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Genomics and the future of medicine

The discovery of genetic material

The development of genetics and genomics as a field of scientific knowledge has taken place over a very long period of time. Its history can be said to have begun in 1865, when Mendel published a paper which is regarded as providing the basis for genetic science. Based on his records of around 28,000 plants, Mendel showed how different characteristics were passed between generations. At the time, Mendel's experimental work was admired for its assimilation and analysis of large amounts of data, but its importance was not recognized until early in the 20th century. Similarly, 19th-century work on identifying the chemicals involved in reproduction was not recognized at the time. Research by Miescher published in 1871 identified deoxyribonucleic acid (DNA) as the chemical in the nucleus of the cell which was responsible for controlling reproduction. Since DNA was a relatively simple molecule, however, until early in the 20th century it was thought that proteins were more likely to control the reproductive process. Research by Watson, Crick and Franklin in 1953 showed the double helix structure of DNA, making it easier to understand how it provided instructions for reproduction. Experiments in the 1960s by Nirenberg and Matthaei provided clear evidence to describe the chemical processes involved in DNA reproduction. Almost a century after Mendel had identified the processes governing genetic inheritance, research had identified the underlying biochemical mechanisms.

The Human Genome Project

The next major step forward in genetic knowledge was the Human Genome Project, which began in 1990. The genome represents the complete set of DNA in each organism; and the activity in every cell in every living organism is governed by the DNA in its nucleus. By aiming to generate a high-quality reference DNA sequence for the human genome, the project aimed to provide knowledge about the most fundamental aspects of life. At the time, the project was seen as extremely ambitious in technical terms. Because the laboratory techniques which were used to map DNA were complex and time-consuming, and depended on highly skilled laboratory staff, it was clear that without new technologies and techniques it would not be possible to achieve the stated objectives by 2005; so, as a first step, major investments were made in computer technology for data processing. This marked the beginning of a new scientific discipline of bioinformatics. By 1998, with less than half of the planned project time remaining, just over 6% of the genome had been mapped. Fortunately, by this time, a significant investment had been made in developing specialized electronic components which could directly analyze DNA without the need for human intervention. Consequently, there was an enormous increase in the speed with which the genome could be mapped. By April 2003, a finished version of the human genome sequence was available, along with much new knowledge. By coincidence or design, it was exactly 50 years since Watson and Crick published their paper on the structure of DNA, which identified the 'letters' of the genomic alphabet.

Epigenetics as a field of study

As the Human Genome Project finished sequencing human DNA, it seemed all of the secrets of how life develops were about to be revealed. While the project revealed some extremely valuable knowledge, however, an enormous amount remained to be understood. For example, when the project was completed, it showed that only around 2% of the genes in the genome were responsible for creating proteins. Although some researchers classified the other 98% of genes as 'junk', it seemed likely that they had some function. A clue to the nature

of this function came from the DNA sequences of different organisms. These showed a remarkable similarity between the genes which code for proteins in humans (around 20,000) and similar genes in much simpler life forms. The main difference between more and less complex life forms was actually the amount of 'junk' or non-coding DNA in the genome. The realization that this non-coding DNA somehow controlled or regulated how the coding genes produced proteins led to a rapid growth in research into epigenetics ('above genetics') to try to understand how this process worked. This research showed that while the underlying DNA sequence of an organism remained fixed, non-genetic factors (including environmental factors) could change how this DNA behaved when producing new cells. Furthermore, these epigenetic changes could be inherited by future generations. As a result, the standard view that genetic inheritance was fixed needed to be revised. While DNA itself was a key factor in inheritance, it was not as central as many had previously thought.

The human microbiome

The technological advances made during the Human Genome Project made it possible to launch a project to map all of the life forms which live in and on the human body. The Human Microbiome Project began in 2007. In its first phase, it aimed to identify what a healthy microbiome looked like and what variations occurred in different types of disease. The research showed that different types of microorganisms are found in different parts of the body and that different individuals have different microbiome profiles. Despite the fact that these profiles are largely acquired early in life, they can change rapidly in certain circumstances. Differences can also be observed between different populations and in different environments. The research was also able to identify associations between changes in the microbiome and different conditions such as autism and cancer. In addition, it found that differences in the microbiome could affect how well certain drugs performed, such as those used to treat heart conditions. The second phase of the research, which began in 2014, is investigating in more detail how the body and the microbiome interact to influence areas such as immunity and metabolism. The knowledge gained from these projects shows that the study of genetics cannot be confined to studies of cells in the human body alone, but must also consider the genetic aspects of the microorganisms which live in and on the body.

The future of genomics

Recent decades have seen a very rapid growth in knowledge about the link between genetics and life itself. Many benefits have already emerged from this research, and there will be many more in future decades. Researchers have already begun to correlate variations in DNA with differences in results from medical interventions. This should allow us to classify individuals into subgroups based on various DNA sequences, for whom drugs could then be customized. A new discipline, pharmacogenomics, is developing around the study of these interactions. However, more work on epigenetics is still needed to understand how the environment and related factors can influence human development. Mapping the different types of life which live in and on humans shows that the interactions between humans and different life forms are far more complex than previously imagined and can have a direct influence on human health. Advances in computing have provided vast quantities of data on the relationships between different aspects of life in a relatively short time. Converting this data into practical knowledge to improve the quality of healthcare is likely to take much longer.