***Department of Biology, Faculty of Medicine in Pilsen, Charles University, Czech Republic***

**Subject: Medical Biology and Genetics (EA0102003); 1st year; 2nd semester; General Medicine**

**Learning goals and outcomes – GENETICS (summer semester)**

**1. Topic: Monohybridism, Determination of Theoretical Genotypic and Phenotypic Segregation Ratios**

Students are able to:

* **Define and use the terms in the right context:** gene, trait, allele, locus, genotype, phenotype, homozygote, heterozygote, complete and incomplete dominance, recessiveness, co-dominance; monohybridism; Mendel's laws, parental and filial generations (1st and 2nd filial generation), hybridization, hybrid, independent assortment, backcross, testcross, B1-generation, reciprocal cross, Punnett square, genotypic and phenotypic segregation ratios; lethal genes, dominant lethal allele, incompletely dominant lethal allele, recessive lethal allele; genomic imprinting, epigenetics, methylation, paternal and maternal imprinting, χ2-test
* **Explain and apply** the first and second Mendel’s laws in the examples
* **Derive** genotypic and phenotypic segregation ratios in the F1-generation using Punnett square assuming complete or incomplete dominance, or co-dominance
* **Derive** genotypic and phenotypic segregation ratios in the F2-generation using Punnett square assuming complete or incomplete dominance, or co-dominance
* **Derive** genotypic and phenotypic segregation ratios resulting from a cross of two individuals of any selected genotypes using Punnett square, assuming complete or incomplete dominance, or co-dominance
* **Explain** the back (test) cross and itsprinciple, and **understand** the importance of the B1-generation segregation ratios
* **Verify** statistically, using the χ2-test, the segregation ratios of the experimental group with the ideal/theoretical segregation ratios, and draw conclusions if the difference between both groups (ratios) is/is not statistically significant
* **List and explain** all types of non-Mendelian inheritance
* **Understand** the deviations from the ideal Mendelian segregation ratios in the case of lethal genes and gene imprinting

**2. Topic: Dihybridism, Polyhybridism and the Forked-Line Method**

Students are able to:

* **Define** and use the correct terms in the right context: dihybridism, dihybrid combination (Punnett) square, random segregation, polyhybridism; branching (forked-line) method (to derive frequency of particular gametic combinations, genotypes, and phenotypes including their segregation ratios); probability rules
* **Derive** the number, type, and frequencies of gametes produced by a dihybrid (polyhybrid)
* **Explain** and **apply** the third Mendel's law in various examples/tasks
* **Draw** a dihybrid Punnett square, and **derive** the genotypic and phenotypic segregation ratios of F2-generation
* **Understand** and to **apply** the branching method in the tasks focused on deriving gametic allelic combinations of any polyhybrid
* **Understand** and to **apply** the branching method in the tasks focused on genotypic and phenotypic segregation ratios of offspring derived from crosses of any two polyhybrids, assuming both complete and incomplete dominance
* **Apply** probability rules in relation to segregation ratios deriving, and **understand** what the probability means for a particular genotype / phenotype of the offspring
* **Explain** the shift in the phenotypic segregation ratio in a cross of two dihybrids where one gene involved is lethal

**3. Topic: Gene Linkage I**

Students are able to:

* **Define** and **use** the terms in the right context: gene linkage, principles of gene linkage and modification of segregation ratios, crossing-over, recombination fraction, linkage strength, Morgan number, Bateson number, centiMorgan (cM), linkage phase, cis (coupling) and trans (repulsion) allelic configurations, three-point test, chromosome map, linkage group, Morgan’s laws, genetic and physical mapping, lod score
* **Explain** why some gametic allelic combinations are more frequent than others, and their frequency relation to the linkage strength (distance of genes)
* **Express** the distance of two genes (linkage strength) using the Morgan and Bateson numbers, and to convert these two numbers; to derive the probability of crossing over from these numbers
* **Deduce** the distance between two genes (strength of linkage) using three point test cross
* **Derive** the frequency of gametic combinations from a genotype of an individual, and from known distances between genes (gene linkage)

**4. Topic: Gene Linkage II**

Students are able to:

* **Apply** knowledge from the previous topic (Gene Linkage I) in various tasks
* **Deduce** genotypic and phenotypic segregation ratios in the F2 generation (crossing two dihybrids in any linkage phase)
* **Construct** a gene map (sequence and order of three or more genes on a chromosome) and express the distance of neighbouring genes in cM using a three-point test cross (for a cis or trans linkage phase of a heterozygous parent)
* **Express** the distance of human genes using the lod score

**5. Topic: Sex and Heredity**

Students are able to:

* **Define** and **apply** the terms: autosomes, gonosomes (heterochromosomes), chromosome X and Y, chromosomal determination of sex (mammalian species - Drosophila and bird - Abraxas), homogametic and heterogametic sex; sex-linked inheritance (completely and incompletely), X-linked inheritance, pseudo-autosomal region (PAR); sex-influenced inheritance, sex-limited inheritance, pseudodominance, hemizygote, holandic inheritance, gonosomal dominant and gonosomal recessive inheritance, direct and indirect heredity; X chromosome inactivation, Barr body, mosaic; maternal and paternal chromosome; haemophilia A, colour blindness (daltonism), woman-carrier; baldness in humans, Xg blood group system
* **Deduce** the segregation ratios for F1 and F2 generations in tasks where the gene responsible for a trait in focus is located on a chromosome X (including reciprocal crosses); explain deviations from expected Mendelian ratios and different results of reciprocal crosses
* **Understand** the process of random chromosome X inactivation (Barr body formation), and its effect on the phenotype of a female heterozygote
* **Deduce** segregation ratios arising from a cross of two parents with known genotypes (gonosomal inheritance – examples: haemophilia A, daltonism, etc.)
* **Explain** the difference between sex-influenced and sex-limited inheritance, give examples; derive segregation ratios
* **Understand** the principle of blood group Xg expression (antigen formation), its inheritance, frequency (probability) in men and women
* Solve tasks combining gonosomal inheritance and gene linkage (two genes located on chromosome X)

**6. Topic: Gene Interactions and Polygenic Inheritance**

Students are able to:

* **Define** and **apply** the terms: gene interaction, reciprocal interaction, dominant epistasis, recessive epistasis, inhibition, complementarity, compensation, gene duplicity, gene multiplicity, gene duplicity non-cumulative, gene duplicity cumulative (with dominance, and without dominance); epistatic and hypostatic gene, pleiotropy, epistasis, modification of phenotypic segregation ratios due to gene interactions, functional relations between interacting genes; additive and multiplicative effects of genes; polygenic inheritance, quantitative traits, multifactorial inheritance, modifier genes, polygene, heritability, heritability coefficient, Pascal triangle, twin studies, monozygotic and dizygotic twins; absolute and relative risk of multiple polygenic trait, Edwards formula, first degree relatives
* **Explain** the changes in F2-generation phenotypic segregation ratios in the above mentioned interactions (in comparison with the expected Mendelian ratios)
* **Derive** phenotypic segregation ratios in all types of gene interactions (cross of any two parents with a known genotype)
* **Explain** the transition from monogenic to polygenic inheritance using the interaction cumulative duplicity without dominance
* **List** some examples of polygenic traits, and to **explain** why the inheritance of these traits is referred to as multifactorial; explain the concept of heritability and describe the method used to estimate the proportion of the hereditary in the phenotype
* **Determine** the proportion of a quantitative trait using the example of additive gene interaction
* **Express** the absolute risk of a complex polygenic trait (disease) occurrence in siblings, and children of an affected proband, using the Edwards formula; to express a relative risk of affection by the same complex polygenic trait

**7. Topic: Blood group system and Multiple Allelism**

Students are able to:

* **Define** and **apply** the terms: multiple alleles, antigen, agglutinogen, glycolipid and glycoprotein, glycosyltransferase; antibody, immunoglobulin, agglutinin, ABO blood group, co-dominance, complete dominance, antigens A, B, H; natural antibodies, IgM, alleles A1, A2, B, O; agglutination, hemagglutination, Bombay phenotype, (non) secretors, recessive epistasis; universal donors and universal recipients; Rh blood group, antigens C, E, D, Rh positivity (Rh +), Rh negativity (Rh-), anti-D antibodies, maternal and foetal blood incompatibility, haemolytic disease (foetal erythroblastosis), immunization; blood group system MNSs
* **Deduce** all potential blood group genotypes of ABO (for blood groups: A1, A2, B, A1B, A2B, O)
* **Understand** the relationship between all ABO blood group system alleles
* **Derive** all potential (possible) ABO blood groups of children of two parents with known blood groups; to deduce all the possible blood groups of a parent knowing the blood groups of the other parent, and their child/children
* **Explain** the expression of erythrocyte antigens A and B as a consequence of recessive epistasis between genes ABO and H
* **Explain** the secretion of antigens A and B as a consequence of recessive epistasis between genes ABO and Se
* **Explain** the inheritance of Rh blood group, and genes CE and D
* **Explain** the inheritance of the MNSs blood groups, and the relation of genes MN and Ss
* **Derive** all possible blood groups (various combinations of blood groups: ABO, Rh, Xg and MNSs) of children knowing the blood groups of both parents, or t all possible blood groups of one parent knowing blood groups of the other parent and their child/children
* Realize the fact that one trait (e.g. ABO blood group) may be inherited more frequently with another trait (e.g. nail-patella syndrome) due to gene linkage

**8. Topic: Immunogenetics and Multiple Allelism**

Students are able to:

* **Define** and **use** in the right context the terms: immunogenetics, multiple alleles, cells specific (adaptive) immunity, B-lymphocytes, B-cell receptor (BCR), plasma B cell, T- lymphocytes (CD4), Tc lymphocytes (CD8), antigen presenting cell (APC), immunogen, autoantigen, autotransplantation, xenoantigen, xenotransplantation, alloantigen, allotransplantation; HLA (Human Leukocyte Antigen), MHC-glycoproteins (MHC I and MHC II), MHC loci, transplantation antigens, histocompatibility (transplant) genes, tight linkage; haplotype, co-dominance, paternity test, transplantation (in)compatibility; immunodeficiency, autoimmune diseases
* **Explain** the inheritance of MHC antigens
* **Explain** the consequences (disadvantages) of a multiple MHC I allele (HLA-genes A, B, C) in the context of allogeneic transplantation
* **Explain** the implications (benefits) of a multiple MHC II gene alleles in relation to the immunity of an organism (population) against severe (e.g. bacterial) infections
* **Derive** possible combinations of HLA genes (haplotypes) in parents and their children
* **Apply** knowledge of HLA-allele combinations on paternity determinations; to decide whether or not the accused man can be the biological father of a child using their phenotypes or genotypes

**9. Topic: Genealogy**

Students are able to:

* **Define** and **apply** the terms in the context: the pedigree, the genealogical scheme, the standard symbols used in pedigrees, proband; types of inheritance: autosomal dominant (AD), autosomal recessive (AR), semidominant or autosomal incompletely dominant (SD), gonosomal dominant (GD), gonosomal recessive (GR), holandric, mitochondrial, sex-influenced and sex-limited; genetic heterogeneity, phenocopy, penetrance (complete and incomplete), variable expressivity, gene dose compensation (inactivation of X chromosome), de novo mutation, lethal genes; coefficient of kinship and coefficient of inbreeding
* **Interpret** symbols used in pedigrees/genealogy schemes
* **Describe** and **explain** the basic characteristics of all types of inheritance mentioned above, the usual patterns of expression/occurrence of a trait (disease) in pedigrees (for each type of inheritance), and to **analyse/complete** selected pedigrees in tasks
* **Identify** the (most probable) type of inheritance according to the occurrence of a trait in a family (genealogy scheme)
* **Calculate** and **explain** the probability of a trait occurrence in offspring of the last generation in a pedigree
* **Apply** the typical expression characteristics of above mentioned types of inheritance in blank or incomplete schemes, fill them to match reality as much as possible, to prove their knowledge

**10. Topic: Population Genetics, Hardy-Weinberg Law**

Students are able to:

* **Define** and **apply** the terms: population, population genetics, gene pool, panmixia, panmictic population, Hardy-Weinberg equilibrium (HW law), genetic equilibrium, allelic and genotypic frequencies; selection, mutation, migration, fitness, heterozygous advantage, genetic drift, genetic disequilibrium
* **Describe** the mathematical expression of the HW equilibrium, all variables, and **derive** and explain basic mathematical formulas
* List assumptions underlying Hardy–Weinberg equilibrium/law and explain deviations from these assumptions in the real world
* **Deduce** the frequency of pathological and healthy alleles, all genotypes and phenotypes in the analysed population in various tasks (calculation based on the known disease frequency in the population, or on the known frequency of a pathological allele) including autosomal or gonosomal completely or incompletely dominant traits (diseases)
* **Apply** mathematical modifications of the HW equilibrium to examples/tasks with multiple alleles (e.g. ABO blood system), including codominance and incomplete dominance, autosomal or gonosomal inheritance

**11. Topic: Genetic prognosis**

Students are able to:

* **Define** and **apply** the terms: genetic counselling, genetic prognosis, medical genetics, genetic prevention - screening programs, prenatal diagnostics; incomplete penetrance; carriers in autosomal recessive diseases, female carriers in gonosomal recessive diseases; probability rules, inbreeding, coefficient of kinship, coefficient of inbreeding
* **Draw** a pedigree according to the selected tasks, to mark the proband, and a trait (disease) in this scheme, to derive genotypes of all members of the family
* **Know** and **apply** the basic characteristics of different types of inheritance in pedigrees; to calculate the probabilities of being carrier/sick/healthy for individual members of the analysed family
* **Express** mathematically the probability of the birth of a sick child in an analysed family

**12. Topic: DNA diagnostics I**

Students are able to:

* **Define** and use in context following terms: DNA denaturation, nucleic acid hybridization in vitro, restriction fragments (restricts), restriction endonucleases (restriction enzymes), nucleotide probe, intragenic probe, complementary nucleotide sequences; direct and indirect DNA diagnostics; restriction fragment length polymorphism (RFLP), restriction maps, DNA fingerprinting, homozygotes and heterozygote in the length of restriction fragments; gel electrophoresis, Southern blotting, autoradiogram; informative and non-informative family; polycystic kidney disease
* **Describe** the difference between direct and indirect DNA diagnostics and their application; Advantages and disadvantages of both methods
* **Describe** the activity and importance of the restriction endonucleases, and the principle of separation of the resulting fragments by gel electrophoresis, their labelling, and visualization
* **Describe** the principle of the indirect DNA diagnostics (RFLP method), explain the implications of the gene linkage (between the gene responsible for the disease in focus, and the probe hybridization site)
* **Analyse** pedigrees (RFLP electropherogram) and to determine whether the individual (member of the analysed family) is a carrier (in recessive diseases) or heterozygote (in dominant diseases with incomplete penetration or late onset) or heathy, or will be ill; to identify an informative and non-informative family, and to be able to suggest alternative method to refine the unsuccessful analysis
* **Calculate** the prognosis based on the genealogy, and on DNA analysis, and compare results of both of methods

**13. Topic: DNA diagnostics II**

Students are able to:

* **Define** and use in context the following terms: DNA replication, polymerase chain reaction (PCR), amplification, amplicon, primers, Taq-polymerase, DNA intercalating fluorescent dye, PCR thermocycler, gel electrophoresis, quantitative (real time) PCR; haemophilia A and B, Huntington's chorea
* **Describe** the principle of the PCR method and its use in direct/indirect DNA diagnostics; to summarize its advantages and disadvantages
* **Describe** how the principle and results of RFLP analysis differ from principal and electrophoretic results of PCR
* **Interpret** the results of PCR analysis - based on the results of gel electrophoresis identify carriers of the pathological allele, and to derive/calculate the prognosis for other members of an analysed family, or for a foetus

**14. Topic: Credit test, and exam topics consultations**