HARNESSING THE POWER OF GENOMICS FOR ANIMAL HEALTH AND FOOD SECURITY

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The field of genomics, that is the study of DNA sequences that make up the genetic code of living organisms, has advanced at a breathtaking pace over the last twenty years. At the beginning of the 90s an international project was launched that took over twelve years to sequence the human genome. Today the same exercise to read the 3 billion letters of the human genetic code can be achieved in less than a week. This relentless advance of the field of genomics, which has revolutionised genetics and offered considerable medical advances, is not limited to investigating human DNA. DNA analysis methods have been used to study many groups of plants, animals and bacteria and these methods are increasingly being applied to test for species identity or the presence of a genetically modified organism. This technology has important applications in the domain of animal health and food security, as exemplified by the use of advanced genomic techniques to identify and understand last year's E. coli outbreak in Germany. Yet it is fair to say, when compared to human disease, direct application of genomics or the knowledge generated from genomics to food security and animal health is still in its infancy. However, we are now in a situation where advances in genomics show tremendous potential to assist in monitoring diseases and rapidly identifying and tracking disease outbreaks.

Two examples of meetings which bring experts together to consider genomics in animal health are the International Symposium on Animal Functional Genomics (ISAFG) and the International Symposium on Animal Genomics for Animal Health (AGAH). The conference websites show that there is a huge amount of research being performed using advanced genomics methods, however the challenge remains in translating this to everyday applications. The last AGAH meeting identified four priority areas for genomics and the associated challenges that need to be overcome to ensure they have maximum impact[1]. These were:

1. Marker-assisted selection of animals with desirable health traits
2. Functional genomics of host-pathogen interactions
3. Translating genomic information to tools for controlling diseases
4. Integrating stakeholder support to advance animal genomics in animal health

This final priority reflects the inherent difficulties associated with introducing "disruptive" albeit highly beneficial transformative innovations into existing well established markets.

There are a few more technical hurdles that need to be overcome before genomics can make a full transition from its current predominant use in research fields to widespread application as a routine screening tool for animal health

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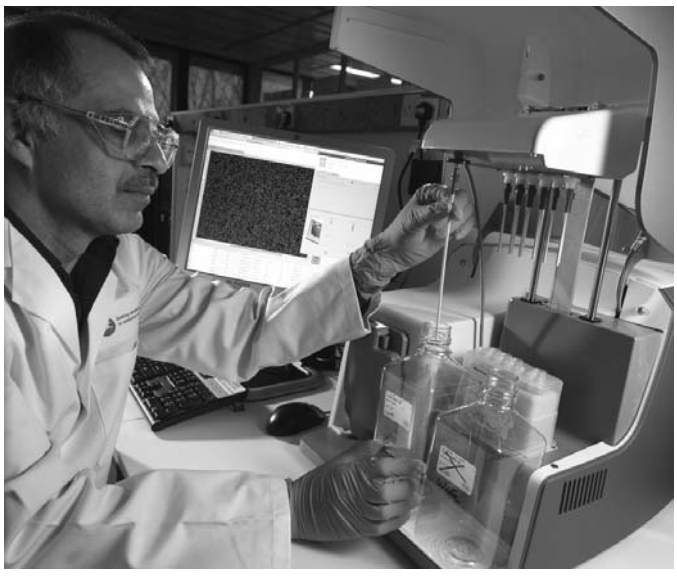

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protection. It requires the analysis of the whole or large parts of a genome and necessarily depends on the power of computing to interrogate the resulting very large data sets. Direct application of genomic techniques to complex issues like selective breeding could offer huge economic benefits. However more research is needed to understand fully the fundamental relationships between genetic sequences and specific biological phenomena, and we are some distance from having robust, simple instruments that would allow routine use by non-experts for the purpose of mass-screening of livestock. Efforts to control for technical variation will also be crucial if more applied applications are to succeed. Identifying mechanisms to facilitate robust data comparison, such as through the development of appropriate reference standards, will be central to this endeavour.

In the short term, the fastest route for translation of the knowledge gained from genomics to assist in animal health is to use this information to complement and improve on more established approaches. Methods, like the polymerase chain reaction (PCR), that are currently used to identify a specific gene, genotype an animal, measure drug resistance or diagnose an infection can all be made more effective using genomics.

We can soon expect to harness the potential of genomics in the field of animal health and reap major economic and societal rewards from improved disease control (reducing and ultimately eradicating outbreaks), tailored medication and selective breeding. UK science has an opportunity to lead the world in this area, with our leading expertise and research infrastructure in genomics. Within the space of a few years computational power will pick up sufficiently to handle the data generated. In the meantime attention to the AGAH priorities with directed public funding will allow our knowledge to mature sufficiently to ensure market acceptance to embrace fully this transformative technology.

1. S. C. Bishop, J. K. Lunney, M. H. Pinard-van der Laan et al., *BMC Proc* **5 Suppl 4**, S1 (2011).

A case study:

Bovine TB – how genomics is helping to fight the disease now and in the future

Genomics is helping in the fight against bovine tuberculosis (TB). Bovine TB is an infectious disease caused by the bacterium *Mycobacterium bovis*. *Mycobacterium bovis* can also cause TB in humans as well as other mammals including badgers and deer. The disease costs the UK government approximately £100 million every year and continues to be one of the most important issues facing the UK farming industry.

TB DNA Fingerprinting: tracking the spread of the disease

Being able to monitor and understand the spread of disease (epidemiology) is a vital part of ultimately controlling them. Epidemiology relies on laboratory tests which allow different strains of organisms to be distinguished and monitored. For TB, the most useful epidemiological tools are based on an understanding of the genomes and genetic variation of *Mycobacterium bovis*, so called molecular epidemiology.

Two techniques are commonly used – TB spoligotyping and VNTR (variable number of tandem repeats). Both are types of TB DNA fingerprinting or genetic typing. Both measure variation in the genomes of TB and allow different strains of TB to be identified and monitored as they spread around the countryside. This information is being used by epidemiologists to identify risk factors and plan the most effective intervention strategies to combat the disease. In Great Britain, the two techniques are routinely used in combination by the Animal Health and Veterinary Laboratories Agency, to support field investigations into the likely source of TB incidents in cattle and other animals.

Using DNA fingerprinting to ensure identified TB infected cattle are removed from farms

DNA fingerprinting can allow genetic identification of individual bovine animals – similar to human DNA fingerprinting used in criminal investigations. This method can be used to detect cases where eartags from TB positive cattle are swapped with less productive animals, sending the less productive (but disease free) animals to slaughter and retaining the infected animals on the farm. To deter strongly this sort of practice DNA samples are now taken from all TB test positive cattle at the time they are disclosed. DNA cross checking (between the animal identified on farm and the animal sent to slaughter) is carried out on a sample basis – or where fraud is suspected – to ensure TB infected cattle are not retained on farms.

The Future….towards better diagnostics, vaccines, medicines and disease control

The two examples above demonstrate how genomics based technology is helping in the fight against TB in the here and now. However, genomics is also underpinning and allowing research to be performed that would have been unthinkable only a few years ago. This research is exploiting techniques based on genomics such as microarrays and next generation sequencing (NGS).

Microarrays can be used to measure the presence or activity of thousands of genes in one experiment (in both *Mycobacterium bovis* and cattle) allowing researchers to understand better how the genome of an organism determines its biology. Using NGS the entire genome of a TB strain can be determined in a matter of hours allowing the differences between strains to be deciphered at a speed and level of detail not previously possible. Interestingly, the improved understanding of how strains differ will lead to molecular epidemiological tools which have advantages over spoligotyping and VNTR – a good example of how genomics can refine and improve current approaches.

Such genomics methods are helping to transform our understanding of fundamental TB biology: how the organism infects cattle, how it causes disease and how the immune response in the cattle fights the disease. These advances in understanding will ultimately lead to development of better TB disease control through improved vaccines, diagnostics and medicines.