**DNA sequencing tackles global challenges**

**Shankar Balasubramanian and Dr David Klenerman**

The first full genome sequence of a eukaryote; *Saccharomyces cerevisiae* First complete chromosome sequence; *Streptomyces coelicolor*. DNA sequencing tackles global challenges

Commercialise a technique to sequence DNA approach to DNA sequencing. Shankar Balasubramanian and Dr David BBSRC funding of £282K awarded to Dr 1996 discoveries enabled researchers to determine foundations of modern bioscience. Subsequent structure of DNA in 1953, they laid the basis. DNA sequencing can also help researchers identify potentially valuable natural products and produced new and improved strains of microbes. Used to manufacture biological drugs such as medicines or industrial enzymes.

DNA sequencing technologies now mean that the human genome can be sequenced in one day.

**BBSRC**

- 2000 ARK Genomics is set up by BBSRC as part of its ‘Innovate Genome Futures’ initiative to provide access to functional genomics technology and measure relevant to the animal health community.
- 2004 Arabidopsis Genome Initiative was part-funded by BBSRC. The Arabidopsis Genome Initiative was part-funded by BBSRC.
- 2009 RootKabalaumann named BBSRC Innovator of the Year for inventing and commercialising new hand-held sequencing technology. He was part of an international team that aimed to understand the genetic basis of cancers and other rare diseases.
- 2012 BBSRC research on an ash dieback fungus showed that the fungus can be sequenced in a single day.

**Examples of genome sequencing supported by BBSRC**

- **2016 RNA sequencing technology shows that the human genome can be sequenced in a single day.**
- **2006**
  - *Saccharomyces cerevisiae* (yeast) genome was sequenced by researchers at the John Innes Centre, which is formally part of the University of East Anglia.
  - *Saccharomyces cerevisiae* first sequenced, part of the *Saccharomyces* genome, is the model yeast used in research globally. The *Saccharomyces* Genome Initiative was part-funded by BBSRC.
- **2000** First complete chromosome sequence of *Saccharomyces cerevisiae* was published, led by researchers at the John Innes Centre.
- **2000** First plant genome to be sequenced; the *Arabidopsis thaliana* genome was published.

**1996**

- **BBSRC funding of £1.25M awarded to Dr Tim Hunt and Dr David Klenerman at the University of Cambridge to support their work developing a new approach to DNA sequencing.**
- **1998**
  - *Saccharomyces cerevisiae* genome sequencing project completed by US researchers, spanning more than 17 years and cost around £2.5M (in 1991 US dollars). The first full genome sequence of a eukaryote; *Saccharomyces cerevisiae* First complete chromosome sequence; *Streptomyces coelicolor*. DNA sequencing tackles global challenges

**BBSRC support for sequencing technology**

- **2005** Oxford Nanolabs Ltd (later renamed Oxford Nanopore Technologies) founded as a spinout from Oxford University research on BBSRC-funded technology.
- **2006** Solis launch their first genome sequencer – the Genome Analyser – capable of sequence one genome a day in a single run. In the same year, Solis acquires Lorn Therapeutics (an instrumentation company) which later becomes an international public company.
- **2007** UK genetics analysis company IlluMi Nova Sports for $600M+.
- **2010** Paul Kariuki Balaumann named BBSRC Innovator of the Year for inventing and commercialising new hand-held sequencing technology. He was part of an international team that aimed to understand the genetic basis of cancers and other rare diseases.
- **2012** Whole genome sequencing technology shows that the human genome can be sequenced in a single day.

**Timeline:**

- **1992** First complete chromosome sequence of *Drosophila melanogaster* (fruit fly) sequenced.
- **1996** First full genome sequence of a bacterium; the *Saccharomyces cerevisiae* genome was published.
- **2000** First plant genome to be sequenced; the *Arabidopsis thaliana* genome was published.
- **2005** The *Hymenoscyphus fraxineus* fungus genome was sequenced at the John Innes Centre, which is formally part of the University of East Anglia.
- **2009** RootKabalaumann named BBSRC Innovator of the Year for inventing and commercialising new hand-held sequencing technology.
- **2012** Whole genome sequencing technology shows that the human genome can be sequenced in a single day.

**BBSRC investments in the early 1990s supported some of the earliest published DNA sequences (yeast and the model plant *Arabidopsis*), used in global biology.** BBSRC’s investments in the early 1990s supported some of the earliest published DNA sequences (yeast and the model plant *Arabidopsis*), used in global biology. By 2000, researchers were using sequencing technologies which was much faster and cheaper than previous methods. More recently, BBSRC-funded research underpinned the formation of Oxford Nanopore to develop and commercialise their innovative new sequencing technology.

- **2015** DNA sequencing technologies now mean that the human genome can be sequenced in one day.

This timeline provides a snapshot of some of the major BBSRC investments in DNA sequencing and its application to some of the most important challenges facing society today.
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Solexa and Illumina

Based on BBSRC-funded research in the 1990s, Professor Balasubramanian and colleagues from the University of Cambridge developed ‘Solexa’ sequencing technology. Using Solexa, researchers could sequence DNA 10,000 faster and much more cost-effectively than was previously possible. In 1998 Professor Balasubramanian and Professor Klenerman founded Solexa Ltd to develop and commercialise the technology. The company was later bought by Illumina for US$600M. According to Illumina, today more than 90% of the world’s sequencing data is generated using their sequencing by synthesis (SBS) technology. Professor Balasubramanian was named as the 2010 BBSRC Innovator of the Year for inventing Solexa sequencing, and for his work in launching Solexa Ltd, and the subsequent commercialisation and dissemination of the technology.

Advances using Illumina sequencing technology:

- Illumina sequencing was used by an international consortium of researchers to sequence the genome of wheat; a staple crop providing 20% of the world’s calories. Using the wheat genome sequence, breeders are beginning to understand the genetics of complex characteristics such as yield stability and resistance to pests and disease. Detailed mapping of the location of these genes is helping plant breeders to develop improved wheat varieties more quickly and efficiently.

- Scientists are studying the genome sequences of the chicken and the chicken pathogen Eimeria (both sequenced using Illumina technology) to improve welfare and efficiency in chicken production by reducing disease in farmed poultry. The Eimeria sequence is being used to identify potential new targets for vaccines or drugs against coccidiosis, a devastating disease of chickens which costs farmers £2Bn per year, contributing to global food security. The chicken sequence has also been used to breed chickens that do not spread bird flu to other chickens. It is also being used to study the avian immune system, with the aim of reducing the quantity of chemicals and antibiotics that are used in poultry production.

- Sequencing is being used to help in the battle against the ash dieback epidemic. Sequencing the fungus responsible for the disease is increasing our understanding of how it infects and is spread between trees, leading the way towards development of effective treatments. Researchers have also sequenced ash trees with naturally high levels of resistance to ash dieback to identify the genes responsible for their resistance. This could help breeders create resistant strains of ash tree to replace those lost to the disease.

Sequencing in the news

In 2012, BBC news reported that researchers had used Illumina sequencing to stop an outbreak of MRSA in a hospital.

By analysing the genome sequences of MRSA isolates from a special baby care unit at Rosie Hospital in Cambridge, researchers traced them all to a single source of infection. This source was identified as a member of staff who was a carrier of MRSA but showed no symptoms; once treated further MRSA infections in the outbreak stopped.

- The UK’s 100,000 Genomes Project, was established in 2014 to sequence the genomes of NHS patients with rare diseases and cancer, as well as their families. Illumina is working with the project to deliver the necessary infrastructure and expertise. The project is the largest such national project in the world and is being managed by Genomics England. It was set up by the UK Government with the aims of establishing a ‘genomics medicine’ service for the NHS, enabling medical research, and building a UK genomics industry. Data analysis for the project is being supported by spinout company Genomics plc, which arose from BBSRC-funded research at the University of Oxford to develop new DNA sequence analysis software.
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