What is Genomics?

• Each cell contains a complete copy of an organism’s genome, or blueprint for all cellular structures and activities.

• The genome is distributed along chromosomes, which are made of compressed and entwined DNA.

• Cells are of many different types (e.g. blood, skin, nerve cells), but all can be traced back to a single cell, the fertilized egg.

• Genomics is the study of molecular information to understand natural human variation and disease.
Cell Morphology

http://probes.invitrogen.com/resources/education/tutorials/4Intro_Flow/player.html
Central Dogma

The Central Dogma of Molecular Biology

DNA → RNA → Protein

Replication
DNA duplicates

Transcription
RNA synthesis

Translation
Protein synthesis

(Amy Vierstraete 1999)
TCAGTTGGAGCTGCCACCGCTCTCTCCTACATCCACGTCCTGTAGCTCTATGACCTCCACCTTTGAGTCCCTCCTCCTACACCTGACATGAAAAGGCACATGAGGATCCTCAAATACCCCGTGATCAGTCTCAGGGTAGCTCTCATAGCCTGGACAGGGCCCCCCTCGGGGGTTGCGCCCAGGTCCAGGCGGGGGATGCACAGCAACAGTCACCGAAGCAGAAGCCGTCACAGTGGTGATGGGCTGGCAGTAGCTGGGCACAGAGCTGCCCATGGCGGTGGACGTTGGGTTCCGAGGGTTGTGAGAACGGGCCCCACGGGGCCTGAGCGGTCCCTATTGCTAGGGCCAGAATGCCCTTCAGTAGAAATTTCAAAAGCGTCTCTGCGCGGTCTGTAGGGGGGTGCGGCCAAGCCTTCTCTAGGGGGATCCCTTCGAGGCTGCTGGCCTTGCCGTCCAGGGGACAAGGAGCCAGAGTCCAGGTGGGGCTGTTGCCGAGGGGTCAAGGGAGGCTGATGTCTGGAGTCCGGATGGACCACCTGCAGAGGAGAGACATAGGTCAACACAGGGAGGTAGGATGGTGGTGATGTTCCACCCACAAAACAAAACCTATTCCTTTAGAAACCTCCAGGATGTGAATCCTGCCTGCACCAGCACAGCTGGCTGGAGGCATATAGCCACTGCCCATAGATCTCAACTTACCCTCAACAACCAACTGCCCCAGGCCCTAAGTTCCTGCCTCAAAACTGCCAAGGCCTGGATAGCCAAGAGCCTGGGTGTCTTGGAAATATGCAACCATAAAATAGTAGCTTTTAGAGTATCGTAAAGCAGAGCAGAAAACTTCCACACAGATAGTGCTGTCTGTTAGGCAATACATCTCTGCTCTGACTATTAGGAATCTGGTTTCTGGGTCATATTAGTGTTGTTTTCACCTGTCCCCAGCCCTAAGGCTGCAGCAGAACAAAACAAAGGCACGACACGAATAAGCCACGAAGACAATAACGATTTTTGTATCAAGCGTCCTCTCCCATTTCAGCTTACCTGACAATGAAATCAAATTCGGACCCTGCAAGCATCAGTACACCCAGCAGAGTGGACACAGCACCGTCCAGAACGGGAGCAGACATGTGCTCCAGAGCGAGCATAGCCCTGTGGTTCTTGTCCCCAATGGCTGTCAGAAAGGCCTGAACAAAGGAGAAAATTGACACGGTCACATTCTGGGTGTGGTAAAGTGCTCAGCTGTGTCTATACTTGGGTTTTGTAT...

Total amount of DNA in human genome: $3 \times 10^9$ base pairs (bp)
DNA (Deoxyribonucleic acids) are molecules to store genetic information of a living organism.

DNA consists of two polymers made from four types of nucleotides: adenine (A) guanine (G), cytosine (C) and thymine (T).

Purines: A, G; Pyrimidines: C, T

Two polymers are complementary to each other and from a double-helix structure

5’ –ACCGTTCGACGGTAA– 3’

3’ –TGGCAAGCTGCCATT– 5’

Watson and Crick 1953
Transcription

DNA: GTAATCCTC
RNA: GUAUCC
Translation

Transcription Factors

TF1

TAATAAAAATACCCACACAAATCTAA

TF2

CCACCCAC

TF1

TTAATAAAAATACCCACACAACTAAGGAT

Gene1

TF2

TAATAAAAAT

Gene2

TF1

TACTACCCACACAAATCTAA

Gene3

TF3

Diseases

Misregulation

Other genes

Activation

Repression

Other Interactions

Transcription factors
Epigenetics

http://nihroadmap.nih.gov/EPIGENOMICS/images/epigeneticmechanisms.jpg
Nucleic acid hybridization

(a) DNA is denatured by heating.
(b) Renaturation on cooling.
(c) Hybridization.

Nucleic Acid Hybridization
Central Dogma

DNA
WG-seq
Exome-seq
SNP-arrays

Goals
SNP
Small indels
Large SV
Copy number

The Central Dogma of Molecular Biology

Replication
DNA duplicates

Transcription
RNA synthesis

Translation
Protein synthesis

DNA → RNA → Protein

RNA polymerase
Nucleus
mRNA
Nuclear membrane
Cytoplasm
ribosome
mRNA
protein

(Andy Viethmese 1999)
Central Dogma

RNA
- RNA-seq
- Expression arrays (exon arrays)
- (tiling arrays)
- miRNA arrays
- shortRNA-seq

Goals:
- Quantify expression
- Changes
- Which genes are active
- Quantify splicing
Central Dogma

ChIP-seq: chromatin IP
Protein-DNA interactions

Main usage
Transcription factors
Histone modifications

Goals:
map TF genomewide
understand gene regulation

DNA methylation arrays, seq
Central Dogma

The Central Dogma of Molecular Biology

- Replication: DNA duplicates
- Transcription: RNA synthesis
- Translation: Protein synthesis

HiC
Long range DNA-DNA interactions

Proteomics
Ribosome profiling
Understand translation