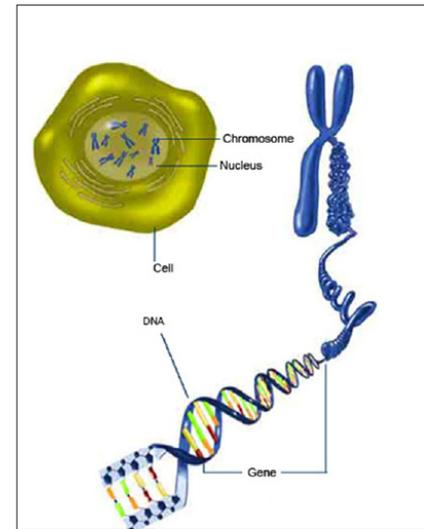


HIGH-THROUGHPUT DNA SEQUENCING

GENES 101

Genes 101 - The 23 pairs of chromosomes in our genome contain a little more than 20,000 genes. Each chromosome consists of a long molecule of double stranded DNA, which in turn is made of a sequence of paired nucleotides. Each nucleotide consists of a sugar molecule, a phosphate group and one of four bases (A=adenine, T=thymine, C=cytosine, or G=guanine). Each base in one strand is always paired with its complementary base on the opposing strand. A on one strand is paired with T on the other strand, T with A, G with C, and C with G. Variations of the nucleotide sequence are a normal feature of DNA. However, if these changes affect the way a gene functions, they can result in disease. These variations may be inherited or occur spontaneously as mutations.



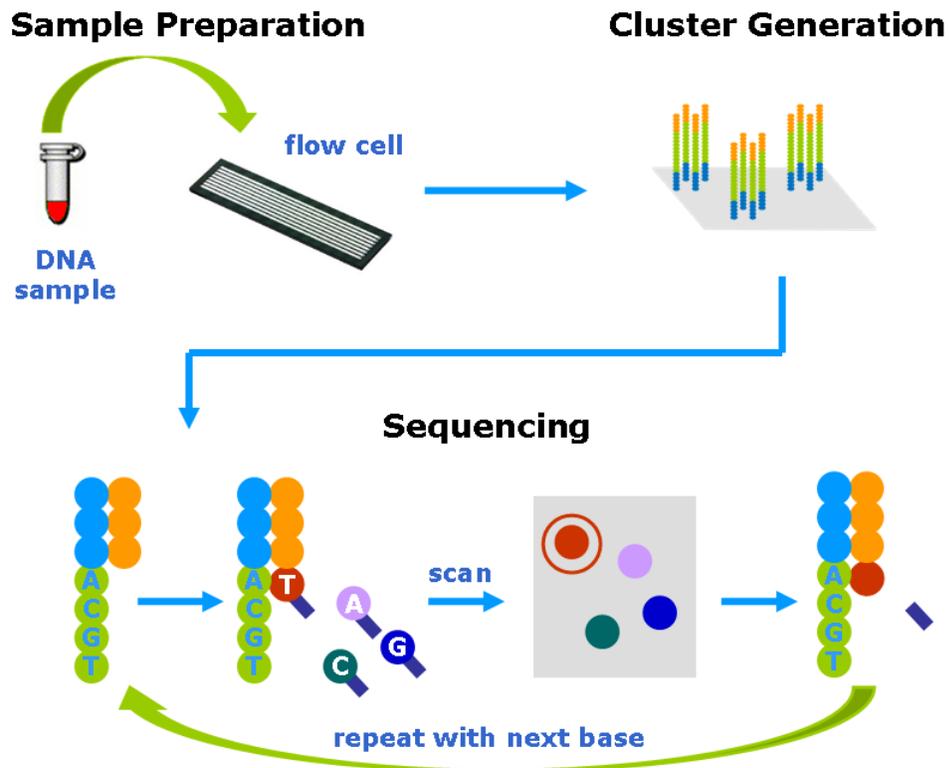
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WHAT IS HIGH-THROUGHPUT SEQUENCING (HTS)?

A new generation of technologies now provide much more rapid and cost-effective determination of the sequence of individual nucleotide bases that make up a genome. Current high-throughput sequencers are 1000 times faster and produce equivalent data at 1/1000 the cost of the sequencers used in the Human Genome Project ten years ago, and even better performance is likely in the near future. This is done by massively parallel sequencing of hundreds of millions of fragments of DNA simultaneously using state-of-the-art nanotechnology, molecular biology, solid-state chemistry, imaging, and computational methods.

HOW DOES IT WORK?

While there are numerous “next generation” sequencing platforms, one of the most frequently used is a “sequencing by synthesis” method. First, the double stranded DNA sample is fragmented and denatured, and the resulting single stranded fragments are attached to the surface of a flow cell. Multiple copies of each attached fragment are made by PCR (an amplification technique), producing discrete clusters of identical strands on the flow cell surface. Sequencing occurs by supplying the flow cell with a solution containing an enzyme that copies the attached DNA strands using nucleotides that have been fluorescently labeled with different colours to indicate whether the nucleotide is an A, T, C or G. The entire flow cell is then scanned every time a nucleotide is added, producing a fluorescent image that can be read using a computer to determine which nucleotide has been added to each cluster of fragments. Next, a chemical step removes the fluorescent group and the next labeled nucleotide is incorporated. This is repeated over and over until the entire fragment has been sequenced. For an illustration of this, see the figure on the reverse side of this fact sheet.



WHAT CAN HTS BE USED FOR?

HTS overcomes previous limitations to allow millions of bases to be sequenced much quicker and at lower cost compared to conventional methods. This technology can be used to uncover a vast amount of germline (sperm/egg cells) and somatic (all other cells) variation for mutation detection in disease genes or to better understand what makes up a normal individual. Pharmacogenetic use of HTS allows the detection of sequence variations that contribute to adverse drug reactions or even those variants that contribute to the relative effectiveness of drug treatments. HTS can be used to identify genomic structural variants such as copy number variations (microduplications, microdeletions), inversions, insertions and other complex DNA rearrangements that may be linked to a disease. Finally, HTS technologies can be used in meta-genomics, which is the sequencing of viral and bacterial genomes to identify novel pathogens that may exist in a sample.

HOW CAN I GET INVOLVED?

For more information about how we can assist you to undertake a genomic research study please call

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