

## The Millennium Prize Laureate 2008

*"For his invention of DNA fingerprinting, used in the identification of criminal suspects and in paternity and immigration disputes, making him one of the most significant figures in modern genetics."*



### **Professor Sir Alec Jeffreys**

Department of Genetics  
University of Leicester, United Kingdom

Born January 1950 in Oxford, United Kingdom

### **Father of DNA fingerprinting**

The DNA fingerprinting technique developed by British geneticist Professor Alec Jeffreys has revolutionized the field of forensic science, as well as playing an important role in the resolution of paternity and immigration disputes.

Jeffreys is clearly a man with science in his genes: "I think I was born to be a scientist, as I was already fascinated by the subject at the age of five." His path was further determined some three years later, when his father gave him a microscope and a large chemistry set. It was while 'experimenting' with sulphuric acid and this set that he acquired the scar he still has today, hidden under his beard.

His interest in experimental chemistry and biology continued to grow and he went on to study biochemistry at Merton College, Oxford, then undertook his PhD on the mitochondria of cultured mammalian cells at the Genetics Laboratory, also at Oxford. Thereafter he moved to the University of Amsterdam, where he worked

as a research fellow on some of the first investigations into mammalian genes. In 1977 Jeffreys moved back to the UK to lecture in the Department of Genetics at the University of Leicester.

### **The "Eureka" moment**

The birth of DNA fingerprinting can be pinpointed exactly to the morning of September 10th, 1984. It was then that Jeffreys had a "eureka" moment in his Leicester lab while examining an X-ray that formed part of a DNA experiment analysing genetic markers for fundamental human studies. What the experiment showed, unexpectedly, were extraordinarily variable DNA patterns showing simple inheritance in his technician's family's DNA. Jeffreys quickly realized the import of this discovery of a biological identification method. "That moment changed my life," he says. And it led to the development of techniques that would fundamentally change this important area of science.

### **DNA fingerprinting – the detail**

The double-stranded, helix-shaped DNA (deoxyribonucleic acid) – that is found in all human and nearly all living cells – stores the body's genetic code.

All humans share extremely similar DNA sequences, with differences between people forming the basis of all inherited variation, including normal variation and inherited disease. However, most of our DNA shows only very subtle variation. Jeffreys discovered that human DNA also contains numerous patches of extremely variable DNA that he called minisatellites. These regions contain stuttered or repeated DNA sequences, and extreme levels of variation can arise through differences in the numbers of stutters between people created by a high rate of mutation when DNA is transmitted from parent to child. He also showed that different minisatellites share a short DNA sequence motif, allowing him to invent a method for detecting many highly variable minisatellites at the same time to produce a highly individual-specific DNA pattern – a DNA fingerprint. These patterns are extremely discriminating, revealing many differences even between very close relatives. The only people who share the same DNA fingerprint are identical twins who of course share the same DNA. Genetic fingerprints are also simply inherited from parent to child, providing a powerful tool for establishing family relationships.

### **How to make a DNA fingerprint?**

The first step is to extract DNA from the cells in a sample of blood, saliva, semen or other appropriate fluid or tissue. These can be found usually from personal items such as toothbrushes or razors, banked samples such as banked sperm or biopsy tissue, blood kin (biological relatives) or human remains.

The traditional way to fingerprint DNA is by doing what is called a Southern blot. The DNA being analyzed must be separated from other material, then cut into many different-sized pieces using restriction enzymes, which are proteins that can cut double-stranded DNA without damaging the bases. Variation in the number of stutters at a minisatellite results in variation in the length of the minisatellite DNA fragment. The next stage therefore is to detect these minisatellite DNA fragments and measure their length.

This is done by electrophoresis: the complex mixture of DNA fragments is separated by putting them into a slab of gel and applying an electric current

across it. Because DNA has a natural slightly negative charge, it will be attracted to the end of the gel. As the smaller pieces will move faster than the larger pieces, finally the pieces will be separated by size, with the larger ones near the beginning of the gel and the smaller ones nearer the end.

After electrophoresis the DNA fragments are transferred from the fragile gel to a strong sheet of nylon or nitrocellulose paper membrane. The gel is discarded and the DNA is ready to be analyzed using a radioactive probe that specifically detects minisatellite-containing DNA fragments. Jeffreys invented two types of probes, those that detect many minisatellites simultaneously to produce a DNA fingerprint, and probes that detect just one minisatellite at a time to produce a much simpler pattern called a DNA profile. A piece of X-ray film is exposed to the membrane after radioactive probing and fragments that have bound to the probe appear as black bands when the X-ray film is developed.

By measuring how far the fragments have moved through the gel one can calculate their sizes and therefore obtain the lengths of the different variants. If one is checking family relationships, for example, one can see if a child has variants shared with both parents.

### **DNA fingerprinting evolves**

The original method of DNA fingerprinting was slow and required significant quantities of high-quality DNA, while the new methods use smaller amounts of DNA and samples that may also be more degraded than those previously used.

DNA fingerprinting took a huge leap forward with the invention of the polymerase chain reaction. Both discriminating power and ability to recover information from very small initial samples was now possible by amplification of specific regions of DNA using a cycling of temperature and a thermostable polymerase enzyme along with fluorescently-labelled sequence-specific primers for DNA amplification.

The most prevalent method of DNA fingerprinting used today is based on the polymerase chain reaction and analyses variation at short tandem repeat regions of DNA, also known as microsatellites. These highly polymorphic regions have short repeated sequences of DNA (the most common is four bases repeated, but there are other lengths in use, such as three and five bases). Because different people have different numbers of repeat units, these regions of DNA can again be used to discern between individuals. These repeat locations are targeted with sequence-specific primers and are amplified. The DNA fragments that result are then separated and detected using electrophoresis; instead of using radioactive probes, the gel is scanned directly and the DNA profile uploaded directly into a computer.

Each variant displayed at a short tandem repeat region is usually quite common in humans. However, when looking at multiple regions, it is the unique combination of these variants in an individual that makes this method highly discriminating as an identification tool. The more repeat regions that are tested in an individual, the more discriminating the test becomes.

Recent innovations have included the creation of primers targeting variable regions on the Y-chromosome, which allows detection of male profiles in some instances of rape where the DNA is very heavily contaminated with the victim. Y-chromosomes are paternally-inherited, so analysis can help in the identification of paternally-related males, but, unlike DNA fingerprinting, Y typing does not allow proof positive of identity.

For highly-degraded samples, it is sometimes impossible to get a complete profile of the short tandem repeats. In these situations mitochondrial DNA is sometimes typed as there are many copies of mitochondrial DNA in a cell, while there are only two copies of a nuclear DNA sequence such as a simple tandem repeat. Mitochondrial DNA can be obtained from material such as hair shafts and old bones/teeth and because mitochondrial DNA is maternally inherited, directly-linked maternal relatives can be used as match references, such as, for example, one's maternal grandmother's sister's son. This technique is useful in determining unclear identities, such as those of missing persons, when a maternally-linked relative can be found.

## **Applications of DNA fingerprinting**

DNA fingerprinting was first put to use when Jeffreys was asked to help in a disputed immigration case to confirm the identity of a British boy whose family was originally from Ghana. The boy had gone back to Ghana and returned to the UK with a suspicious-looking passport and the authorities suspected that it might not in fact be the same child who originally left. It was a tough case but Jeffreys was quickly able to prove, using this new science of his, that the boy was who he claimed to be.

DNA fingerprinting was first used as a police forensic test in 1986 in a double rape and murder case. Jeffreys was brought in by the UK police to assist in identifying the culprit. His testing exonerated an innocent man who has falsely confessed to one of the murders and eventually led to the entrapment of the true murderer.

It has played a key role in many high publicity cases. In one early achievement, Jeffreys confirmed the identity for German prosecutors of the Nazi Dr. Josef Mengele, who had died in 1979, by comparing DNA obtained from a femur bone of his exhumed skeleton with DNA from his widow and son, in a similar way to paternity testing. In another controversial case, DNA analysis was performed to determine if Thomas Jefferson had sired a son with one of his slaves. And mitochondrial DNA testing was used in determining that Anna Anderson was not the Russian princess Anastasia Romanov she had claimed to be.

The most recent ethnogeographic research uses DNA profiles to trace origins of population groups looking at geographic variations in human genome. And the method can also be applied to many non-human species, for example in wildlife forensics and conservation biology.

Before DNA fingerprinting was commercialized in 1987, the laboratory of Prof Jeffreys was the only centre in the world conducting DNA fingerprinting. Now, however, DNA fingerprints are examined everywhere, even in portable laboratories, and the equipment for genetic fingerprinting is being made by dozens of companies around the world.

DNA fingerprinting has a vital role to play in contemporary society; genetic research continues, making DNA-related applications more common in many areas of life. This has raised also some ethical questions, particularly regarding the potential for genetic information to be used to limit freedoms and invade privacy.

Jeffreys is one of those who opposes the extension of police DNA databases to cover whole populations, given the presumption of future guilt this implies. However, he does suggest that a separate national DNA database, containing encrypted DNA profiles, might provide an answer to problems of identification in

times of disaster.

## **Jeffreys today**

Jeffreys is Professor of Genetics at the University of Leicester and continues to work at the genetics laboratory. When not working, he enjoys surfing (not often in Leicester) and philately. He is a Distinguished Supporter of the British Humanist Association and likes to boast that he is one of the top Twister players on staff at Leicester University!

"I have to confess that I simply haven't grown up. I think deep inside I'm still stuck at age 14 with my chemistry set; it's just curiosity that keeps me going! The ability to keep experimenting and discovering things about the universe in which we live is a great privilege – as well as a fantastic hobby. So that's why I love what I do.

## **Further reading**

<http://protist.biology.washington.edu/fingerprint/dnaintro.html>

[http://en.wikipedia.org/wiki/Genetic\\_fingerprinting](http://en.wikipedia.org/wiki/Genetic_fingerprinting)

<http://science.howstuffworks.com/dna-evidence.htm>

<http://www.faqs.org/health/topics/24/Genetic-fingerprinting.html>

Sally Morgan: From Mendel's Peas to Genetic Fingerprinting (ISBN 1403488371); Heinemann/Reintree (2006)

Gerald Sheindlin: Genetic Fingerprinting: The Law and Science of DNA (ISBN 1887750045); Rutledge Books (July 1996)

## **CV - Professor Sir Alec JEFFREYS**

British citizen

Born 9th January, 1950 at Oxford, England

Married, two children

- 1968 Admitted to Merton College, Oxford
- 1972 Gained Honors B.A. (Oxon) Class I in Biochemistry
- 1972 Awarded Christopher Welch Scholarship for postgraduate research.  
D. Phil. research programme commenced in the Genetics  
Laboratory, Department of Biochemistry, Oxford University
- 1975 D. Phil. degree gained
- 1975 - 1977 Awarded Postdoctoral Research Fellowship by the European  
Molecular Biology Organization. Commenced research programme  
in University of Amsterdam
- 1977 - 1984 Lecturer in the Department of Genetics, University of Leicester
- 1982 - 1991 Lister Institute Research Fellow, Dept. of Genetics, University of  
Leicester
- 1984 - 1987 Reader in Genetics, University of Leicester
- 1987 - Professor of Genetics, University of Leicester
- 1991 - Royal Society Wolfson Research Professor, University of Leicester
- 1993 - 1999 Howard Hughes International Research Scholar

### **Notable prizes**

- 1986 Elected Fellow of the Royal Society, London
- 1991 Elected Fellow of the Royal College of Pathologists
- 1992 The Allen Award by the American Society of Human Genetics
- 1993 Elected an Honorary Fellow of the Royal College of Physicians
- 1993 The Albert Einstein World of Science Award by the World Cultural  
Council, Mexico City
- 1998 The Australia Prize (with profs E. Blackburn, S. Cory and G.  
Sutherland)
- 2004 Louis-Jeantet Prize for Medicine, Fondation Louis-Jeantet de  
Médecine, Geneva, Switzerland
- 2004 Royal Medal awarded by the Royal Society
- 2005 Elected Foreign Associate of the National Academy of Sciences,  
Washington, USA
- 2005 Albert Lasker Award for Clinical Medical Research
- 2006 Dr H P Heineken Prize for Biochemistry and Biophysics awarded by  
the Royal Netherlands Academy of Arts and Sciences
- 2008 Candidate for Millennium Prize 2008

### **Other awards and recognition**

- 1992 An honorary freeman of the City of Leicester 1992
- 1994 Knighted for services to science and technology
- 2004 Daily Mirror Pride of Britain Lifetime Achievement Award
- 2006 Great Briton Award, Greatest Briton of 2006

### **Patents**

- "Polynucleotide Probes", October 1985
- "Improvements in Genetic Probes", March 1987
- "Polynucleotide Probes", October 1989
- "Characterization of genomic DNA", November 1989
- "Method of Characterization", August 1991

"Sequences", December 1993

"Simple Tandem Repeats", November 1994

"DNA enrichment by allele-specific hybridisation", January 2003