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Case Study

PUSHING BACK THE BOUNDARIES IN FOOD RESEARCH

Food poisoning remains a serious problem in the UK. Foodborne illness costs the British economy about £ 1billion a year and Salmonella Typhimurium is one of the most common causes. The bacteria's resistance to antibiotics has increased at an alarming rate and it now kills more people in the west than any other food-born pathogen.

This bacteria is commonly found in the environment so why, in some environments does it become so virulent? Scientists at the Institute of Food Research (IFR) have been trying to determine how Salmonella survives in the body and why it causes disease.

Their research is being assisted by a new technology, BlueFuse for Microarrays, developed by British bioinformatics company BlueGnome.

BlueFuse uses statistical modelling techniques for analysing genetic data. It has made the initial stages of the investigation faster, potentially saving the IFR 6 months of a scientist's time each year. It also improves the accuracy of the results and reduces the tedium of much of the analysis.

Food poisoning

Food poisoning begins when food infected with Salmonella is eaten and moves into the gut. Samonella invades the epithelial cells lining the walls of the gut. These cells are designed to absorb nutrients not fight disease. The epithelial cells die and detach from each other leaving holes in the gut wall, which triggers the bloody diarrhoea characteristic of Salmonella food poisoning.

World first at IFR

The team at IFR have made a major breakthrough in their research. Salmonella has 4,644 genes and until recently only 100 had been identified as being involved in disease. During an infection some of the genes are 'switched on' and this gives the scientists important information about what is happening within the bacteria, and offers the potential to create vaccinations for livestock to prevent outbreaks of the disease.

Just a year after the entire genome sequence of Salmonella was published, scientists led by Dr Jay Hinton at the Institute of Food Research (IFR) in Norwich identified the 919 genes which were switched on or off during an infection:

"This was the first time that anyone had created a complete picture of gene expression in any organism during infection. This detailed snapshot of what the bacteria are actually doing during infection gives us the first clue of the importance of these 919 genes, and this technique can be applied to any infectious disease." Dr Hinton explains.

The findings are considered by the academic community to be as important as early work by Edward Jenner and Louis Pasteur.

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The research

The technique used to study genes is called DNA microarrays; these are glass slides from which all the genes in an organism can be studied at one time. The slides have a pattern of minute dots, each one representing a different gene. The slides are washed with a marker, which differentially colours the genes, which are activated in an infection.

As pioneers in this field, scientists at IFR had to build the microarray facility from scratch. They have continued to push the boundaries of what can be done and this includes being one of the first laboratories in the country to license BlueFuse following its launch earlier this year.

One Salmonella DNA microarray contains nearly 5,000 spot shaped features. Before BlueFuse, researchers such as Arthur Thompson at IFR would have to manually examine each spot to a make a judgement about whether the gene was switched on or not.

He explains, "Examining each microarray by eye and eliminating features that were caused by the washing process, dust or hairs could take two hours and gave me a headache! With BlueFuse this process is done automatically in 20 minutes."

The solution

Dr Jay Hinton, says BlueFuse makes the work faster and more accurate:

"At least 100 people die a year in the UK from Salmonella and the problem may worsen as resistance to existing antibiotics increases. People have already used the obvious approaches to reduce Salmonella infection, so we are looking for new information on how these bacteria causes disease.

The starting point is to look at the animal cells and identify which Salmonella genes change during an infection and to see what this tells us about the bacterial process. Armed with this we hope to discover the 'Achilles Heel' of Salmonella and develop a new antibiotic or vaccine.

This work is pushing microarrays to the limit using very small quantities of the genetic material (RNA). We already use less RNA than anyone has tried before, but BlueFuse may help us reduce further the level of RNA required for gene expression analysis.

BlueFuse is particularly useful in our research as it extracts more information, from poor quality data. One of the challenges of using DNA microarrays is to look at genes that are expressed at low levels. We have identified 919 genes that change during infection, but with BlueFuse we may be able to find more. We are now getting good data from small amounts of RNA, which is very exciting.

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"We are always striving to improve the quality of the microarray data we produce. The software has a novel way of assigning confidence to the quality of data obtained from microarrays, which lets us be really sure that the Salmonella genes we are studying are really being switched on or off during the process of infection.

BlueFuse enables our computers to analyse three times more microarrays per day. Last year we used some 3000 microarrays in the Institute of Food Research, we estimate that BlueFuse would have saved us six months of a scientist's time, that's two months in my laboratory alone.

It has also given a boost to staff morale, no longer has someone got to sit for hours infront of a computer – bored, not always making the right decisions suffering from eye strain and headaches. The new batch facility looks good and as we are working with hundreds of arrays it will make a big difference, we can run it over night and do more experiments.

"Our research is aimed at eliminating Salmonella from farm animals by developing a new vaccine to which it should not develop resistance. A better Salmonella vaccine will be a major advance for world science."

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