HISTORY OF GENOMICS

1. Hello, welcome to Module 5 of Introduction to Human Genetics. This is the first lecture in this Module and here we'll look at the key events in the history of genomics and genetic research. Although genomics and genetics may sound similar and are related, they focus on different information and should not be confused with each other. What's the difference?
Genetics is a study of single genes and their roles in inheritance, so the way that certain traits or conditions are passed down from one generation to another.
Genomics, which is a more recent term, addresses genome as a whole structure, so it is a study of all of a person's genes and their interactions with each other and with the person's environment.

2. History of genetics dates back to the second half of the 19th century, when Gregor Mendel, recognized as the father of modern genetics, conducted his experiments on pea plant varieties and published his classic paper in 1865. In this work, he demonstrated a number of statistical patterns underlying inheritance and developed a theory involving hereditary factors in the germ cells to explain this patterns. You may learn more about his experiments in Module 1 of our course.

3. Friedrich Miescher was the first researcher to isolate and identify nucleic acid. He was interested in studying the chemistry of the nucleus of leucocytes. As white blood cells were known to be one of the main components in pus, for his research Miescher collected bandages with infectious materials from a nearby clinic. In 1869, he isolated a new molecule from the cells' nuclei and called it "nuclein". Now we know this substance to be DNA. Although Miescher studied it throughout his career, he and other scientists of that time believed proteins were the molecules by which traits are passed from parents to children. The importance of DNA was unrecognized until 1940s.
Once DNA was identified as the genetic material, many scientists sought information that might clarify how it serves as a basis for the process of heredity. The answer was believed to depend strongly on the nature of the chemical structure of the DNA molecule.

4. Rosalind Franklin who mastered X-ray diffraction techniques in Paris, accepted a research scholarship at King's College in London where Maurice Wilkins was using X-ray crystallography to study DNA. In 1952 Franklin took two sets of high-resolution photos of crystallized DNA fibers and looked at the dimensions of DNA strands, with phosphates on the outside of what appeared to be a helical structure.

5. This discovery helped Francis Crick and James Watson model the structure of DNA. Using cutouts of the bases and metal scraps from a machine shop, they constructed the model that represented DNA as a double helix, with sugars and phosphates forming the outer strands of the helix and the bases pointing into the center. Their 1953 paper notes that the model "immediately suggests a possible copying mechanism for the genetic material."

6. In the early 1960s, Marshall Nirenberg and National Institutes of Health colleagues focused on how DNA directs protein synthesis and the role of RNA in these processes. Their 1961 experiment, using a synthetic mRNA strand that contained only uracils, yielded a protein that contained only phenylalanines. Identifying three uracil bases in a row as the RNA code for phenylalanine was their first breakthrough. Within a few years, Nirenberg's team had cracked the 60 mRNA codons for all 20 amino acids. In 1968, Nirenberg shared the Nobel Prize in Physiology or Medicine for his contributions to breaking the genetic code and understanding protein synthesis.

7. The history of genomics begins in the 1970s with the first, classical method of DNA sequencing devised by Frederick Sanger. Sanger method mimics the natural process of DNA replication using polymerase, radioactively labeled nucleotides, and chemically altered "terminating" bases. In 1977

Sanger and his group used it to sequence the first complete genome – that of bacteriphage called phiX174.

8. In 1983 Kary Mullis conceived the Polymerase Chain Reaction – PCR. It is relatively simple and inexpensive technology used to amplify or in other words make billions of copies of a DNA segment. You may learn more about this method in Module 4 of our course. PCR revolutionized the study of DNA and together with the automated Sanger sequencing method allowed researchers to believe that sequencing the entire human genome could be possible.
Beginning in 1984, the U.S. Department of Energy, National Institutes of Health, and international groups held meetings about studying the human genome.

9. Finally, in 1990 the Human Genome Project was launched. The project would develop technology for analyzing DNA; map and sequence human and other genomes – including fruit flies and mice; and study related ethical, legal, and social issues.

10. First draft and initial analysis of the human genome sequence was published in 2001. A wealth of information was obtained. For instance, the number of human genes was estimated to be less than 30,000. Researchers also reported that the DNA sequences of any two human individuals are 99.9 percent identical.

11. The Human Genome Project's ambitious goals had all been met in 2003, two years ahead of its original schedule. The sequences produced by the project covered about 99 percent of the human genome's gene-containing regions. The project successfully undertook a wide range of additional goals: from sequencing the genomes of organisms used in disease research, to developing new technologies for studying whole genomes.

12. The next stage of genomic research was to derive meaningful knowledge from the DNA sequence. New huge research programs based on bioinformatic tools proliferated to address this challenge. The ENCyclopedia Of DNA Elements – ENCODE consortium was launched in 2003, to carry out a project to identify all functional elements in the human genome sequence.

13. Another spin-off from the Human Genome Project was the 1000 Genomes Project launched in 2008. Its goal was to comprehensively characterize human variation by capturing data from at least 1000 people from all over the world. This effort became feasible, as next-generation sequencing platforms sharply reduced sequencing costs. What's more, increasing sequencing capacity led to repeated revisions of initial plans to the current project scale of 2500 individuals...

14. ...and development of even more ambitious projects such as UK10K aiming to compare the genomes of 4,000 healthy people with those of 6,000 people living with a disease of suspected genetic cause,

15. or the 100,000 Genomes Project focusing on patients with rare diseases, and their families, as well as patients with common cancers.

16. In 2012 ENCODE study published 30 research papers describing the active regions of the human genome, including confirmation that the human genome contains 20,687 protein-coding genes.

17. As we find out more about our genes and how we react differently to diseases and to treatment, personalised medicine becomes increasingly important. Its challenge is to infuse genomic information into medical practice. It is thought that in the future access to our own genetic information could become a routine part of everyday healthcare and that personal

genomics could allow us to optimise our health on a whole different level to improving our diet and doing more exercise.