**Short content of Lection**

**Lecture 1. Chromosome studies**

Chromosome studies are used in the general genetics clinic to determine a cause for developmental delay/mental retardation, birth defects, dysmorphic features, and/or autism. Chromosome analysis is also performed in the prenatal setting to determine whether a fetus is affected with aneuploidy or other chromosome rearrangements. Finally, chromosome abnormalities are often detected in cancer samples. A large number of different methods have been developed for chromosome analysis:

* Chromosome analysis using a [karyotype](http://en.wikipedia.org/wiki/Karyotype) involves special stains that generate light and dark bands, allowing identification of each chromosome under a microscope.
* [Fluorescence in situ hybridization](http://en.wikipedia.org/wiki/Fluorescence_in_situ_hybridization) (FISH) involves fluorescent labeling of probes that bind to specific DNA sequences, used for identifying aneuploidy, genomic deletions or duplications, characterizing chromosomal translocations and determining the origin of [ring chromosomes](http://en.wikipedia.org/wiki/Ring_chromosome).
* Chromosome painting is a technique that uses fluorescent probes specific for each chromosome to differentially label each chromosome. This technique is more often used in cancer cytogenetics, where complex chromosome rearrangements can occur.
* [Array comparative genomic hybridization](http://en.wikipedia.org/wiki/Array_comparative_genomic_hybridization%22%20%5Co%20%22Array%20comparative%20genomic%20hybridization) is a new molecular technique that involves hybridization of an individual DNA sample to a glass slide or microarray chip containing molecular probes (ranging from large ~200kb [bacterial artificial chromosomes](http://en.wikipedia.org/wiki/Bacterial_artificial_chromosome%22%20%5Co%20%22Bacterial%20artificial%20chromosome) to small oligonucleotides) that represent unique regions of the genome. This method is particularly sensitive for detection of genomic gains or losses across the genome but does not detect balanced translocations or distinguish the location of duplicated genetic material (for example, a tandem duplication versus an insertional duplication).

**Lecture 2-4. Basic metabolic studies**

Biochemical studies are performed to screen for imbalances of metabolites in the bodily fluid, usually the blood (plasma/serum) or urine, but also in cerebrospinal fluid (CSF). Specific tests of enzyme function (either in leukocytes, skin fibroblasts, liver, or muscle) are also employed under certain circumstances. In the US, the [newborn screen](http://en.wikipedia.org/wiki/Newborn_screening) incorporates biochemical tests to screen for treatable conditions such as [galactosemia](http://en.wikipedia.org/wiki/Galactosemia) and [phenylketonuria](http://en.wikipedia.org/wiki/Phenylketonuria) (PKU). Patients suspected to have a metabolic condition might undergo the following tests:

* Quantitative amino acid analysis is typically performed using the ninhydrin reaction, followed by [liquid chromatography](http://en.wikipedia.org/wiki/Liquid_chromatography%22%20%5Co%20%22Liquid%20chromatography) to measure the amount of amino acid in the sample (either urine, plasma/serum, or CSF). Measurement of amino acids in plasma or serum is used in the evaluation of [disorders of amino acid metabolism](http://en.wikipedia.org/wiki/List_of_amino_acid_metabolism_disorders) such as [urea cycle disorders](http://en.wikipedia.org/wiki/Urea_cycle_disorders), [maple syrup urine disease](http://en.wikipedia.org/wiki/Maple_syrup_urine_disease), and [PKU](http://en.wikipedia.org/wiki/Phenylketonuria). Measurement of amino acids in urine can be useful in the diagnosis of [cystinuria](http://en.wikipedia.org/wiki/Cystinuria) or renal [Fanconi syndrome](http://en.wikipedia.org/wiki/Fanconi_syndrome) as can be seen in [cystinosis](http://en.wikipedia.org/wiki/Cystinosis).
* Urine organic acid analysis can be either performed using quantitative or qualitative methods, but in either case the test is used to detect the excretion of abnormal [organic acids](http://en.wikipedia.org/wiki/Organic_aciduria). These compounds are normally produced during bodily metabolism of amino acids and odd-chain fatty acids, but accumulate in patients with certain [metabolic conditions](http://en.wikipedia.org/wiki/Inborn_error_of_metabolism).
* The acylcarnitine combination profile detects compounds such as organic acids and fatty acids conjugated to carnitine. The test is used for detection of disorders involving fatty acid metabolism, including [MCAD](http://en.wikipedia.org/wiki/Medium_chain_acyl_dehydrogenase_deficiency).
* Pyruvate and lactate are byproducts of normal metabolism, particularly during [anaerobic metabolism](http://en.wikipedia.org/wiki/Lactic_acid_fermentation). These compounds normally accumulate during exercise or ischemia, but are also elevated in patients with disorders of pyruvate metabolism or mitochondrial disorders.
* [Ammonia](http://en.wikipedia.org/wiki/Ammonia) is an end product of amino acid metabolism and is converted in the liver to [urea](http://en.wikipedia.org/wiki/Urea) through a series of enzymatic reactions termed the [urea cycle](http://en.wikipedia.org/wiki/Urea_cycle). Elevated ammonia can therefore be detected in patients with [urea cycle disorders](http://en.wikipedia.org/wiki/Urea_cycle_disorders), as well as other conditions involving [liver failure](http://en.wikipedia.org/wiki/Liver_failure).
* Enzyme testing is performed for a wide range of metabolic disorders to confirm a diagnosis suspected based on screening tests.

**Lecture 5-8. Molecular studies**

* [DNA sequencing](http://en.wikipedia.org/wiki/DNA_sequencing%22%20%5Co%20%22DNA%20sequencing) is used to directly analyze the genomic DNA sequence of a particular gene. In general, only the parts of the gene that code for the expressed protein ([exons](http://en.wikipedia.org/wiki/Exons%22%20%5Co%20%22Exons)) and small amounts of the flanking untranslated regions and [introns](http://en.wikipedia.org/wiki/Introns) are analyzed. Therefore, although these tests are highly specific and sensitive, they do not routinely identify all of the mutations that could cause disease.
* [DNA methylation](http://en.wikipedia.org/wiki/DNA_methylation) analysis is used to diagnose certain genetic disorders that are caused by disruptions of [epigenetic](http://en.wikipedia.org/wiki/Epigenetic) mechanisms such as [genomic imprinting](http://en.wikipedia.org/wiki/Genomic_imprinting) and [uniparental disomy](http://en.wikipedia.org/wiki/Uniparental_disomy).
* [Southern blotting](http://en.wikipedia.org/wiki/Southern_blotting) is an early technique basic on detection of fragments of DNA separated by size through [gel electrophoresis](http://en.wikipedia.org/wiki/Gel_electrophoresis) and detected using radiolabeled probes. This test was routinely used to detect deletions or duplications in conditions such as [Duchenne muscular dystrophy](http://en.wikipedia.org/wiki/Duchenne_muscular_dystrophy) but is being replaced by high-resolution [array comparative genomic hybridization](http://en.wikipedia.org/wiki/Array_comparative_genomic_hybridization) techniques. Southern blotting is still useful in the diagnosis of disorders caused by [trinucleotide repeats](http://en.wikipedia.org/wiki/Trinucleotide_repeat).
* [Short tandem repeats](http://en.wikipedia.org/wiki/Short_tandem_repeat) are unique markers that can be used to determine [haplotypes](http://en.wikipedia.org/wiki/Haplotypes) and are used in identity testing for maternal cell contamination.

**Lecture 9. Treatments**

Each cell of the body contains the hereditary information ([DNA](http://en.wikipedia.org/wiki/DNA)) wrapped up in structures called [chromosomes](http://en.wikipedia.org/wiki/Chromosomes). Since genetic syndromes are typically the result of alterations of the chromosomes or genes, there is no treatment currently available that can correct the genetic alterations in every cell of the body. Therefore, there is currently no "cure" for genetic disorders. However, for many genetic syndromes there is treatment available to manage the symptoms. In some cases, particularly [inborn errors of metabolism](http://en.wikipedia.org/wiki/Inborn_errors_of_metabolism), the mechanism of disease is well understood and offers the potential for dietary and medical management to prevent or reduce the long-term complications. In other cases, [infusion therapy](http://en.wikipedia.org/wiki/Infusion_therapy) is used to replace the missing enzyme. Current research is actively seeking to use [gene therapy](http://en.wikipedia.org/wiki/Gene_therapy) or other new medications to treat specific genetic disorders.