

In the first of the tutorial series on genetics, genomics and proteomics, Andrew Webb, PhD, Professor of Biological Sciences, Wellesley College presented an overview talk entitled: "From Mendel to Microarrays: the Basic Concepts & Tools of Molecular Genetics". The historical landmarks in genetics include: 1865, Mendel's laws of heredity; 1910, the chromosomal theory of inheritance; 1953, the Watson and Crick discovery of the double helix structure of DNA and 2000, the initial sequencing of the human genome. Some of the concepts discussed are summarized below. The central dogma of molecular biology is that genetic information flows from DNA to RNA to proteins. Genes are the region of DNA that controls the production of a discrete hereditary characteristic, usually a single protein. Genes lie along chromosomes, threadlike linear structures within the cell nucleus. Each of the 4 bases in DNA can pair with only one specific base, allowing DNA to act as a template for its own duplication. DNA replication produces two double helices from each original DNA molecule. RNA is an intermediate in the flow of information from DNA to protein. Transcription is the process by which RNA is formed from DNA; translation is the process by which proteins are formed from RNA. Genetic information is carried by codons, 3-letter-word regions of RNA which specify the specific amino acid sequence to be used in forming proteins. This amino acid sequence is the primary structure of the protein. The function of the protein is related to its 3-D structure and the rules of protein folding which determine this structure are still poorly understood. The secondary structure is described by alpha helices and beta sheets. The tertiary structure describes the folding in space. The efficiency of gene expression varies from gene to gene and depends on both general and gene-specific factors.

DNA analysis involves a number of steps. The material must be isolated and then cut into pieces using restriction enzymes. The fragments are separated by molecular weight using gel electrophoresis. The DNA sequence must be determined and then localized to find where the gene is. Recombinant DNA describes the production of DNA from different sources using restriction enzymes to cleave DNA at specific sites and then recombining them using an enzyme. DNA cloning depends upon having methods to isolate, amplify and express specific DNA sequences. Cloning for many applications of DNA technology may be done by inserting the DNA fragment of interest into circular double-stranded plasmid DNA, inserting the recombinant plasmid DNA into a bacterium and replicating the bacteria in cell culture. A more recent technique, PCR (polymerase chain reaction) allows the amplification of a given nucleotide sequence in a test tube and has allowed such amplification to be done on the time scale of hours rather than the days required previously. In addition to speeding the cloning process, PCR has applications in forensics and diagnosis.

Gene chips are microarrays of 10,000-60,000 DNA-specific binding sites on silicon or glass for DNA analysis. The large number of sites allows parallel processing, vastly speeding the analysis process. The analysis process often involves obtaining mRNA from a cell and using reverse transcriptase to produce cDNA which is then analyzed. The hope is to find a signature that can be used for diagnosis or for identifying drug targets; however the measured RNA expression has a poor correlation with proteomics.