milk is only about one-tenth that in human milk. A New Zealand research group developed a genetically modified dairy herd capable of producing 'medicinal milk' containing recombinant human lactoferrin (rhLF) by transgenic technology. Now Argentinean scientists have developed a cow which can secrete human insulin in its milk. This insulin will be purified from cow milk and used for treatment of Diabetes Mellitus. When compared to conventional methods of insulin production this method is much more cost effective.

In 2001, two scientists in Canada spliced spider genes into the cells of lactating goats. The goats began to manufacture silk along with their milk and secrete tiny silk strands from their body by the bucketful. By extracting polymer strands from the milk and weaving them into thread, the scientists can create a light, tough, flexible material that could be used in such applications as military uniforms, medical micro sutures, and tennis racket strings. The major advantage of transgenic technology is that proteins can be produced at a low cost compared to the method using mammalian cell culture. However various ethical, legal and social aspects of biotechnological research need to be addressed before the implementation of transgenic herds.

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