ILRI

International Livestock Research Institute

Deciphering the code of life to benefit the poor

2000

Annual Report

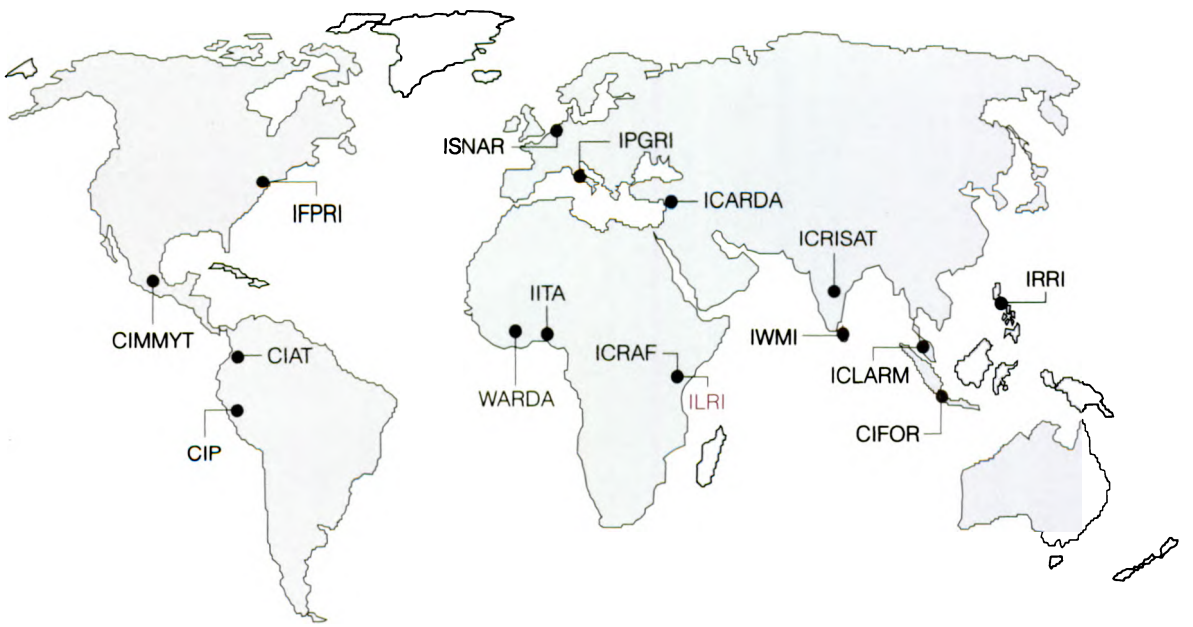
2001

About ILRI

The International Livestock Research Institute (ILRI) is a public-sector international agricultural research centre under the aegis of the Consultative Group on International Agricultural Research (CGIAR). ILRI's mandate is to enhance the well-being of present and future generations in developing countries through research to improve sustainable livestock production. It works in partnerships and alliances with other organizations, national and international, in the fields of livestock research, training and information exchange. ILRI was formed in 1994 and is headquartered in Nairobi, Kenya.

About the CGIAR

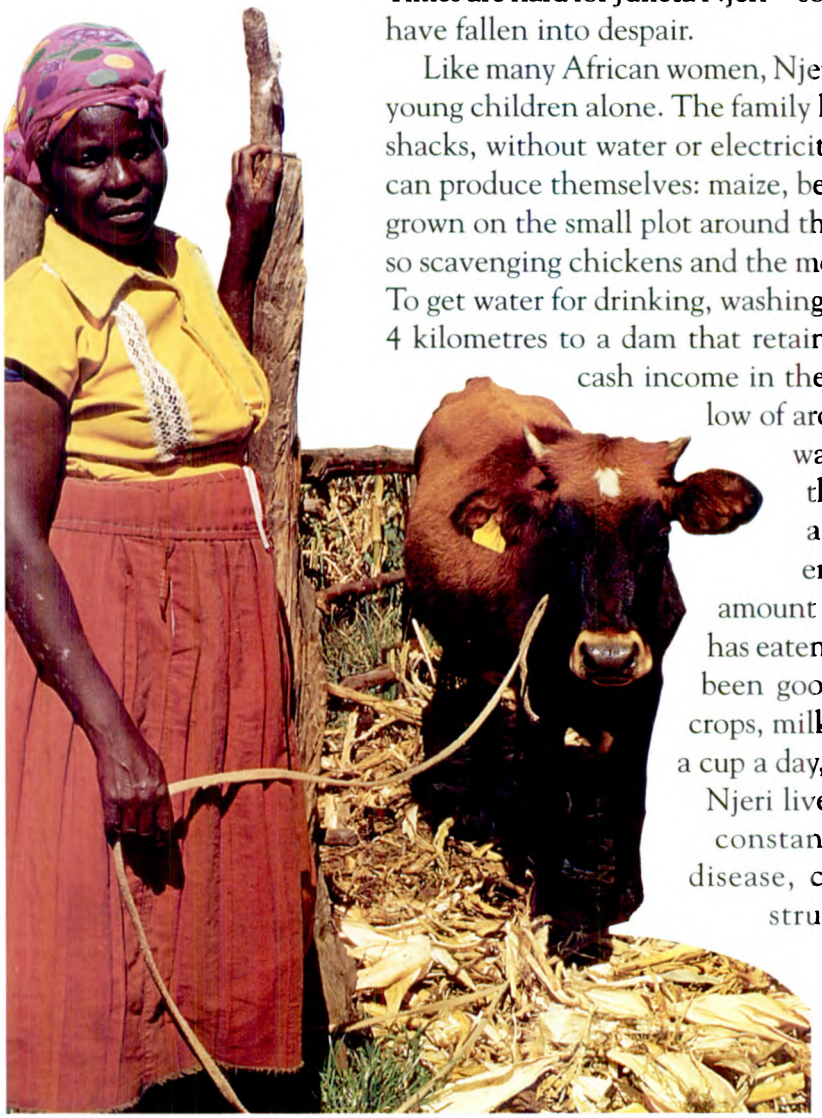
Established in 1971, the Consultative Group on International Agricultural Research (CGIAR) is an informal association of public- and private-sector members that supports a network of 16 international agricultural research centres. The CGIAR's mission is to contribute to food security and poverty eradication in developing countries through research, partnership, capacity building and policy support. It promotes sustainable agricultural development based on the environmentally sound management of natural resources.



FUTURE HARVEST **ILRI is a Future Harvest centre**

Deciphering the code of life to benefit the poor

Living on hope



Times are hard for Julieta Njeri—so hard that a lesser woman might have fallen into despair.

Like many African women, Njeri struggles to bring up her three young children alone. The family lives in two cramped tin-roofed shacks, without water or electricity. They eat only the food they can produce themselves: maize, beans and some green vegetables grown on the small plot around their homestead, eggs from 20 or so scavenging chickens and the meagre milk from two zebu cows. To get water for drinking, washing and cleaning, Njeri must walk 4 kilometres to a dam that retains a small, stagnant pond. Her cash income in the year 2000 sank to an all-time low of around KSh 1500 or US$ 20 and was derived almost entirely from the sale of a few surplus eggs. In a good year, Njeri also harvests enough beans to have a small amount left over for sale after the family has eaten. But the past few years haven't been good: drought has shrivelled her crops, milk yields have fallen to less than a cup a day, and the dam has silted up.

Njeri lives on the very edge of survival, constantly at risk from hunger and disease, constantly exhausted by the struggle to keep body and soul together. Yet, far from despairing, she is sustained by hope—hope that her circumstances are about to change for the better.

Njeri plans to increase her income by selling milk. Last year, she took a big step towards realising that plan by cashing in her mature zebu bull and buying a crossbred dairy calf instead. If she can successfully raise this animal to maturity and feed it properly, it will produce a bucket of milk a day instead of a cupful. She will retain a share of the extra milk in the household, enabling her to raise healthier children as well as eat better herself. The rest she will sell, using the cash to increase the family's food security still further and to buy other long neglected necessities such as clothing and shoes. When her mature cow calves, she may either keep the calf, if it is female, so as to produce still more milk or, more probably, sell it for a lump sum, especially if it is male. With luck, she might then be able to pay the children's school fees.

'Anyone who has ever struggled with poverty knows how extremely expensive it is to be poor.' — James Baldwin, American essayist.

But Njeri's plan could yet be thwarted. Her village, in the Maragua District of Kenya, lies in an area at high risk of East Coast fever (ECF), an often fatal disease of cattle to which crossbred animals are particularly susceptible. The disease is caused by a single-celled parasite called *Theileria parva*, which is transmitted to cattle through the saliva of biting ticks. At the height of the last dry season, when feed resources on her farm ran out, Njeri had no choice but to take her calf to graze with other farmers' cattle on nearby common land. Born of sheer necessity, her action was nevertheless a risky one, since this land is prone to infestation with ticks. Her calf promptly went down with the disease, threatening the loss of the investment on which her future depends.

On this occasion Njeri was lucky. She was taking part in a research project (Box 1), which came to her rescue by providing the expensive drugs needed to save the animal. But the experience has dented her confidence. She knows that, if she is to run a profitable small-scale dairying enterprise in the future, she must be able to protect her animals from the disease independently of external support.

Millions of other would-be small-scale milk producers in eastern and southern Africa share Njeri's predicament. Some 29 million cattle in the region are thought to be at risk from ECF, which annually causes losses estimated at US$ 200 million in dead animals and foregone milk and meat production.

At present, little can be done to prevent the disease. The drugs that can cure it are too costly for the vast majority of small-scale producers. The tick vector can be controlled with acaracide sprays,

Box 1: A risk reducer

ILRI's epidemiology team has been working with the Kenya Agricultural Research Institute (KARI) to monitor the risk of infection with ECF in four Kenyan environments suitable for small-scale dairying. The aim is to provide a basis for assessing the potential impact of a new vaccine against the disease.

The first environment is the high-potential central and eastern highlands, which have plentiful rainfall and easy access to the urban market of Nairobi. Here cows are mainly stall-fed rather than grazed on communal pastures, so the risk of infection is relatively low. But if the disease does occur it is usually fatal, since the animals kept are high-grade Friesians, which are highly susceptible. In such production systems, a single tick can spell the end of the enterprise.

The second environment is the lower-altitude medium- to low-potential highlands, where rainfall is less certain and land pressure is rising as the zone fills up with migrants from higher lying areas. Farmers here are attempting to keep crossbred cows, but tick challenge is high and many animals succumb, especially when grazed along roadsides or on communal pastures. A vaccine made available in this environment—the home of Njeri—would have a tremendous impact.

In the third environment, the western highlands, dairy production is more extensive, since land is more plentiful. Again, the risk of infection for grazed animals is high, especially for exotic purebreds. Wealthier farmers use acaricide sprays to rid their animals of ticks. Here a vaccine would considerably reduce the costs of disease control.

The fourth environment is the basin of Lake Victoria, also in western Kenya. Disease incidence is relatively low, but farmers are nonetheless reluctant to keep crossbred animals because of the perceived risk of infection. Introducing a vaccine might persuade them to change their minds.

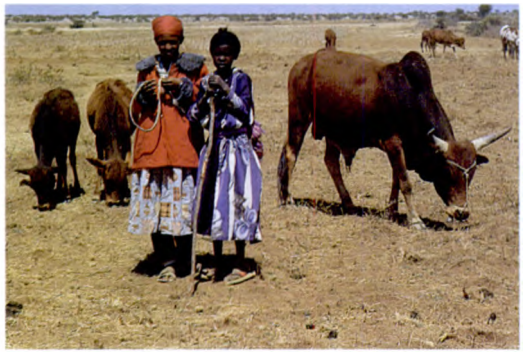
but these too are expensive and they have damaging side-effects on the environment and human health. There is a vaccine against ECF—but it is a 'live' one, risky and difficult to deliver under African conditions. Because it entails inoculation with the causative parasite, this vaccine risks bringing on the very disease it is intended to cure. It also requires delivery via a 'cold chain', to ensure that it is still live when injected into the animal. And, to block the development of full-blown ECF, it has to be administered in conjunction with tetracycline, another expensive drug.

But all that could be about to change. A team of scientists at ILRI has been working with national and international colleagues to develop a better vaccine—one which, because it is based on a component or subunit of the parasite, will be cheaper, safer to use and easier to deliver. That work, which has made slow progress in

the past because of its great complexity, now stands poised on the brink of success. It does so thanks in large measure to the new tools of genomics research, which are enabling scientists to take a quantum leap forward in their understanding of the genetics of ECF.

New weapons in the war on poverty

ILRI's genomics research, like all its research, starts with the problems that confront poor livestock producers such as Njeri. The Institute and its partners identify these problems through participatory diagnostic studies conducted in farming communities in Africa, Asia and Latin America. They use the results of these studies to assess the potential impact of different lines of research, to decide on priorities and to drive the agenda of research in the laboratory.



The raw materials used in the research are the natural resources of which poor livestock producers are the custodians. On ILRI's doorstep, in the vast dry rangelands and steppe pastures of Africa and Asia, live hundreds of breeds of domestic livestock and their wild relatives—a genetic heritage rich in the characteristics of stress resistance and tolerance of value in these harsh habitats. These animals, like their cousins in wetter environments, feed on forage plants that vary greatly in their growth habits, adaptation to different niches, nutritional characteristics and suitability for other functions besides livestock feed. ILRI has one of the world's largest and most diverse collections of forage germplasm—over 13,000 accessions belonging to 1000 different species. Besides these animals and plants, the Institute studies the gut microbes that aid the digestion of feed in ruminants, and the worms, protozoa and other parasites that curb production and cause diseases in livestock. In seeking access to all these resources and using them in its research, ILRI is guided by the 1993 Convention on Biological Diversity (Box 2).

ILRI 2000–2001

Deciphering the code of life to benefit the poor

ILRI
INTERNATIONAL LIVESTOCK RESEARCH INSTITUTE

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Cover picture: Delia Wasawo, a Kenyan technologist who heads ILRI's DNA Sequencing Unit, loads a gel into an automatic sequencer at ILRI's Nairobi laboratories. Delia received training in advanced sequencing techniques at The Institute for Genomic Research (TIGR) in the USA. She is now applying these techniques in an ILRI–TIGR collaborative project to decode the DNA of the *Theileria parva* parasite, a major scourge of livestock in tropical Africa.

ISBN 92–9146–092–3

Correct citation: ILRI (International Livestock Research Institute). 2001. *ILRI 2000–2001: Deciphering the code of life to benefit the poor*. ILRI, Nairobi, Kenya.

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The need to improve the productivity of these resources was never more compelling. Despite the gains made through past research, an estimated 1.3 billion people, or nearly a third of the population of the developing world, continue to live on less than US$ 1 a day—a fact described at the recent Davos World Economic Forum as the greatest single moral challenge facing human-kind. Predictably, the statistics are worst for sub-Saharan Africa, where per capita incomes have been falling for the past 25 years and over 50% of the population now lives below the poverty line. But the absolute numbers of poor people are highest in Asia (excluding West Asia), where an estimated 801 million poor now live. Clearly, ILRI's research must address the needs of both these regions (Box 3).

Box 2: ILRI and the Convention on Biological Diversity

The Convention on Biological Diversity (CBD) established the principles of national sovereignty over genetic resources and the equitable sharing of the benefits that flow from their conservation and use. ILRI respects these principles and abides by them in its work.

In keeping with the spirit of the CBD, ILRI considers its collection of forage germplasm (which was acquired before the Convention came into force) to be held in trust for human-kind and especially for the world's poor. Following an agreement signed with the Food and Agriculture Organization of the United Nations (FAO), it has placed its collection under FAO trusteeship. Reflecting its belief in the value of an open global system of germplasm exchange, ILRI makes limited quantities of germplasm available to all who request it, provided they undertake not to claim ownership of the material or intellectual property rights over it and provided they ensure that others to whom they pass on the material are bound by the same conditions. These conditions also apply to information about the material.

ILRI recognises and supports the indispensable role of farmers in domesticating and conserving genetic resources, including those of livestock, microbes and parasites in addition to forage species. In seeking access to these resources, the Institute abides by the principle of 'prior informed consent' and the terms and conditions defined under national policies. It undertakes to negotiate materials transfer agreements with appropriate national bodies and to conduct collection missions in a participatory manner.

For millions of poor rural people, livestock represent an opportunity to accumulate assets. Without the security provided by their animals, they will always be liable to a sudden slide back into poverty at the whim of climatic, market or family setbacks. But more than this, livestock production also represents an opportunity for the poor to raise their incomes by entering an expanding market. Three factors—rising human populations, urbanisation and incomes—are driving a rapid increase in the demand for livestock products throughout the developing world (Table 1). As consumers switch away from traditional cereals into a more diverse diet in which meat, milk, fish and eggs will

Box 3: Out of Africa, benefits for Asia

For historical reasons, ILRI's staff and programmes are concentrated mainly in Africa and most of its research is conducted there. However, the Institute's basic and strategic research, especially in genomics, is becoming increasingly global in its applications, with strong potential benefits for Asia emerging alongside those for Africa.

For example, research to develop a vaccine against *T. parva* in Africa should benefit the control of *T. annulata*, a similar organism that affects an estimated 200 million cattle in Asia (see p. 35). Similarly, work on worm resistance in the Red Maasai sheep of eastern Africa should eventually benefit millions of sheep and goat producers in Asia and world-wide (see p. 35). And research to explore the genetic diversity of indigenous livestock is now reaching beyond African cattle to encompass Asian species such as the yak and the Bactrian camel (see p. 27).

Since it was founded in 1994, ILRI has strengthened its presence in Asia, basing regional projects for South Asia at the International Crops Research Institute for the Semi-Arid Tropics (ICRISAT) in India and for East and South-East Asia at the International Rice Research Institute (IRRI) in the Philippines.

Research in South Asia addresses the needs of dairy and small ruminant production systems in rainfed and irrigated areas. The principal project currently under way is identifying the genetic basis of palatability and feed value in cereal crop residues and is expected to have considerable impact throughout the drier areas of Asia, with benefits flowing back towards Africa and other regions (see p. 36). Research in East and South-East Asia emphasises the mixed crop–livestock systems of the rainfed areas and addresses problems of disease control, nutrient availability and the policy environment. Two core projects are responsible for this research: the Crop–Animal Systems Research Network (CASREN) and the Sustainable Parasite Control in the Tropics (SPC) project. A range of additional support activities has developed round these projects, with strong emphasis on information dissemination.

Foreword

'New developments in modern biotechnology...are revolutionising global research and development in agriculture and natural resources research.'— Serageldin and Persley (2000).

ILRI's 1999 Annual Report dealt with the Livestock Revolution. Before we introduce the theme of this year's report, it is worth reflecting briefly on what we mean by this term.

Driven by rising incomes and population growth, the demand for meat and milk in developing countries is expected to double by the year 2020. This simple fact has tremendous implications. In the developing countries, it presents poor livestock producers with perhaps the most significant income-earning opportunity they will see in their lifetimes—an opportunity they can grasp, because livestock are an enterprise with which they are familiar and in which, by and large, they can afford to invest. For the governments of these countries, it implies regulating the livestock sector effectively so as to protect human health and the environment. It also implies allocating more resources to livestock-oriented research and development (R&D). If the Revolution is to be an equitable one, governments must focus their efforts on the needs of poor producers, enabling them to participate on equal terms with large producers in the expanding market for livestock products. And for those of us in the developed world who support those efforts, the Revolution also means placing more emphasis on livestock R&D, including policy issues.

To seize the opportunity provided by the Livestock Revolution, poor producers need to increase the productivity of their herds and flocks. There are two main routes to increased productivity: reducing the losses caused by diseases and parasites, and improving the quantity and quality of animal feeds, together with their utilisation. Both are the subject of research by ILRI and its partners.

ILRI is in a unique position to conduct this research. Based in the developing world, it is well placed to study the needs of poor producers and to work with their resources—the plants and animals they raise. At the same time, it has the necessary expertise and equipment to tap into scientific advances in the developed world and so to bring new knowledge to bear on the problems faced by its beneficiaries.

This brings us to our theme for this year's Annual Report: deciphering the code of life to benefit the poor. If this theme seems audacious, we make no apology. The astonishing progress in genomics over the past few years has created powerful new tools for understanding and solving basic biological problems in both human medicine and agriculture. By revealing the similarities between the genomes of different organisms, these tools have opened up new fields of common interest between ILRI and the advanced institutes that developed them. We believe our partnerships with these institutes are bringing forward the day on which we will be able to deliver substantial gains in the productivity of the herds and flocks kept by

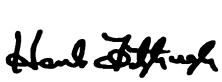
poor livestock producers in developing countries. The prospects of seeing an early impact from investments in ILRI have brightened immeasurably.

The highlight of the past year at ILRI, and hence of this report, is the exciting progress made towards a subunit vaccine against East Coast fever (ECF)—progress that would not have been possible without the vision and commitment shown by our new partner in this work, The Institute for Genomic Research (TIGR). But genomics also contributes to many other aspects of our programme, enabling us to characterise indigenous livestock breeds, to increase the range of forages available to smallholders and to improve feed quality and utilisation, as well as to solve other pressing problems in animal health. These fields too have recently seen encouraging advances.

The year has brought other significant, if more mundane, achievements: the new ILRI strategy was accepted by the research group to which ILRI belongs, the Consultative Group on International Agricultural Research (CGIAR); a medium-term plan based on the strategy was developed; and ILRI was reorganised to reflect the integrated nature of its programme and to sharpen its focus on impact at the farm level. These developments equip the Institute to face an increasingly uncertain world in the confidence that its mission and programme are clearly articulated and forward-looking. This should provide welcome stability at a time when the CGIAR system stands on the brink of major changes.

Anchored in the needs of the poor yet reaching out to advanced research institutes, ILRI's programmes span the spectrum from adaptive research on the farm to basic research in the laboratory. The only way in which the Institute can draw these contrasting worlds together is through the strength of its partnerships. To get the most out of its partnerships, ILRI has pursued the concept of catalytic leadership—inspiring gifted people in other institutions to work with us to achieve shared aims. We believe this report testifies to the success of this approach.

To all our stakeholders and partners, we express our gratitude for your support. ILRI has an exciting programme on the verge of major advances through science. Stay with us!



Hank Fitzhugh
Director General
ILRI

John Vercoe
Chairman
ILRI Board of Trustees

Table 1. Projected trends in meat and milk consumption in different regions of the world, 1993–2020.

Region	Projected annual growth of total production, 1993–2020		Total production in 2020		Per capita production in 2020	
	Meat	Milk	Meat	Milk	Meat	Milk
	(percent per year)		(million tonnes)		(kilogrammes)	
China	2.9	3.2	86	19	60	13
Other East Asia	2.4	3.9	7	3	55	29
India	2.8	1.6	8	172	6	135
Other South Asia	2.6	3.1	4	46	9	92
South-East Asia	3.1	2.9	16	3	25	5
Latin America	2.2	2.0	39	80	59	121
WANA	2.5	2.6	11	46	18	72
Sub-Saharan Africa	3.4	4.0	11	31	10	30
Developing world	2.7	3.2	183	401	29	63
Developed world	0.7	0.4	121	371	87	267
World	1.8	1.6	303	772	39	100

Source: Delgado et al. (1999).

feature ever more largely, producers are responding by trying to increase supplies. ILRI and its partners have dubbed this fundamental shift in the pattern of demand and supply the Livestock Revolution.

The key to enabling poor, small-scale livestock producers to benefit from the Livestock Revolution is to find ways of increasing the productivity of their animals. The two main challenges are to reduce the losses caused by diseases and parasites and to improve the quantity, quality and utilisation of animal feeds. ILRI's scientists and their partners are using the tools of modern genomics to respond to both these challenges.

What is genomics? The word is a new one, coined by scientists to describe the use of molecular tools to delve beneath the

appearance of an organism so as to study the structure of its genome—the sum total of its DNA—and the functions of its individual genes. Today's molecular tool-kit has its origins in the 1953 discovery by Crick and Watson of the double-helix structure of DNA and the four nucleotides or base-pairs—C, T, A and G—of which it is made. The history of the tools' development is one of dramatic advances in the speed and accuracy with which genes can be identified and manipulated (Box 4).

To unlock the secrets of a genome, scientists must first decipher the sequence of bases along the single strand of DNA contained in each chromosome, then distinguish and attribute functions to individual genes. 'If the unsequenced genome is a kind of alphabet soup, what sequencing does is set the letters in order,' says Subhash Morzaria, leader of ILRI's Livestock Health Programme. 'That is the structural part of genomics. But at this stage the letters are still all run together. Functional genomics is the art of separating them so that they form individual words, enabling us to read the book.'

Setting the letters in order was, until recently, a slow and laborious business. The first sequencing machines, developed in the 1970s, were manually operated and could process only segments of a genome. Nor did learning to read the book come easily: scientists had to proceed empirically, fishing for genes using individual markers, then testing the markers for their correlation with traits by conducting field trials.

The pace began to quicken in the early 1990s, with the advent of bioinformatics—the computer-based discipline that has evolved to analyse complex biological information. Powerful new computers and software became available that enabled scientists to automate the sequencing process.

'Powerful computers are unravelling the digital codes of life at a pace so breath-taking we can hardly absorb its riches.'
— Claire Fraser, President, TIGR.

Then, in 1994, sequencing technology took a giant leap forward. The man who made the leap is Craig Venter, founder of the US-based public-sector research institute, The Institute for Genomic Research (TIGR), and now Chief Executive Officer (CEO) of the private-sector company Celera Genomics. In what Venter calls the 'shotgun approach' (Figure 1), the whole genome of an organism is first mechanically shredded into minute fragments. These fragments are then sequenced individually, before being reassembled by purpose-built computers—among the most powerful ever built—that 'recognise' the points at which the sequences overlap. This operation is conducted repeatedly, to arrive at a picture of the genome that is 95–98% complete.

The shotgun approach has transformed the business of sequencing into a high-speed affair. As a measure of the pace of

'It has been estimated that, at the rate of one word per second for eight hours per day, it would take a century to read the human genome. Fortunately, we have ways of speed-reading.'
— Claire Fraser, President, TIGR.

Box 4: From RFLPs to micro-arrays

In the late 1960s and early 1970s, scientists developed the first enzymes for chopping and splicing DNA. These were used mainly to modify bacteria for use in industries such as brewing, bread making and the manufacture of washing powder.

By the early 1980s, techniques for sequencing and modifying more complex genomes, including whole plants and animals, became available. Molecular markers—specific sequences of DNA that act as pointers—for the first time allowed scientists to identify and track segments of DNA known to be associated with specific traits. These segments are called QTLs—quantitative trait loci.

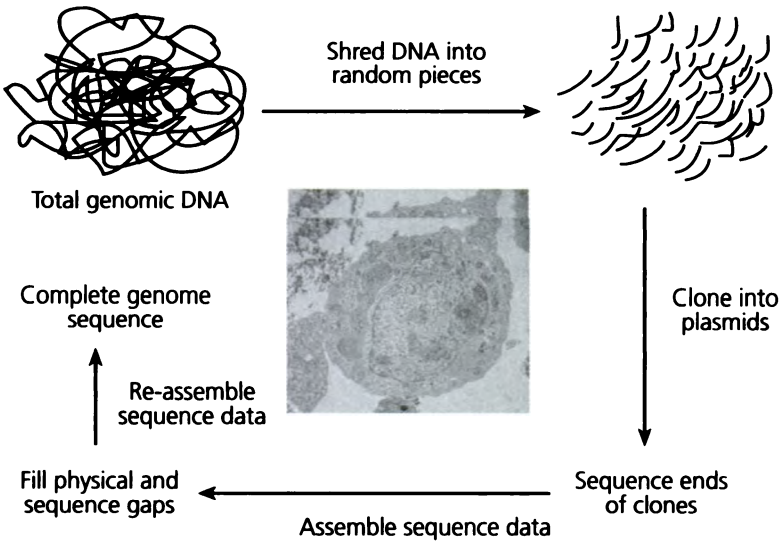
The first generation of markers were restriction fragment length polymorphisms (RFLPs), which were relatively slow and cumbersome to use. They depended on the use of plasmids—small, circular pieces of DNA—into which the DNA sequence of interest had to be transferred. The cells containing the plasmids were then cultured until sufficient DNA was available for experimental purposes.

A decade later, in the early 1990s, came the breakthrough that laid the basis for today's far more rapid sequencing operations—that of polymerase chain reaction or PCR. In nature, DNA is copied as cells divide. By reproducing this copying function in the laboratory, scientists were able to bulk up DNA quickly and accurately for experimental purposes.

PCR gave rise to a new generation of more powerful markers. Among the most widely used are random amplified polymorphic DNA (RAPDs), useful, as the name suggests, for running a quick check to detect unspecified variation, and amplified fragment length polymorphisms (AFLPs), which combine the speed of PCR with the accuracy of restriction enzymes. Closely akin to AFLPs are microsatellites, which consist of simple, repeated sequences of base pairs that are ubiquitous in the genome and highly polymorphic (having many minute variations). The first characteristic allows whole genomes to be covered evenly with these markers, while the second makes them easy to distinguish from one another, enabling scientists to track the inheritance of characteristics from different parents and to use this knowledge to detect performance-related QTLs.

A further set of markers, developed only recently, allows scientists to pinpoint individual genes and to explore their functions at different stages of a biological process or of the life-cycle of an organism. Genes that express a protein do so via messenger ribonucleic acid or mRNA, which is then 'translated' to make the protein. DNA expression arrays are markers that reveal which genes are 'switched on' or, in other words, are producing mRNA in a cell at a given time. The most commonly used form of DNA expression array is the micro-array, consisting of unique signatures of thousands of genes mounted on a glass slide, which can be read using a laser scanning microscope.

Figure 1. Shotgun genome sequencing



Shotgun sequencing

This process is now being used to unravel the genetic code of organisms as diverse as bacteria, fruit flies and human beings. Total genomic DNA is randomly fragmented into numerous short lengths of 2000 to 3000 base pairs, which are then cloned into plasmids. Sequences are then determined for large numbers of plasmids, each carrying a different piece of DNA, and the results are assembled by computer into overlapping sequences. The random or 'shotgun' nature of the process ensures that each base pair is sequenced several times—a factor that contributes to the accuracy of the overall genome sequence. Additional sequence data derived from plasmids containing longer pieces of DNA may be used to ensure correct sequence assembly. Gaps in the data that remain after the shotgun phase are filled by a targeted sequencing strategy, often using PCR.

change, it was in 1994 that scientists at TIGR first decoded the entire DNA sequence of a microbe, realising what had been described by their peers as an impossible dream. In the 6 years since then, they and others around the world have sequenced around 50 genomes, including over 40 microbes, various more complex organisms such as yeast, nematodes and fruit flies, a plant species and—the ultimate prize—the human genome.

In contrast, the task of finding out the functions of individual genes remains a bottleneck. But thanks to bioinformatics and the Internet, this too is easing. The latest software packages enable scientists not merely to decode DNA but also to analyse it and to predict which genes will perform specific functions. This predictive capacity will, in time, largely replace the empirical approach on which functional genomics has so far relied. Meanwhile, the

Internet allows complete sequences of genomes to be published world-wide as soon as they become available. As a result, scientists scattered about the globe are now able to pick up minute differences in genomes by comparing the sequences on which they are working with those already in the public domain. These differences are the key to working out the functions of individual genes. 'We still have much to learn in the field of functional genomics,' says John Gibson, who co-ordinates the Livestock Genetics and Genomics Programme at ILRI. 'But the current state of the art does allow us to narrow down the selection of genes likely to be associated with key traits. And this work, instead of taking 25 years as it used to do, can now be done in a matter of weeks.

'Environments rich in ideas produce chain reactions of innovation. But as with nuclear reactions, a critical mass of ideas and technology is needed first.'—
Jeffrey Sachs,
The Economist,
22/7/00.

The new precision tools of genomics are the fruit of investments many times the size of ILRI's budget and were developed to serve purposes far removed from the needs of poor livestock producers in the developing world. But through its partnerships with advanced institutes such as TIGR, ILRI is able to harness these tools and apply them to the needs of its constituency. These partnerships typically serve multiple purposes, providing benefits to both veterinary and human medical science or to both livestock and crop production (Box 5). They also provide training and jobs for developing-country scientists, augmenting national capacity to absorb and apply new science (Box 6). Thus, by entering these partnerships, ILRI helps close the 'technology gap' between the world's rich and poor nations.

Box 5: Shotgun marriage

ILRI's partnership with TIGR began in 1999. The two institutions are now collaborating on the following projects:

- Sequencing of the *T. parva* genome
  Specific objective: Accelerated development of an ECF subunit vaccine
  General objectives: Insights useful in human medical research, including research on malaria and leukaemia; increased understanding of *T. annulata* genome
- Search for genetic markers for feed quality in cowpea
  Specific objective: Improved dual-purpose varieties of this drought-resistant legume
  General objectives: Increased ability to predict the locations of genes coding for feed quality in other legumes
- Sequencing of rumen microbe molecules
  Specific objective: Probe for presence of useful rumen bacteria
  General objectives: Improved digestion of fibrous and antinutritional components of forages; increased choice of feeds available to smallholders
- Use of mice to study the genetic mechanisms underlying malaria and leukaemia*
  Specific objective: Possible vaccines, drugs and diagnostic kits for these diseases
  General objectives: Better understanding of the body's immune and resistance mechanisms

* In collaboration with the Institute of Molecular and Cell Biology–Africa (IMCB–A). ILRI's contribution is to breed and house the mice and to provide laboratory facilities

Box 6: Closing the technology gap

In 1996, a Kenyan scientist named Delia Wasawo joined ILRI as a research technician, soon graduating from her initial post in an assistant capacity to managing all ILRI's sequencing work.

Over the next 4 years, Delia processed a steadily increasing flow of DNA data, using old-fashioned manual equipment. Then, in 2000, ILRI purchased a new automatic DNA sequencer of the kind in use at TIGR. This sequencer had the power to greatly speed up the sequencing task, freeing Delia for more work on the functional side of genomics.

To prepare her for her new work, ILRI sent Delia on an 8-week course at TIGR's sequencing centre in Rockville, Maryland, USA. TIGR generously agreed to provide the training free of charge. Working alongside TIGR staff, Delia learned not only how to operate the new machine but also the procedures used in shotgun sequencing. During her visit she contributed to the building of two new gene 'libraries'—the stock of unanalysed DNA that results from sequencing.

Now back at ILRI, Delia represents a precious investment in the future of Kenya: someone with the know-how to apply modern genomic science to the country's pressing needs for more productive livestock and crops.

'Young scientists so often lured by research to the north may now decide to stay at home—where the action is.'—Claire Fraser, President, TIGR.

For a non-profit making public-sector institute such as ILRI, genomics research, and the partnerships it involves, raise complex issues of intellectual property (IP) rights. The Institute has recently taken steps to improve its ability to deal with these issues (Box 7).

ILRI's Medium-term Plan 2001–2003 outlines seven key areas critical to enhancing the productivity and sustainability of livestock production in developing countries. Four of these are areas in which genomics is already making exciting contributions to ILRI's research. They are:

- Improvement of livestock feeds and nutrition
- Management of natural resources (as this relates to the livestock sector)
- Improvement of animal health
- Characterisation and utilisation of livestock genetic potential.

We will now draw on these areas to illustrate ILRI's problem-solving genomics research. We cannot cover the full range of activities under way, so we'll restrict ourselves to a few that have recently shown rapid progress.

Box 7: ILRI and intellectual property rights

ILRI has developed a new policy statement on IP rights and established an IP management unit to implement the policy.

The statement outlines the Institute's policies on all the materials and ideas used in and resulting from its research. It emphasises ILRI's mission as a non-profit public-sector research institute whose activities benefit poor producers and consumers in developing countries. It pledges the Institute to make the information, inventions and materials derived from its research freely available in the public domain, except where they contain proprietary materials developed by others. The statement nevertheless recognises that ILRI may seek to protect its IP to ensure the continuing availability of materials and prevent their misappropriation by others, or to create a 'bargaining chip' in negotiations to secure access to other proprietary rights and technologies. Confidentiality agreements and materials transfer agreements are identified as the appropriate vehicles for defining access to and use of all materials and ideas, including those shared with private-sector partners. IP policies in relation to staff members and visitors are also outlined.

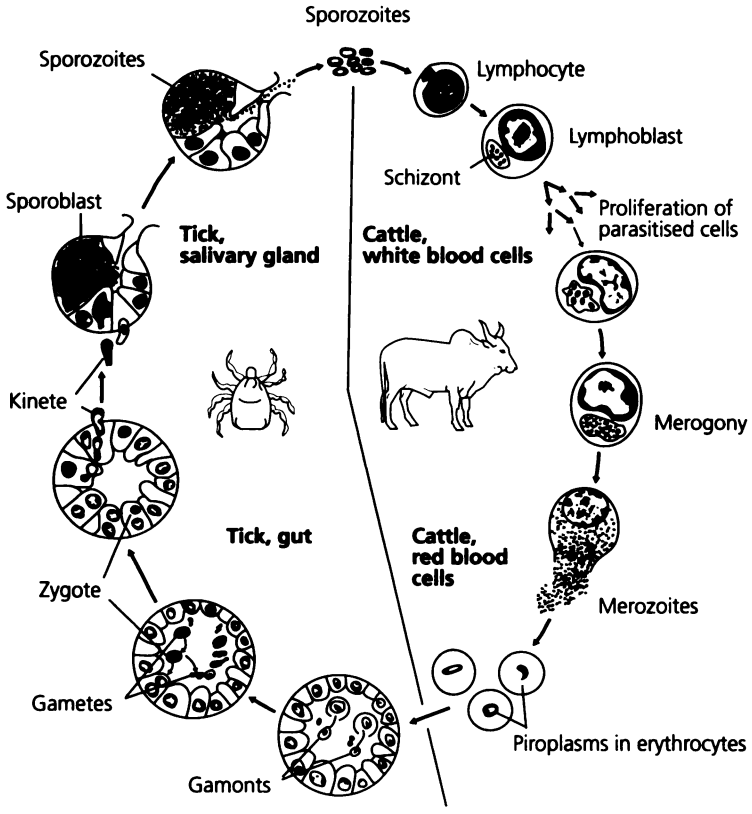
The main tasks of the IP management unit are to evaluate inventions or discoveries made by ILRI scientists, to build awareness of and familiarity with IP issues among the Institute's scientists and their national partners, to ensure proper laboratory and administrative procedures with respect to IP issues and to negotiate and draft contracts or agreements between ILRI and its partners. The unit's work is overseen by an IP committee.

Countdown to a vaccine

The life cycle of *Theileria parva*, the parasite that causes ECF, offers two possible points at which the infected animal's natural defence system can leap into action to fight the disease (Figure 2). A first antibody response occurs at what is called the sporozoite or early infective stage of the parasite, as soon as it enters the animal through the saliva of a biting tick. This response is not often successful because, within seconds of getting under the animal's skin, the sporozoites penetrate its new host's white blood cells, where they are protected. Unless large concentrations of antibodies are already present near the site of the bite, the response is likely to be too little and too late.

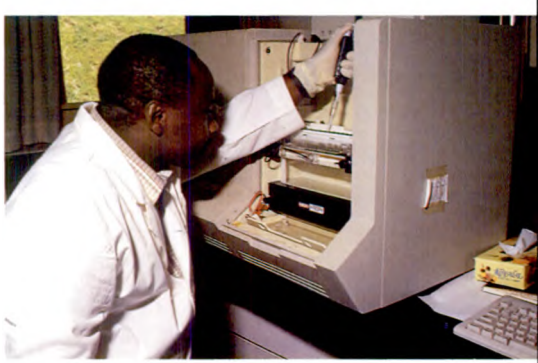
The second immune response is cell-mediated. Once inside a white blood cell, the single-celled sporozoite starts to differentiate into a larger, multinucleate body called a schizont. This body causes the white blood cells to divide and proliferate, lending ECF a strong resemblance to the human disease, leukaemia. The schizont typically

Figure 2. Life cycle of *Theileria parva*



interacts with its host white blood cell via secreted proteins, which are broken down into smaller fragments in the process. When these fragments become associated with a specific category of host cell surface protein called class I MHC (major histocompatibility complex) proteins, the animal's immune system perceives these protein complexes as foreign and responds by bombarding them with killer cells known as cytotoxic lymphocytes (CTLs). If the CTLs are successful, the infection is overcome and the animal recovers. More often, however, the cancerous proliferation of the white blood cells outpaces the work of the CTLs, and the animal dies.

In the mid-1980s, the study of the first of these immune responses led to the discovery of p67, a surface coat protein of the parasite which acts as an antigen at the sporozoite stage of infection. When tested as a vaccine in the field, p67 reduced the incidence of severe ECF by around 50% in cattle. This is not enough to allay the fears of poor livestock producers such as Njeri, who are exposed to high levels of financial risk when the disease strikes. ILRI therefore decided to expand its research, with the aim of identifying the migrant protein targeted by the CTL T-cells during the host's second immune response. If this protein, or schizont antigen, can be combined with p67, it should prove possible to develop a multi-valent subunit vaccine that will confer protection of 90% or more in smallholders' animals.



The task of finding a schizont antigen proved extremely complex. So much so that ILRI's 1999 External Programme and Management Review (EPMR) asked whether research with such an uncertain outcome should be continued. ILRI's response was to commission a further, more specialised external review to examine the question more thoroughly. Two expert panels were constituted, one to determine whether a vaccine was technically feasible and the other to consider whether or not it could be commercially manufactured and delivered to users.

The commercial panel, consisting largely of representatives from private-sector companies, concluded that these companies would not have been willing to invest in research to develop a vaccine against ECF because of the vaccine's relatively small market potential, but that they would be interested in manufacturing and

distributing a vaccine if such research were successful. In other words, they confirmed the value of the public-sector investment made by ILRI's donors. The technical panel noted that the development of a subunit vaccine was the most rational approach to controlling ECF. It also recognised that the complex nature of the disease's causative agent had made for slow progress in achieving this aim. But despite this slow progress, the panel voted overwhelmingly in favour of continuing the research.

The panel's vote of confidence was based on two technological breakthroughs whose timing seemed almost providential. The first was the development of the shotgun approach to genome sequencing, the second the discovery of a new and more effective way of delivering subunit vaccines into animals.

The reason for the slow progress noted by the EPMR was, as mentioned above, the difficulty of identifying a schizont antigen. The *T. parva* parasite has around 6000 genes, the vast majority of which express a protein. In the 15 years to 1999, ILRI had succeeded in identifying less than 1% of them, using PCR markers and conventional gene mapping techniques. 'Completing the job this way would have taken us several more decades,' says Morzaria.

Then, in 1999, came one of those chance meetings between scientists that change the course of research—and its outcome. ILRI molecular biologist Vish Nene attended a conference in the UK on recent developments in malaria research to see if he could learn anything useful for ILRI's work. The four protozoans that cause malaria, which belong to the *Plasmodium* genus, are first cousins to *T. parva*, having similar life cycles in which two types of host cell are successively infected. Also at the conference was Malcolm Gardner, a scientist from TIGR who had been involved in molecular research on *P. falciparum*, the most serious of the four. One evening, after the last conference session of the day had ended, the two met up at the pub across the road. A few beers later, the idea of a partnership between ILRI and TIGR to sequence the *T. parva* genome was born.

'A lot of ideas look good after a few beers,' says Nene. 'But ours still looked good the next morning, in the cold light of day.' What attracted Nene to TIGR as a partner was that the shotgun approach developed by its founder, Craig Venter, had the potential to slash the time needed to sequence the *T. parva* genome from decades to a few months.

Back at ILRI, Nene and his colleagues tried to raise funds to turn the idea into a reality, but were initially unsuccessful. Recognising the strategic importance of the work, ILRI awarded a

small research contract to TIGR to get the ball rolling. By mid-2000, Claire Fraser, TIGR's Director, had become so enthusiastic about the project that she convinced TIGR's Board of Trustees to fund the work to completion. Craig Venter, by now CEO of Celera Genomics, lent his support to the venture by donating the proceeds of the King Faisal Award for Science, which he won in 2000 for his contributions to biology. The vision and commitment of these two leaders of genomics research have brought ILRI within reach of one of its most cherished research goals—a product vital to the future of the smallholder dairying sector in Africa.

But there is still some way to go and success isn't yet guaranteed. The immediate challenge is to close the gaps in the sequence that remain after the automated shotgun sequencing operation. This part of the process is highly demanding in human time and brainpower. The gaps are filled using PCR, which requires painstaking experimentation to find the right choice of primers.

Then comes the most difficult task—closing in on the few genes of interest for creating a schizont vaccine. 'Despite recent progress, our ability to predict protein functions from DNA sequences is still limited,' says Nene. The sequenced genome will have around 6000 genes, the functions of well over half of which will remain unknown. The scientists will use a two-stage process to narrow the field.

The first stage is to find out which genes are actually expressed at the schizont stage of the parasite's development. 'The protein fragments escaping from the schizont are likely to be secreted,' explains Nene. 'Secreted proteins have a distinct signature that can be detected by scanning gene sequences.' Through rapid scanning, using a combination of micro-arrays and the bioinformatics capacity at TIGR, it should be possible to reduce the number of genes of interest to a few hundred. In the second stage, ILRI scientists will use three different approaches to determine which among these genes are actually antigens (Box 8).

If all goes well, the outcome will be a short-list of four or five candidate genes, ready for combining with the p67 gene in vaccine trials on cattle.

The second major breakthrough that convinced the review panel concerned the delivery of the new subunit vaccine into the animal. The vaccine cannot simply be injected but will have to be delivered intracellularly, because the critical gene(s) will only be able to express the schizont antigen from within the animal's white blood cells.

Box 8: Towards a short-list

Three approaches to the creation of a final short-list of candidate genes are needed because no single approach on its own can be trusted to yield completely reliable results.

The first is a direct or *in vitro* immunological assay. Potential candidate genes are transferred first into a plasmid, then into animal cells taken from bovine, monkey or mouse tissue. These cells are then pitted against characteristic CTLs taken from an immune cow, to find out whether they are targeted and killed. However, if the tissue cells are not killed, this does not mean that the gene being screened is irrelevant for vaccine development. The variability of CTLs, different types of which have evolved to deal with different forms of antigen, means that the antigen might be recognised if the CTLs were taken from a different animal.

The second method, also conducted *in vitro*, again uses tissue cells containing parasite genes. This time the cells are used to determine whether blood from an immune animal contains CTLs that can recognise them. This method, sometimes called a 'recall assay', complements the first method and also attempts to eliminate the biases caused by the variability of CTLs.

ILRI's third method, which remains to be tested, will use transgenic mice. Candidate genes will be isolated, placed in plasmids, then inoculated into laboratory mice. Cells from the mice will be tested *in vitro* to determine whether they can kill infected bovine cells.

A research group at the University of Oxford, headed by immunologist Professor Adrian Hill, has developed a new and apparently highly effective way of delivering antigens. Hill and his colleagues have successfully demonstrated their method, known as 'prime–boost', in rabbits and even in human beings, on whom they have used it to test a malaria vaccine. Routine delivery of a vaccine uses a first injection to prime the body's immune responses and a second booster injection, typically a few weeks or months later. In these delivery systems, the same method is used for both injections. The Oxford team, in contrast, administers the primer as 'naked DNA'—inserting the whole gene directly into the cell. The booster is administered by a different method, involving the use of a 'disabled' *Vaccinia* virus as a vector to penetrate the host's cells. (*Vaccinia* is the causative agent of smallpox, but the gene causing the disease is removed.)

'No one yet knows exactly why this approach works,' comments Morzaria. 'If you reverse the two methods, using the virus vector first followed by the naked DNA, the vaccine is not as effective.'

ILRI has now entered a partnership with the University of Oxford to test the prime-boost method in cattle. Trials will go ahead as soon as candidate genes become available.

The major contributions made by its partners have boosted the confidence of the ILRI team. 'We now have a reasonable certainty of obtaining both a candidate vaccine and an effective

means of delivering it,' says Morzaria. The outcome of the review process was unanimous agreement that ILRI should now go all out for a vaccine. The ILRI team is cautiously optimistic that it will soon be celebrating V-day.

Gut reactions

As dusk falls at Dukam, in the central Ethiopian highlands, Negussie Driba and his wife bring in a donkey-cart laden with teff straw, needed to feed their 20-strong herd of local zebu bullocks. The couple do a lively trade as specialised livestock producers, selling their animals either to other farmers, for fattening or ploughing, or to traders, who trek them up to the nation's capital, Addis Ababa, for slaughter. But teff straw isn't enough to meet their animals' needs and must be supplemented by other feeds that are richer in protein. Leguminous trees could fulfil this requirement, but few species are adapted to the difficult conditions of the highlands. At present, Negussie has to buy in high-protein feed, getting through expensive concentrates by the truckload. 'I wish we could produce more on our farm,' he says. 'It would reduce our costs greatly.'

Not far away, at ILRI's Debre Zeit research station, a possible answer to Negussie's needs is under research. It's *Acacia angustissima*, a highly nutritious and rapidly growing tree legume from Central America. Some 20 accessions from ILRI's germplasm collection are being grown on the station to assess their adaptability to African highland environments.

The trees are flourishing—but there's a snag: *A. angustissima* contains a toxic compound that can kill animals if they eat too much of it. The precise identity of the compound isn't yet known, but there are two possible culprits, one a tannin and the other a non-protein amino acid. The amino acid resembles that found in *Lathyrus sativa*, a grain legume widely grown and eaten by people in Ethiopia and a few other countries, where it can cause paralysis or death if overeaten or insufficiently soaked before cooking. However, previous research at ILRI has shown that animals can adapt to a diet containing quite high levels of *A. angustissima*. In an experiment at Debre Zeit, sheep introduced suddenly to a diet with a high proportion of the legume fell ill within days, whereas

those in which the amount was increased gradually remained well and productive. When rumen fluids were removed from these animals and transferred to other animals who were then introduced suddenly to a high-*angustissima* diet, these animals too showed no symptoms. This finding strongly suggested the presence of a rumen microbe which was able to break down the toxic compound and render it harmless.

Finding such microbes is the task of Agnes Odenyo, a rumen microbiologist based at Debre Zeit. It's not an easy task, since the rumens of domestic herbivores contain millions of these organisms, all engaged in a ceaseless assault on the raw feed particles consumed by their hosts. Odenyo's approach has been to cast the net widely, covering a range of wild animal species in addition to domestic sheep adapted to a diet containing A. *angustissima*. The rationale for this approach is that wild species, surviving in harsh environments, can be expected to have developed the ability to digest plants with antinutritional qualities.

'We are sampling the rumen fluids of three groups of wild herbivores,' Odenyo explains. 'The first is a group we call concentrate selectors, which eat only browse. This consists of giraffe, bush duiker and dik-dik. Second is an intermediate group, consisting of impala, eland and gazelle, which prefer browse but also graze pastures. And third is a large group of grazers, including buffalo, zebra, hartebeest and wildebeest.'

It is in the first group, the concentrate selectors, that Odenyo and her colleagues expected to find relevant microbes. And they have not been disappointed. In the gut of an Ethiopian bush duiker they have identified a strain of bacterium called EAT2 which, when tested *in vitro*, grows well in the presence of tannins. Six other candidate bacteria have also been found, some of them in the gut of free-ranging goats. The next steps will be to transfer these bacteria to sheep and to test the sheep on a high-A. *angustissima* diet.

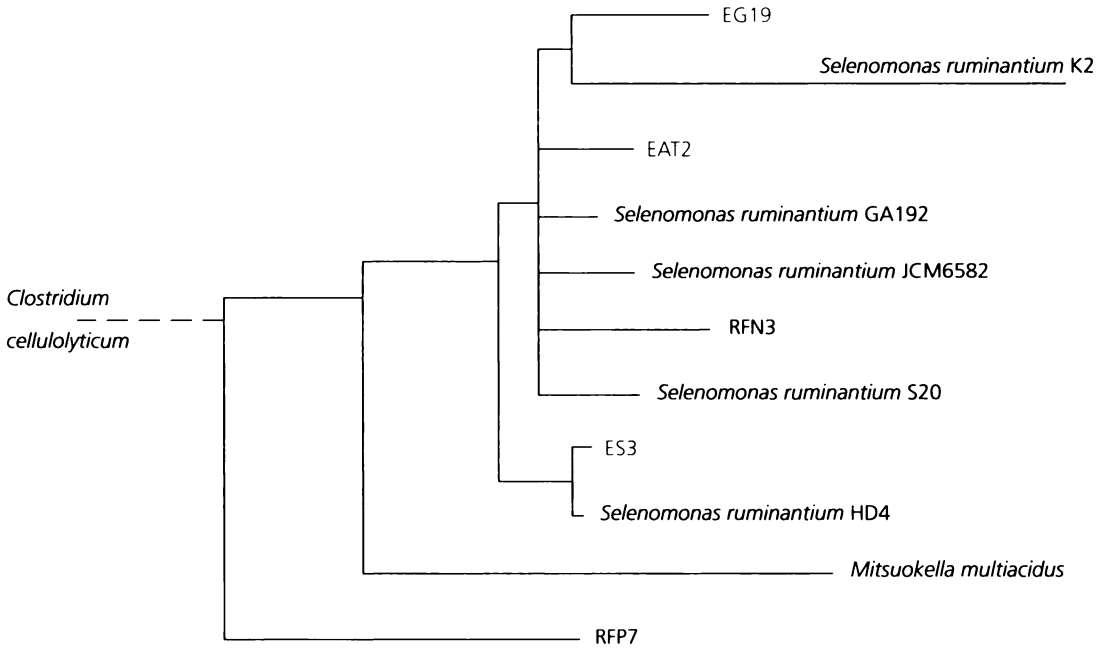
A critical issue associated with this research is whether bacteria transferred from animals on a diet with a high content of antinutritional elements will persist in their new hosts. The continuity with which plants such as A. *angustissima* are fed could

prove crucial in maintaining bacterial populations at high enough levels to avoid toxicity problems.

Working with ILRI's Nairobi-based microbiologist Richard Bishop, Odenyo is addressing this issue by developing a molecular probe to test for the continuing presence of bacteria. The probe is targeted to a molecule found in all bacteria known as 16S rRNA, for which mapped sequences have been published on the Internet. The scientists are using a range of markers to sequence the molecule in bacteria from a range of wild species, from sheep fed on *A. angustissima* and from sheep fed a normal diet. Experiences so far suggest that minute differences in the sequences—changes of just a few base pairs—can be used to identify different isolates and species of bacteria, which can then be compared for their genetic relationships using a dendrogram (Figure 3). The ultimate aim is to identify the genes that make certain bacteria tolerant.

At the same time, the plant itself is also being analysed using molecular markers. 'We have found a lot of variation in our genebank accessions,' says ILRI molecular biologist Ramni Jamnadass, responsible for this part of the work. 'Now we plan to see if any of these variations are correlated with toxicity. If they

Figure 3. Genetic relationships between gut bacterial isolates found by ILRI and those already published



Found by ILRI:
EG19 : Tannin-tolerant bacterial isolate from the rumen of a free-ranging domestic goat
EAT2 : Tannin-tolerant bacterial isolate from the rumen of a bush duiker
ES3 : Tannin-tolerant bacterial isolate from the rumen of a sheep fed on *A. angustissima*

are, then a marker should become possible.' A third line of attack is pursued in partnership with plant chemists and nutritionists in the USA, who have joined ILRI in research to identify the precise nature of the compound that causes toxicity.

If research to detoxify A. *angustissima* is successful, it will add a valuable new high-protein feed to the repertoire available to small-scale livestock producers. A. *angustissima* could be in especially hot demand as a replacement for *Leucaena leucocephala*, a popular leguminous species that has fallen prey to insect attack. Indeed, A. *angustissima* could prove more widely adaptable than leucaena since it has the added advantages of tolerating acid soils, drought and waterlogging—stresses to which leucaena often succumbs. And, by virtue of its antinutritional characteristics, it may also prove better at tolerating insect attack.

Striking back at smut

It was the visit of Peter Ndung'u that brought home the seriousness of smut disease to David Miano Mwangi. KARI's forage agronomist was sitting in his office at the Muguga research station when the farmer knocked on his door, unannounced. 'I've come with a truck,' said Ndung'u, 'to collect the Napier.'

Ndung'u and his fellow farmers had clubbed together to hire the truck and drive over to the research station from their home 100 kilometres away, near Gatundu in Kenya's high-potential highlands. They knew that Mwangi had been conducting trials on something they wanted badly—a cultivar of Napier grass called Kakamega-1. The cultivar is resistant to smut, a devastating disease of Napier grass.

Forming the staple diet of crossbred dairy cows, clumps of tall-growing broad-leaved Napier grass are a familiar sight in farmers' fields around Gatundu, which lies at 1800 metres in prime dairy farming country. Easy to establish and a prolific provider of nutritious biomass, the grass forms a dense green stand about 3 metres high at the height of the rainy season.

But when smut disease strikes, the plant becomes almost unrecognisable. Infected stems harden and shoot to a premature flowering, turning thin and fibrous instead of thick and juicy. The plant produces almost no leaves and the flower head

is filled with black spores. The result is a catastrophic decline in biomass that strikes at the heart of the smallholder dairying sector.

Combined with the recent severe drought, the disease has already led to falling milk production. Some farmers have had to sell their crossbred cows—an act of desperation that plunges them back into poverty. Others have taken to grazing their cattle on sparse communal pastures and along roadsides, a practice that exposes them to increased risk of ECF (see p. 3). And the problem looks set to get worse: smut disease is gradually spreading, reaching down from its epicentre around Gatundu to lower lying areas.

'Smut is extremely serious,' says Naomi Njeri Kibunja, a farmer in the area. 'If we don't get a cure soon the dairy industry will collapse. We have no alternative feed.'

Caused by the fungus *Ustilago kamerunensis*, smut disease was first detected in Napier grass in Kenya in about 1996, during on-farm surveys conducted by Mike Scarr and Graham Farrell, two scientists seconded to KARI under a project funded by the UK's Department for International Development (DfID). The two sent the fungus to a laboratory in the UK for identification and turned to ILRI and KARI colleagues for assistance in tracking down resistant strains of the grass.

ILRI's germplasm collection of Napier was being screened at Kakamega, in Kenya's western highlands, while KARI's was held at Muguga. Farrell selected five high-yielding cultivars from the two sites and tried to infect them with fungal inoculum in the laboratory. When two cultivars, including Kakamega-1, appeared resistant, Scarr decided to give a few cuttings to farmers in Gatundu. The favourable results obtained in the laboratory were confirmed in farmers' fields, prompting Ndung'u and his neighbours to try to augment the supply of cuttings by the truckload.

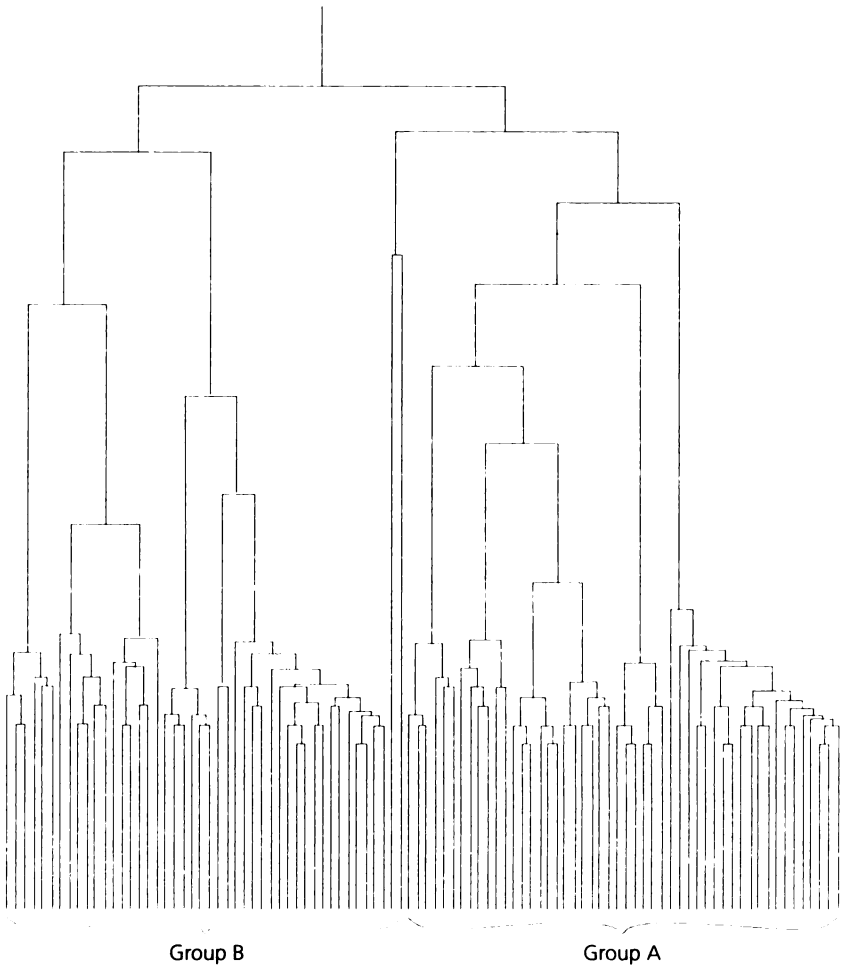
Mwangi is now testing these and other cultivars with two groups of farmers in neighbouring villages. 'We can already see dramatic differences between the performance of resistant and susceptible varieties,' he says. 'Kakamega-1 continues to show good resistance, while another accession, Clone 13, has been confirmed as susceptible.'

Meanwhile, Scarr and Farrell had also approached ILRI's Ramni Jamnadass and Jean Hanson, who leads the Institute's work on

forage genetic resources, for assistance in analysing the accessions at the molecular level. The aim was to detect any genetic differences between resistant and susceptible accessions, in the hope of finding a molecular marker for resistance. Napier grasses are often difficult to distinguish in the field, so a genetic probe that could do the job instead would be extremely useful.

Through an initial analysis conducted using RAPDs, Jamnadass and her colleagues identified two genetically distinct clusters of accessions (Figure 4). Resistant and susceptible accessions fell into different clusters, indicating a genetic difference between them. 'We can't yet be sure whether this difference is due to smut resistance and susceptibility or to some other trait, but it does at least seem possible that we will be able to

Figure 4. Genetic relationships between different accessions of Napier grass



Source: Jamnadass (1999)

identify a marker,' says Jamnadass, who has short-listed candidate primers for further testing.

Both KARI and ILRI are keen to continue the research, if funding for it can be found. Jamnadass has outlined the next steps to be taken, which include field testing the other accessions in each cluster to check whether they are resistant or tolerant. 'This will help establish whether the clustering is due to resistance or not,' she explains. Further progress in closing in on a marker can be made by marker analysis of two closely related clones, one of which has resistance while the other does not. 'Any differences between them are likely to be markers,' she says. Jamnadass also recommends the creation of a core Napier germplasm collection to serve as a basis for further work on the development of accession-specific markers. This will make it easier to apply the probe for smut resistance, enabling scientists to provide better advice to farmers on what accessions to grow.

Critics sometimes say that genomics research is supply driven and takes too long to deliver usable results. The experience with smut in Napier grass shows how strong farmer demand, coupled with responsiveness on the part of a national research group, can ensure that laboratory research at the international level responds rapidly to changing needs.

Exploring livestock diversity

Asia and Africa are home to hundreds of domestic livestock breeds and wild relatives, each harbouring potentially valuable genetic diversity. ILRI and its partners are using molecular markers to explore this diversity.

'The new technologies will enable greatly increased efficiency of selection for valuable genes.'—Serageldin and Persley (2000).

'There are two main reasons for conducting this research,' says Olivier Hanotte, a molecular geneticist at ILRI. 'The first is to identify the genes for useful traits such as disease resistance or heat tolerance. The second is to help governments make difficult conservation decisions.'

Conservation is urgently needed: studies on indigenous African cattle by ILRI animal geneticist Ed Rege show that a third of all breeds are threatened with extinction. But conserving livestock is more expensive and more difficult than conserving plants. Most efforts must take place *in situ*—with owners or herders acting in a dual role as both producers and conservationists. The big problem with this approach is that the drive to increase productivity tends

to take precedence, leading producers to discard animals they see as 'useless'. Yet it is precisely these 'useless' animals that are likely to have valuable genes for stress resistance. Appearances can be deceptive in other ways too: it's often impossible to tell from the look of an animal whether it truly represents a given genotype or not. Nor can individual producers know whether other producers beside themselves are maintaining the type.

All this means that governments need to step in to support the conservation of indigenous livestock breeds. But when and where to intervene? ILRI's molecular research is intended to help them identify how to deploy their scarce resources to maximum effect.

The research focuses mainly on pastoralists' and smallholder herds kept under low-input production systems, predominantly in the dry areas. 'These animals tend to be a better reservoir of survival traits than those raised in wetter areas or on large farms and research stations,' says Rege, who works closely with Hanotte on the project. 'Pastoralists' animals, in particular, are subject to intense selection pressure whenever drought or epidemic diseases strike, whereas producers in more favoured environments or in larger-scale enterprises tend to prevent selection by using inputs to overcome stresses.' So far, research has been restricted mainly

to ruminant species in Africa, but a study launched recently covers additional species and extends activities to Asia (Box 9).

Another study by Hanotte and his colleagues has thrown new light on the history of cattle domestication in Africa. It now seems likely that what is today the Sahara was once the centre of domestication of a distinctively African population of *Bos taurus*.

The classical map of cattle domestication in Asia and Africa shows two centres of domestication in Asia—one in the Indus

Box 9: Wild about those Asian genes

Just as they did in crops, when people first domesticated livestock they captured only a fraction of the diversity that was 'out there' in nature. Much of that diversity has since disappeared. But the surviving wild relatives of today's domestic livestock may contain useful genes for introduction into a higher-yielding genetic background.

The wild ancestor of cattle, the auroch, has long been extinct. But there are other species, including the yak and the two-humped or Bactrian camel, for which wild gene pools still exist, living alongside the modern domestic population. This is the case in north-west China and Tibet, where ILRI and national partners have launched a case study that scientists believe will reveal much about the reduction in biodiversity associated with domestication, the importance of keeping wild livestock as a gene reservoir, and the need to make more funds available for conservation.

The wild relatives of the yak and the Bactrian camel are under severe threat. In the case of the Bactrian camel, only 1000 or so animals are left. Both species are fully protected under the Convention on International Trade in Endangered Species (CITES), but in this vast and barren region, where fresh food is scarce and policing next to impossible, they are in danger of being hunted to extinction. Conserving the wild yak is especially important, since it may soon be needed to replenish the genetic stock of the domestic yak, which is also in decline. There are two reasons for this decline: the nomads who herd yak often crossbreed their animals with cattle to improve the quality of milk; and inbreeding in the remote valleys of this mountainous region is leading to dwarfing and infertility.

ILRI has launched preliminary studies on yak in collaboration with Gansu Agricultural University, in north-west China. Studies on the Bactrian camel have yet to begin, but will be closely linked to existing work on the one-humped camel, being conducted in northern Kenya at the request of KARI.

Valley for *Bos indicus* and the other in the Fertile Crescent for *Bos taurus*—but none in Africa. According to the classical scenario, zebu animals came to Africa by a variety of routes over land and sea, reaching the Horn of Africa and other east coast destinations between around BC 2000 and AD 1000, while longhorned and shorthorned taurine animals migrated in an arc round the north and west African coasts in two successive waves, around BC 6000–5000 and BC 3000–2500. The Sanga breed, found today in southern Africa, was considered to be a hybrid between the taurine and zebu types that had originated in the Horn of Africa and migrated southwards, possibly with the Bantu-speaking peoples.

'Because they were thought to have arrived relatively recently in the region, African cattle as a whole were considered to be no more than a subset of cattle from Asia and so, despite a few useful local adaptations, little worth conserving in their own right,' says Hanotte.

That picture began to change in the early to mid-1990s, when a research team at Ireland's Trinity College, Dublin conducted a study that suggested the existence of a uniquely African genetic component in African cattle. This study was based on a small number of breeds and focused on mitochondrial DNA, which can only be inherited from the female side. In ancient times as today, most of the animals imported and transported for mating purposes were males. So by analysing mitochondrial DNA, scientists are able to distinguish the genes that have long been present in a population from those introduced more recently.

Although this Dublin study was intriguing, it was not conclusive. In particular, it did not rule out a major influence of cattle from the Fertile Crescent on today's African genepool through the male lineage. As part of its strategic research to aid government decision making, ILRI therefore decided to collaborate with the Dublin group and with national programmes in Africa to conduct a broader study, covering 22 countries and focusing on two additional types of DNA: the Y-chromosome, which would reveal patterns of male inheritance, and autosomal microsatellites, a form of DNA marker inherited from both the paternal and the maternal sides.

To analyse the microsatellite marker data, the team used a statistical method called Principal Component Analysis to derive a more subtle picture of the complexity of cattle evolution than can be portrayed using a conventional dendrogram. This analysis revealed that the first and most significant genetic component in African cattle is, to use Hanotte's words, 'something typically Asian zebu in origin'. The second component, however, is 'something typically African'—confirming the tentative conclusions reached by the earlier mitochondrial DNA study.

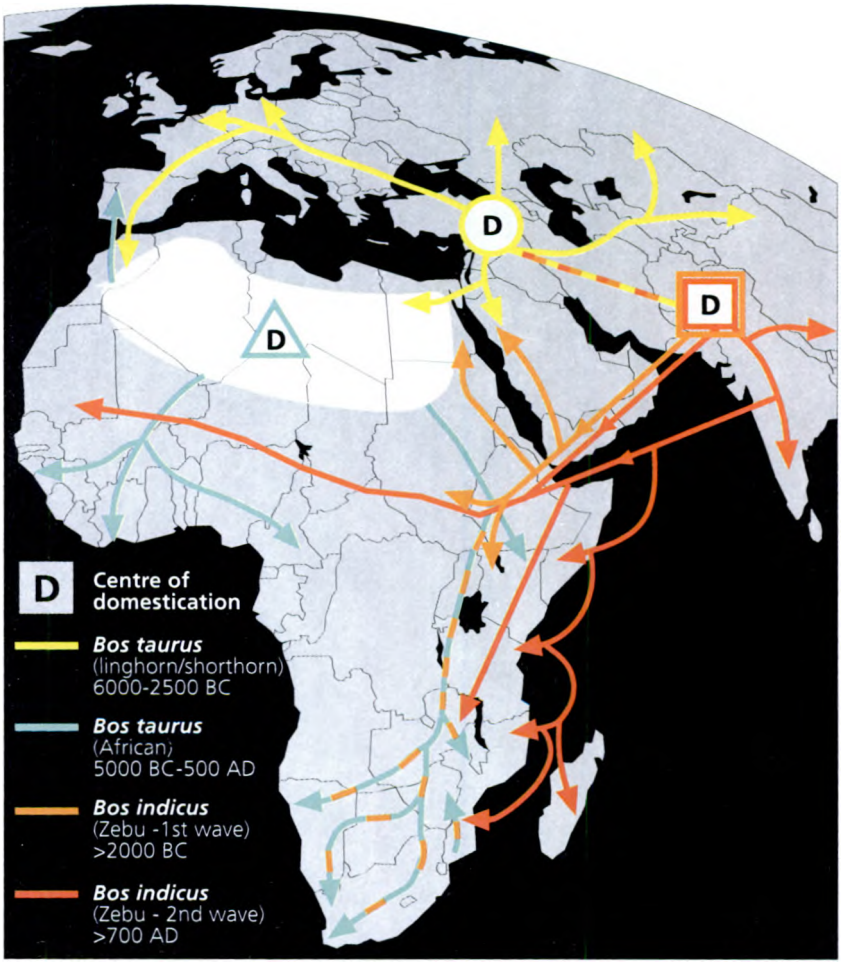
Several findings showed how misleading appearances can be as a basis for deciding on conservation priorities. The last remaining taurine breed in East Africa, the Sheko, in fact turned out to have a strong zebu background. 'If a taurine "version" of this breed is to be conserved, it will be

necessary to act fast and to choose the right animal,' says Hanotte. The taurine animals that live near the northern edge of the tsetse-infested zone of West Africa also showed a surprisingly high degree of zebu introgression, suggesting a strong influence from the zebu populations of the Sahelian belt. Most striking of all was the finding that the supposedly hybrid Sanga animals of southern Africa tend to have a taurine Y-chromosome, suggesting they arrived here before the major incursion of zebu animals through the Arabian Peninsula. These animals are thus far less 'zebu' than they look.

'The genomics revolution has unprecedented potential for allowing African countries to both conserve and exploit their gene-rich continent.'— Onesmo ole-MoiYoi, Director, Institute of Molecular and Cell Biology–Africa.

What are the overall implications? The study has helped to redraw the classical map of cattle domestication to show a third area of domestication in North Africa (Figure 5). The molecular evidence for this area is supported by recent archaeological findings

Figure 5. A new map of cattle domestication and migration in Africa



in southern Egypt, where cattle remains of supposedly domestic origin have been found dating back to BC 6000–9000—at least contemporary with, and possibly before, the earliest West Asian records of domestication. Probably descended in part directly from the native auroch, the cattle of Africa are thus a unique, genetically distinct group, well worth further exploration. Despite intermixing, three major subgroups are still discernible—the West African taurine, the 'taurine' Sanga and the East African zebu—each containing significant genetic diversity. Conservation efforts are needed to capture this diversity, which could prove immensely valuable in future selection and breeding programmes but is currently threatened with extinction. The research also casts Africa's marginalised pastoral peoples in a new light, as the custodians of a genetic heritage whose value to human-kind is only just beginning to be appreciated.

More for your money

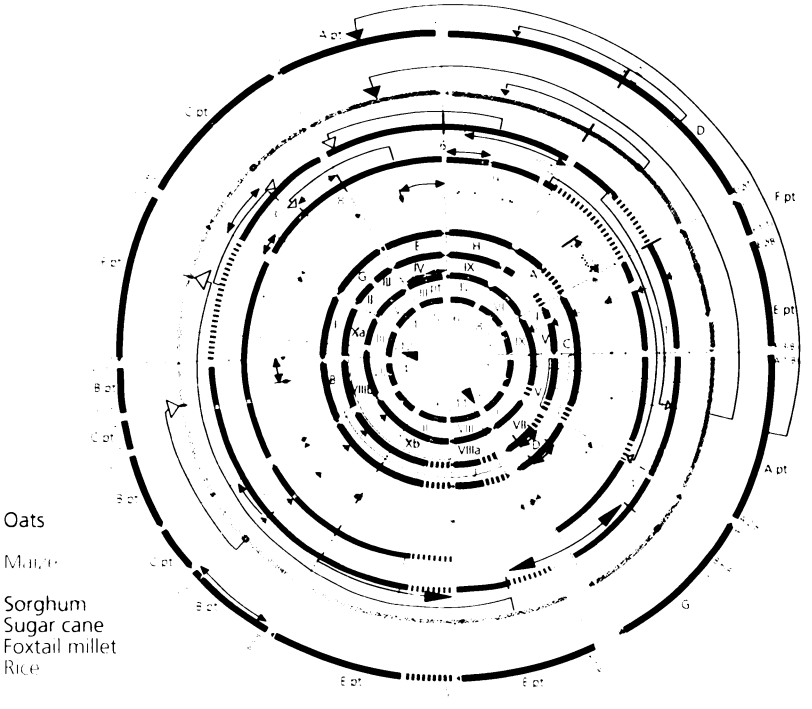
Genomics has greatly accelerated the rate at which we can gain and apply new knowledge. This in itself has substantially increased the potential returns to investments in research. But the genomics revolution is associated with several other factors that promise to increase research impact and efficiency still further.

As genome sequencing progresses, scientists are uncovering remarkable similarities between the genomes of different life forms. These similarities take two forms, known as synteny and homology. Synteny is the tendency for genes in related organisms to occupy similar locations of the genome, while homology refers to the observation that the more closely related are two organisms, the

more similar in form are their genes. These two phenomena provide scientists with short cuts in their search for the genes that code for key traits. For example, research by ICRISAT and ILRI to locate the genes for drought tolerance in the genome of pearl millet will help scientists searching for the same genes in other cereal species, such as sorghum, rice and maize. This is why Jean Hanson sees the plant collection in her care as having immense value for improving world food production, not just livestock feed resources (Figure 6). 'Many grasses are similar to cereal crops; many forage legumes are similar to food legumes,' she says. And these similarities are not limited to plants but extend throughout the plant and animal kingdoms, even to microbial organisms.

Synteny and homology are leading to an exciting period of cross-fertilisation between human and animal disease research. For example, TIGR's interest in sequencing the *T. parva* genome lay partly in its probable resemblance to *P. falciparum*, the principal causative agent of malaria and the subject of much of TIGR's own research. Both partners therefore stand to benefit by the research.

Figure 6. Synteny of globally important grasses and cereals



Source: Gale and Devos (1998). Excerpted and adapted with permission from *Science* 282 (5389), p.657, © 1998, American Association for the Advancement of Science.

One person who appreciates these mutual benefits is Onesmo ole-MoiYoi. Formerly a scientist with ILRI's predecessor, the International Laboratory for Research on Animal Diseases (ILRAD), ole-MoiYoi now heads a new institute that is becoming a leader of advanced biomedical research in Africa. The Institute of Molecular and Cell Biology–Africa (IMCB–A), founded in 1999 with sponsorship from the United Nations Scientific and Cultural Organization (UNESCO), makes use of ILRI's Nairobi laboratories to conduct research on leukaemia and malaria. 'The study of *T. parva* is leading us to the discovery of new pathways for the evolution of leukaemia and could shed light on the mechanisms of cell-mediated immunity,' says ole-MoiYoi (Box 10).

No one knows the value of modern genomics research better than ole-MoiYoi, who began life as the son of a settled Maasai farmer in northern Tanzania. He traces his interest in modern medicine to his paternal grandmother, who was a traditional healer. 'There is no real difference between what she was attempting to

'38% of yeast proteins...are similar to mammalian proteins; 60% of human disease genes have equivalents in flies and plants. We are finding that nature conserves: what's good enough for the humble fruit fly works just as well for us.'—
Claire Fraser, President, TIGR.

Box 10: ECF research throws light on leukaemia

In 1983, Philip Leder, a professor of genetics working at the Howard Hughes Medical School in Boston, USA, discovered the high prevalence of a gene known as *myc* in leukaemic blood cells. However, Leder was unable to use this gene to trigger leukaemia. The search began for another gene that might conspire with *myc* to cause the disease.

During the 1990s, research by ole-MoiYoi and his colleagues at ILRI established that casein kinase II (CK II), a common multifunctional protein whose levels are strictly controlled in normal cells, is markedly increased in the white blood cells of cattle infected with *T. parva*. Their findings suggested that CK II could be contributing to the cancerous proliferation of cells that characterises this stage of ECF.

Following a seminar at Harvard University at which these results where presented, Leder and his colleague, David Seldin, decided to introduce the CK II gene into mice, which were then mated with mice carrying the *myc* gene. The combination of genes proved deadly, with offspring carrying both genes dying rapidly of a leukaemia-like condition in which CK II protein was produced uncontrollably.

A valuable by-product of ILRI's research on *T. parva*, this discovery could prove a breakthrough in the search for a cure to a disease that kills thousands of people every year.

'I believe genomics will make astonishing progress possible in our lifetime, in both medicine and agriculture.'— Onesmo ole-MoiYoi, Director, Institute of Molecular and Cell Biology-Africa.

'A new strategy of technology promotion must be based on an interplay of academia, government and industry, with participation from rich and poor alike.' — Jeffrey Sachs, The Economist, *22/7/00.*

do and what we are doing now,' he says. 'The difference lies in *how* we are doing it: we have the more accurate tools for the job.'

Together, synteny and homology are one of the major factors prompting advanced institutions in the developed world to form partnerships with ILRI. Generally, the public and private institutions responsible for human medical research command resources far greater than those available to livestock research. But the mutual interests to which synteny and homology give rise enable ILRI to harness a share of those resources to the cause of increasing livestock productivity in the developing world. Through its partnerships with these institutions, ILRI is able to access powerful technology without having to invest the money needed to develop the technology.

To deliver the products of its genomics research, ILRI will need partnerships with the private sector. For example, if it is to reach poor producers, a new ECF vaccine must be mass-produced and made locally available at low cost in rural areas—a job best done by commercial companies. Of necessity, the main motive driving private-sector partners to collaborate with ILRI will be the potential for profit. But there are now other predisposing factors too, including the companies' desire to contribute to poverty eradication as a means of building future markets and influencing public opinion in their favour. This trend towards a more compassionate private sector increases ILRI's opportunities to forge private–public partnerships that will genuinely benefit the poor and hungry in developing countries.

A further source of the efficiency gains associated with genomics research is the humble domestic mouse, which serves as a model

for other mammals in research to identify genes and develop vaccines and drugs. ILRI is one of many laboratories around the world taking part in a rapid increase in the use of these animals for research purposes. 'The advantage of mice is that they are small and hence cheaper to house and feed than are cattle,' says Fuad Iraqi, the ILRI scientist responsible for this work. 'They also breed rapidly, creating very considerable time savings.' Mice are thought to share around 80% of their genes with human beings and most domestic livestock species. The efficiency of research on mice will be given a further boost in 2001, when an international consortium is due to publish the complete sequence of the mouse genome.

Using mice, Iraqi and his colleagues are close to a breakthrough in the search for the genes that code for tolerance of trypanosomosis—the other major parasitic disease on which ILRI conducts research (Box 11).

Box 11: Closing in on trypanotolerance

ILRI's search for the genes that confer trypanotolerance began in 1988, when scientists working for its predecessor, the International Laboratory for Research on Animal Diseases (ILRAD), crossed a resistant cattle breed, the West African N'Dama, with another African breed, the East African Boran, that is susceptible to the disease.

The cattle genome was at that time thought to contain around 60,000 genes on 30 chromosome pairs. In 12 years of work with the progeny of the cross it proved possible to narrow the search down to around six chromosomal regions with an estimated total of between 6000 and 12,000 genes.

In 1994, ILRI's scientists turned to the mouse model in the hope of achieving faster progress. That hope has been more than realised, with the work on mice overtaking that on cattle in only 6 years. The first stage, completed in 1.5 years, was to develop a second-generation (F2) population of mice in which the trait could be roughly mapped. This exercise narrowed the search to three QTLs probably containing 3000–6000 genes. The scientists then bred the mice still further to develop advanced intercross lines (AILs). Inter-crossing has the effect of recombining the QTLs so that each region of interest occupies a still smaller segment of the chromosome. The F6 generation allowed a more accurate map to be made, reducing the candidate genes to around 400. Since then the number has been reduced still further, to some 20 genes in the case of one chromosome region. Once the mice genes have been identified, it should be relatively easy to identify the equivalent genes in cattle, using the recently developed techniques of comparative genomics.

Understanding the genetic basis of trypanotolerance should bring major benefits. It should prove possible to combine molecular and conventional breeding techniques to develop cattle breeds with improved productivity as well as disease tolerance, which can be used to improve the livelihoods of poor farmers in tsetse-infected areas. The benefits may extend to Asia and to Latin America, which suffer from related forms of the disease. And they could also spill over to human medical science: trypanosomosis in cattle is the same disease as sleeping sickness in humans, so the same genes for resistance are likely to be at work in both.

The results of basic genomics research are applicable on a global as well as a regional or local scale. This allows huge gains from the transfer of knowledge from one region to another. Perhaps the most striking example of this potential in the ILRI research portfolio is that research on a vaccine against *T. parva* greatly increases the chances of controlling its close relative, *T. annulata*. Over 200 million cattle are thought to be at risk of infection from this organism, which is found across a swathe of land from the Mediterranean basin through West Asia to the Indian subcontinent and large parts of China and Central Asia. 'Of the two organisms, *T. annulata* is actually the more significant economically,' says Morzaria. Research at the UK's Sanger Institute and the University of Glasgow, where *T. annulata* is being sequenced, suggests that their genomes are highly similar. 'The information we have will be extremely useful for their work,' notes Morzaria. 'A homologue of the p67 gene in *T. parva* has already been found and shown to give protection to cattle.'

Transregional benefits should also emerge from ILRI's research on worm resistance in the Red Maasai sheep of eastern Africa. This breed is renowned for its ability to flourish on infested pastures that cause other animals to weaken and die. Over the past decade, researchers have confirmed the breed's resistance and begun the search for genetic markers to assist in selection and breeding. A mouse model is being used alongside the experimental population of sheep developed for this purpose—and it looks as if, once again, the work on mice may overtake that on sheep. The researchers expect to identify the genes for resistance in the near future. That will open the way for their use in other breeds—a prospect that should be of interest to sheep breeders and farmers across the world. The results may also prove transferable to goats, which suffer similar losses from worm parasites. Already, 10 countries in Asia are participating through a networking project in a search for similar genes in their own indigenous breeds.

A third example of the global benefits that can be expected from genomics research is provided by work on the feed value of cereal crop residues. This work, conducted with a range of partners including ICRISAT in India, focuses mainly on pearl millet, a dual-purpose cereal grown by millions of resource-poor farmers in the drylands of the Indian subcontinent and the African Sahel. An *ex ante* impact assessment of this research put a figure of up to US$ 208 million on the benefits if the results were widely adopted in both continents. And that is to reckon without the spillover benefits made possible through synteny and homology, which should allow the knowledge gained in pearl millet to be transferred to a host of other crops including maize, sorghum, rice, wheat, barley, sugarcane and various forage grasses. 'It should be particularly easy to transfer useful traits into Napier grass, which is the same genus as pearl millet,' Hanson says. Similar work has already started on maize, in partnership with the International Wheat and Maize Improvement Center (CIMMYT), and on sorghum, with ICRISAT. On the legumes side, research on cowpea is under way in partnership with the International Institute of Tropical Agriculture (IITA).

'We chose pearl millet as our priority species for this research because of its great importance for livestock feed,' says Jimmy Smith, co-ordinator of the CGIAR's System-wide Livestock Programme (SLP), which supports this work. 'Producers in the dry areas where pearl millet is grown have very few other options available to them.' But ILRI and its partners were able to apply the tools of genomics to their task at low cost because ICRISAT had already developed mapping populations of pearl millet for its

research to improve grain yields. Thus livestock research can piggy-back on the investments made in human food crop research, just as it can on those made in human medical research. Moreover, the livestock component of the joint project should greatly increase the payoff to human food research: socio-economists have found that the adoption rates of improved millet varieties are often disappointingly low at present, largely because plant breeders concentrated on increasing grain yield and neglected the importance to producers of the feed value of the residue. This lesson is applicable to several other crops besides millet, including sorghum, barley and maize. 'Integrating crop and livestock research is the key to increasing impact throughout much of the CGIAR system,' notes Smith.

Hope rekindled

By 2005, Julieta Njeri could be among the first of Africa's poor livestock producers to test a new subunit vaccine against ECF on their crossbred cows. In that year too, Negussie Driba and his family could be growing more of their own forage, in the form of a nutritious yet harmless *Acacia angustissima*. And Peter Ndung'u and his friends could once again be enjoying a plentiful supply of disease-free Napier grass to feed their animals.

We say 'could', because the basic and strategic nature of genomics research makes its outcome uncertain. But assuming our research is successful, what will these new technologies mean to our beneficiaries?

For poor livestock producers, better technologies for feeding their animals and protecting them against disease will mean, first of all, reduced risk. The path they must tread out of poverty crosses dangerous passes. They are attracted to livestock production chiefly because of its potential to increase their incomes. But to secure those higher incomes they must first invest in more productive animals. Technology that helps them protect their investment will be highly prized. Indeed, for many it will create the enabling environment that will give them the courage to embark on a livestock enterprise.

Next, the technologies will mean a better standard of living. This works in two principal ways. First, farming families will eat better, enjoying a more diverse diet that gives improved health. Research has shown that the nutrients in milk are vital for the physical and mental development of young children, getting them

off to a better start in life. Working adults too will be able to give more to their daily labours, both on and off the farm. And second, the families will earn more, spending the cash raised through the sale of milk and meat on a whole range of needs. Njeri's purchases will start small and will at first be confined mainly to additional food items, but they will grow in size and scope as her income rises, moving beyond food to other basic household necessities, then to clothing and shoes, then to home improvements. Perhaps one day she will be able to start life afresh in a new house. Above all, she will invest in education for her children, equipping them to get more out of life than she has done.

Lastly, the technologies mean something that isn't tangible and can't be measured but is perhaps the most important benefit of all from ILRI's research: rekindled hope. An improved livestock enterprise can provide poor people, even the desperately poor, with something to live and work for, something that allows them to aspire to better things, something that gives them a taste of what it means to be a success in life.

We at ILRI believe research to improve livestock productivity is one of the best investments that well wishers of the developing world can make. Critics often argue that laboratory-based research does not address the needs of poor farmers. The stories of Julieta Njeri, Negussie Driba and Peter Ndung'u give the lie to that accusation. Those stories are far from over yet; let us do all we can to make sure they end more happily than they began.

'We have a glittering trove of new discoveries that promise to transform our understanding of basic biology, medicine and agriculture. But whether we will use this knowledge to benefit all mankind, ultimately depends on our wisdom and foresight.'— Claire Fraser, President, TIGR.

'The study of genomics is the first line of defence against parochialism.' — Claire Fraser, President, TIGR.

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Livestock Genetics and Genomics
People, Livestock and the Environment
Livestock Policy Analysis
Strengthening Partnerships for Livestock Research
System-wide Livestock Programme

ILRI production-to-consumption projects in 2000

Market-oriented Smallholder Dairy
Market-oriented Livestock Systems in West Africa
Crop–livestock Systems in Mountain Regions
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[14] Seconded and financed by SDC (Swiss Development Corporation), Switzerland
[15] 50% joint appointment with IITA (International Institute of Tropical Agriculture)

Graduate fellows at ILRI in 2000

Name/ Nationality	University/ Institute of Registration	Degree	Project Title	Location	Date of Departure
Guy-Erik Akouégnon, Nigerian	Hohenheim, Germany	PhD	Using feedback to refine innovation and recommendation domains: Assessment of farmers' reactions experimenting with herbaceous legumes as a strategy to promote legume utilisation in West Africa	Nigeria	2002
Washingtone Arodi, Kenyan	Kenyatta, Kenya	MSc	Characterisation of monoclonal antibodies to bovine interleukin 2 (IL-2) and the development of a sensitive ELISA assay	Kenya	2001
Frederick Atieno, Kenyan	Nairobi, Kenya	MSc	Effects of land-use changes on plant species diversity and vegetation structure in Kenyan rangelands: A case study of Kajiado District	Kenya	2000
Isabelle Baltenweck, French	Auvergne, France	PhD	Patterns of intensification in smallholder dairying: Spatial analysis of determinants of change	Kenya	2000
Mody Barry, Ivorian	Oklahoma State, USA	PhD	Urban livestock production systems and food security in the Zone Dense of Khorogo (northern C0ôte d'Ivoire)	Côte d'Ivoire	2000
Bockline Bebe, Kenyan	Wageningen, Netherlands	PhD	Herd dynamics of smallholder dairy cows in the Kenya highlands	Kenya	2001
Belay Duguma, Ethiopian	Alemaya, Ethiopia	MSc	The assessment of water resources quality and management of water for livestock in Ginchi watershed area	Ethiopia	2001
Corrina Botha, German	Hohenheim, Germany	MSc	Evaluation of selected herbaceous legumes for their potential to combat *Striga hermonthica*	Nigeria	2000

Graduate fellows (continued)

Name/ Nationality	University/ Institute of Registration	Degree	Project Title	Location	Date of Departure
Anthea Broadhead, British	Liverpool, UK	PhD	Positional cloning of trypanotolerance quantitative trait loci	Kenya	2000
Shauna Burnsilver, American	Colorado State, USA	PhD	Land use change and wildlife conservation in Kajiado District, Kenya, as part of the integrated modelling and assessment programme in East Africa	Kenya	2002
Sebastian Chenyambuga, Tanzanian	Sokoine, Tanzania	PhD	Genetic characterisation of East African goat populations	Kenya	2000
Boukader Diarra, Malian	Cheikh Anta Diop, Senegal	PhD	Characterisation of drug resistance in trypanosomes in West Africa	Burkina Faso	2001
Eden Ephraim, Ethiopian	Addis Ababa, Ethiopia	MSc	Isolation and characterisation of bacteria that degrade non-protein amino acids and tannin from adapted indigenous African ruminants	Ethiopia	2001
Gebrejohannes Gebreegziabber, Ethiopian	Alemaya, Ethiopia	MSc	Study on components of days open in relation to postpartum body weight dynamics and modeling lactation curves in zebu and crossbred cows	Ethiopia	2001
Getachew Eshete, Ethiopian	Alemaya, Ethiopia	MSc	Feed resources management in Ginchi watershed area	Ethiopia	2001
John Githiori, Kenyan	Swedish Agricultural University, Sweden	PhD	Anthelmintic properties of ethnoveterinary preparations used by smallholder farmers to treat internal parasites of their livestock	Kenya	2002
Bridgette Gnoumou, Burkinabé	Wisconsin, USA	PhD	Cattle and manure management strategies to increase soil fertility in western Niger	Niger	2000
Simon Irvin, British	Wye, UK	MSc	Case study: Assessing demand for forages and constraints to adoption in the Soddo/Areka area of Ethiopia	Ethiopia	2000

Graduate fellows (continued)

Name/ Nationality	University/ Institute of Registration	Degree	Project Title	Location	Date of Departure
Andreas Jenet, Argentinian	Swiss Federal Institute of Technology, Switzerland	PhD	New concepts for sustainable efficient smallholder dairy nutrition	Ethiopia	2003
Stephen Kaba, Ghanaian	Wageningen, Netherlands	PhD	Immunogenicity and vaccine potential of a recombinant *Theileria parva* surface antigen (p67) produced in the baculovirus-insect cell expression system	Kenya	2000
Misrak Kabede, Ethiopian	Addis Ababa, Ethiopia	MSc	Isolation and characterisation of bacteria tolerant to toxic compounds in an extract fraction from *Acacia angustissima* leaves, from free-ranging sheep and goats	Ethiopia	2000
Alex Kahi, Kenyan	Hohenheim, Germany	PhD	Evaluation of alternative dairy cattle	Kenya	2000
Lucy Kamau, Kenyan	Kenyatta, Kenya	PhD	Isolation and characterisation of genes encoding candidate vaccine antigens from *Rhipicephalus appendiculatus*	Kenya	2001
Simon Kang'a, Kenyan	Kenyatta, Kenya	PhD	Development and application of genetic markers linked to bovine trypanotolerance genes	Kenya	2001
Victor Konde, Zambian	Brunel, UK	PhD	Molecular genetic aspects of isometamidium resistance in *Trypanosoma (Nannomonas) congolense*	Kenya	2000
Isaac Koskey, Kenyan	Wageningen, Netherlands	PhD	Breeding objectives and breeding strategies for small ruminants in the tropics	Kenya	2003
Delphin Koundande, Beninese	Wageningen, Netherlands	PhD	Opportunities for marker-assisted introgression of trypanotolerance in mice and cattle	Kenya	2000

Graduate fellows (continued)

Name/ Nationality	University/ Institute of Registration	Degree	Project Title	Location	Date of Departure
Géraud Laval, French	Lyon, France	MSc	Cost analysis of contagious bovine pleuropneumonia (CBPP)	Ethiopia	2001
Ben Lukuyu, Kenyan	Greenwich, UK	MPhil	Evaluation and improvement of feeding strategies for optimising feed intake in crop–livestock systems	Kenya	2000
Noreen Machila-Eisler, Zambian	Edinburgh, UK	PhD	Tools to improve targeting of drugs for African bovine trypanosomiasis	Kenya	2003
Amos Mbugua, Kenyan	Nairobi, Kenya	MSc	Analysis of receptors in the flagellar pocket of *Trypanosoma congolense*	Kenya	2001
Solomon Melaku, Ethiopian	Humboldt, Germany	PhD	Supplementation of selected multipurpose trees to Ethiopian highland sheep maintained on a basal diet of teff straw (*Eragrotis tef*): Effects on rumen fibre degradation, rumen and blood metabolites, live weight gain and reproductive parameters	Ethiopia	2000
David Menge, Kenyan	Kenyatta, Kenya	PhD	Genetic mapping of quantitative trait loci (QTLs) controlling resistance to gastro-intestinal (GI) nematodes in a mouse model	Kenya	2003
Felix M'mboyi, Kenyan	Nairobi, Kenya	MSc	The impact of structure, conduct and performance of the delivery systems for tsetse and trypanosomiasis control inputs and services on livestock production in Kenya	Kenya	2001
Sam Mugasi, Ugandan	Makerere, Uganda	PhD	Community actions in disease control and natural resource management: Economic issues	Uganda	2002
Anne Muigai, Kenyan	Kenyatta, Kenya	PhD	Genetic diversity of sheep populations in sub-Saharan Africa	Kenya	2001

Graduate fellows (continued)

Name/ Nationality	University/ Institute of Registration	Degree	Project Title	Location	Date of Departure
Wellington Mulinge, Kenyan	Nairobi, Kenya	PhD	Identifying the determinants of competitiveness in intensifying dairy production	Kenya	2001
Winnie Musoke, Ugandan	Makerere, Uganda	PhD	Community assessment of sleeping sickness in Uganda	Uganda	2002
William Mwangi, Kenyan	Nairobi, Kenya	MSc	Characterisation of polymorphism in the genes encoding cattle FC gamma receptors (CD16/CD32/CD64): Implications for vaccine development and genetic diversity	Kenya	2000
Leah Ndungu, Kenyan	Pretoria, South Africa	PhD	The socio-economic, infra-structural and policy effects on the demand for, and delivery of, the p67 *T. parva* vaccine in small-scale, large-scale and pastoralist zones of Kenya	Kenya	2001
Joseph Ngang'a, Kenyan	Kenyatta, Kenya	PhD	Positional cloning of trypanosomosis resistance QTLs, Tir1, 2 and 3, in the mouse	Kenya	2003
Margaret Ngigi, Kenyan	Nairobi, Kenya	PhD	The effects of transaction costs on market participation of smallholder Kenyan dairy farmers	Kenya	2001
Olawole Obembe, Nigerian	Wageningen, Netherlands	PhD	Modification of lignin biosynthesis in cowpea	Nigeria	2003
David Odongo, Kenyan	Brunel, UK	PhD	Assessing the impact of ECF immunisation with an improved subunit vaccine on smallholder production in eastern Africa	Kenya	2003
Margaret Okomo, Kenyan	Wageningen, Netherlands	PhD	Mapping quantitative trait loci controlling genetic resistance to helminthiasis in the Red Maasai sheep of Kenya	Kenya	2002
Fredrick Onyango, Kenyan	Nairobi, Kenya	MSc	T-cell responses in cattle immunised with recombinant p67	Kenya	2001

Graduate fellows (continued)

Name/ Nationality	University/ Institute of Registration	Degree	Project Title	Location	Date of Departure
Denis Ouedraogo, Burkinabé	Ouagadougou, Burkina Faso	PhD	Socio-economic analysis of animal health management practices and factors affecting the development of drug resistance in cattle: The case of Kenedougou Province, Burkina Faso	Burkina Faso	2001
Lawrence Owowye, Nigerian	Ahmadu Bello, Nigeria	PhD	Evaluation of selected legumes for sustainable weed ecology/soil fertility/livestock management interactions in crop–livestock systems of the northern Guinea savannah	Nigeria	2002
Stephen Park, British	Trinity, Dublin, Ireland	PhD	Fine mapping of a cattle trypanotolerance QTL on *Bta*07	Kenya	2001
Sefan Ramme, German	Georg August, Germany	MSc	An ecogeographical survey of the legume *Lablab purpureus* (L.) Sweet (1827) in East Africa: Geographical distribution, actual and potential use	Ethiopia	2001
Berhan Retta, Ethiopian	Wageningen, Netherlands	MSc	Genetic resistance to endoparasites	Ethiopia	2001
Karin Rottengatter, German	Hamburg, Germany	PhD	Development and application of genetic markers linked to bovine trypanotolerance genes	Kenya	2000
Patrick Sakwa, Ugandan	Pretoria, South Africa	PhD	Designing strategies for integrated control of ticks and tick-borne diseases at the farm level: An *ex ante* assessment of the impact of an integrated control programme in a mixed crop–livestock farming system in Uganda	Uganda	2003
Beatrice Salasya, Kenyan	Wageningen, Netherlands	PhD	System prototyping and impact assessment for sustainable alternatives in mixed farming systems in high-potential areas of eastern Africa	Kenya	2003

Graduate fellows (continued)

Name/ Nationality	University/ Institute of Registration	Degree	Project Title	Location	Date of Departure
Catrin Schreiber, German	Humboldt, Germany	MSc	Sources of innovation in livestock production	Kenya	2001
Zewdu Sisay, Ethiopian	Brunel, UK	PhD	Managing the rumen eco-system to improve the utilisation of thornless acacias	Ethiopia	2002
Tom Smucker, American	Michigan, USA	PhD	Land use change and wildlife conservation in Kajiado District, Kenya, as part of the integrated modelling and assessment programme in East Africa	Kenya	2002
Florence Tangka, Cameroonian	Wisconsin, USA	PhD	The food security impacts of dairying with crossbred cows	Ethiopia	2000
Tesfaye Kumsa, Ethiopian	Copenhagen, Denmark	PhD	On-farm use of multi-purpose crossbred cows: Implications for herd productivity, food security and environmental sustainability in the crop–livestock mixed highland production systems of Ethiopia	Ethiopia	2001
Christa Utiger, Swiss	Swiss Federal Institute of Technology, Switzerland	PhD	Nutrient cycling and nutrient balance analyses in intensive and semi-intensive tropical maize–dairy production systems	Kenya	2001
Lisbeth Waaij, Dutch	Wageningen, Netherlands	PhD	Balanced breeding for trypanotolerance in cattle	Kenya	2001
Rosemary Wangeci, Kenyan	Limburgs, Belgium	PhD	The frailty model in animal breeding research	Kenya	2003
Claudia Weidow, German	Rostock, Germany	PhD	Morphological characterisation of *Lablab purpureus* to assess the variation in the collection at ILRI	Kenya	2002
Jeff Worden, American	Colorado State, USA	PhD	Land use change and wildlife conservation in Kajiado District, Kenya	Kenya	2002

ILRI's investors in 2000

Unrestricted contributions

Australia
Austria
Belgium
Brazil
Canada
China, People's Republic
Denmark
Finland
Germany
India
Ireland
Italy
Japan
Norway
Sweden
Switzerland
The Netherlands
United States of America
World Bank

Targeted contributions

African Development Bank
Asian Development Bank
Australia
Belgium
Canada
Common Fund for Commodities (CFC)
Denmark
European Union
Finland
Food and Agriculture Organization of the United Nations (FAO)
Ford Foundation
France
Germany
International Development Research Centre (IDRC)
International Fund for Agricultural Development (IFAD)
Italy
Japan
Kenya
Korea
Leverhulme Trust
Luxembourg
Norway
Organization of Petroleum Exporting Countries (OPEC)
Rockefeller Foundation
South Africa
Spain
Sweden
Switzerland
The Netherlands
United Kingdom
United States of America
World Bank
World Health Organization (WHO)

Subgrants from CGIAR inter-centre initiatives

African Highlands Initiative[1]
CGIAR Central Asia–Caucasus (CG–CAC)
Collective Action for Property Rights[2]
Desert Margins Programme
NRM Small Grants[3]
System-wide Genetic Resources Programme[4]

Non-CGIAR organisations contracting ILRI

Common Fund for Commodities
Global Livestock Collaborative Research Support Program (GL-CRSP)
- Colorado State University
- Michigan State University
- Texas A&M University
- University of Denver
- University of Florida
- University of Massachusetts

Institute of Molecular and Cell Biology–Africa

Leverhulme Trust
Organization of African Unity/Inter-African Bureau for Animal Resources (OAU/IBAR)
Oromia Agricultural Development Bureau of Ethiopia (OADB)
University of Liverpool
University of Nottingham
World Health Organization

Footnotes to list of subgrants

[1] Convened by ICRAF
[2] Convened by IFPRI
[3] Convened by CIAT
[4] Convened by IPGRI

Financial summary

INTERNATIONAL LIVESTOCK RESEARCH INSTITUTE
STATEMENT OF ACTIVITIES
for the year ended 31 December 2000
(US$ '000)

Revenue	2000			1999
	Unrestricted	Restricted	Total	Total
Grants	11,443	11,873	23,316	26,518
Other revenue and support	1,783	0	1,783	1,453
Total revenue	13,226	11,873	25,099	27,971
Expenses and losses				
Programme-related expenses	8,582	11,873	20,455	20,401
Management and general expenses	6,450	0	6,450	6,091
Other expenses and losses	189	0	189	203
Indirect cost recovery	(411)	0	(411)	(127)
Total expenses and losses	14,810	11,873	26,683	26,568
(Decrease)/Increase in net assets	(1,584)	0	(1,584)	1,403
Net assets at beginning of the year	31,333	0	31,333	29.930
Net assets at end of the year	29,749	0	29,749	31,333

INTERNATIONAL LIVESTOCK RESEARCH INSTITUTE
STATEMENT OF FINANCIAL POSITION
at 31 December 2000
(US$ '000)

Assets	2000	1999
Current assets		
Cash and cash equivalents	10,349	16,185
Accounts receivable		
Donors	4,724	3,456
Employees	636	530
Others	1,188	1,057
Inventories	1,378	1,367
Prepaid expenses	235	464
Total current assets	18,510	23,059
Non-current assets		
Property and equipment (net)	17,303	18,081
Intangible assets (net)	361	116
Investment in subsidiary	1,816	1,816
Total non-current assets	19,480	20,013
Total assets	**37,990**	**43,072**
Liabilities and net assets		
Current liabilities		
Accounts payable		
Donors	1,863	5,141
Employees	1,803	1,277
Others	1,506	1,824
Accruals	2,229	2,621
Funds in-trust	339	356
Total current liabilities	7,740	11,219
Non-current liabilities		
Accounts payable—employees	501	520
Total liabilities	8,241	11,739
Net assets		
Unrestricted—appropriated	20,013	20,013
—unappropriated	9,736	11,320
Total net assets	29,749	31,333
Total liabilities and net assets	**37,990**	**43,072**

INTERNATIONAL LIVESTOCK RESEARCH INSTITUTE
2000 FUNDING (US$)

Donor	Unrestricted	Programme restricted	Project restricted	Total
African Development Bank			213,981	213,981
Asian Development Bank			374,867	374,867
Australia	222,040		224,898	446,938
Austria	175,000			175,000
Belgium	162,914		112,041	274,955
Brazil	21,485			21,485
Canada	747,603		7,888	755,491
CG-CAC			99,980	99,980
China, People's Republic	30,000			30,000
CIAT			10,485	10,485
Common Fund for Commodities (CFC)			67,411	67,411
Denmark	533,404		10,655	544,059
Desert Margins Programme			13,324	13,324
European Union			1,459,332	1,459,332
FAO			40,000	40,000
Finland	315,806		38,162	353,968
Ford Foundation		1,000,000		1,000,000
France		336,962	25,622	362,584
Germany	194,175	202,020	372,579	768,774
GL-CRSP			146,897	146,897
ICRAF			7,500	7,500
IDRC			156,099	156,099
IFAD			531,326	531,326
IFPRI			121,473	121,473
India	37,500			37,500
Institute for Molecular Cell Biology–Africa			26,804	26,804
IPGRI			5,511	5,511
Ireland	344,780			344,780
Italy	220,000		413,565	633,565
Japan	380,308	966,161	72,604	1,419,073
Kenya		252,000		252,000
Korea			55,257	55,257
Leverhulme Trust			44,078	44,078
Luxembourg			4,243	4,243
Norway	988,347		174,836	1,163,183
OADB			3,147	3,147
OAU/IBAR			13,604	13,604
OPEC			69,980	69,980
Rockefeller Foundation			74,137	74,137
South Africa		50,000		50,000
Spain		40,000		40,000
Sweden	666,476		247,391	913,867
Switzerland	914,480	243,161	418,626	1,576,267
Texas A&M University			126,769	126,769
The Netherlands	63,394	112,718	159,496	335,608
United Kingdom		1,045,708	782,435	1,828,143
United States of America	2,975,000		175,735	3,150,735
University of Liverpool			34,215	34,215
University of Nottingham			29,379	29,379
World Bank	3,015,200			3,015,200
World Health Organisation			20,538	20,538
Others				72,754
Total	12,007,912	4,248,730	6,986,870	23,316,266

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Credits

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Text: Simon Chater, Green Ink, UK

Cover design: Eric Ouma/ILRI, Kenya

Layout: Christel Blank, Green Ink, UK

Filming: Peninsular Services, UK Ltd

Printing and binding: ILRI, Ethiopia

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Printed at ILRI, Addis Ababa, Ethiopia