

Course Goals

1. Describe the physiological relevance of basic biological processes discussed in this course, including how they are regulated by physiological signals, what their physiological consequences are, and how their dysregulation might result in disease states.
2. Apply knowledge about basic cell physiological systems learned in class to predict outcomes for physiological conditions not discussed in class.
3. Explain how perturbations (i.e., genetic mutations or environmental stimuli such as diet and exercise) affect the specific functions of cells, and how dysregulation of these processes can lead to disease through pathological changes in cell function.
4. Explain how biological structure is related to biological function for cells, organelles, and macromolecules.

Part I Topic Goals**A. Predict whether an organism is prokaryotic vs. eukaryotic and unicellular vs. multicellular and explain why.**

1. In your own words, define the term cell.
2. Compare and contrast prokaryotes and eukaryotes in terms of size, complexity, presence of a nucleus or organelles, and whether they can be unicellular or multicellular.
3. Give examples of different types of unicellular and multicellular organisms.
4. Explain the primary functions of eukaryotic cells.

B. Relate the composition (structure) to the function for organelles and macromolecules found in a typical cell.

1. Describe the basic structure and function of macromolecules (lipids, nucleic acids, proteins).
2. Describe how the levels of protein structure (primary, secondary, tertiary) influence protein function.
3. Describe how protein structure can be modified (phosphorylation/dephosphorylation, binding/unbinding of another protein, proteolytic cleavage).
4. Compare and contrast DNA and RNA in terms of their chemical composition, structure, and function.
5. In your own words, define the term gene, and be able to label the different parts of a gene and gene regulatory region.
6. Describe how phosphorylation can change the activity of a transcription factor.
7. Diagram the structure of the nucleus and the nuclear pore complex (NPC).
8. Compare and contrast the structure and function of the types of RNA (messenger, transfer, and ribosomal) involved in protein translation.

C. Identify how the sequence of macromolecules conveys biological information and how this information affects the biological function of the macromolecule.

1. Describe the Central Dogma of Biology. Explain the function DNA, RNA, and proteins and discuss how each can be modified by biological processes.
2. Explain how the following affect nuclear import and export of proteins:
 - a. Nuclear localization signals (NLS) and importins
 - b. Nuclear export signal (NES) and exportins
 - c. Phosphorylation/dephosphorylation
3. Describe the location and function of untranslated regions (UTRs) in RNA processing.
4. Describe the components (codons) and characteristics (non-overlapping, degenerate) of the Genetic Code.
5. Predict how mutations (missense, nonsense, frame-shift, and splicing) affect the RNA sequence, and subsequently, the resulting protein.
6. Describe the proteins and RNA sequences involved in alternative splicing and the physiological regulation of splicing

D. Identify and/or diagram and explain the steps by which a cell creates, transports, and destroys macromolecules through the processes of transcription, translation, and RNA and protein degradation.TRANSCRIPTION

1. Describe the primary function of general transcription factors (GTFs) (TATA binding protein (TBP), TFIIIs, and TFIIH helicase).
2. Diagram the steps involved in transcription beginning from binding of TBP to the TATA box and ending at creation of an RNA by the polymerase.
3. Describe how transcription factors can activate or repress transcription.
4. Describe the role of histone acetyl transferases (HATs) and histone deacetylases (HDACs) in chromatin (DNA) packing and be able to predict what effect each would have on transcription.

IMPORT/EXPORT

1. Illustrate the steps involved in the general import of any given protein into the nucleus beginning at binding of importin to the cargo protein and ending with the cargo protein engaging in its nuclear function.
2. Describe, compare, and contrast all of the steps involved in the nuclear import/export of STAT (transcription factor), FoxO (transcriptional activator), and NFAT (transcriptional activator).

RNA PROCESSING

1. Compare and contrast the types of RNA processing (5' capping, 3' polyadenylation, and RNA splicing) in terms of when they occur, proteins involved, and their primary functions.

RNA REGULATION/SPLICING

1. Diagram the steps involved:
 - a. Physiological regulation of RNA stability and describe the sequences and proteins involved in this process.
 - b. RNA splicing including the proteins and RNA sequences involved
 - c. Alternative splicing of fibronectin
2. Provide reasons (or biological benefits) for why alternative splicing occurs. (NOTE: These are different from the FUNCTION of splicing, which is to create a mature mRNA that codes for a functional protein).
3. Describe the process and protein sequences involved in mRNA export from the nucleus, and differentiate how mRNA export differs from protein export.

TRANSLATION

1. Diagram the steps of protein translation (initiation, elongation, termination) including the proteins and sequences involved in each.
2. Diagram the steps and proteins involved in IGF-I regulation of protein synthesis/translation.

PROTEIN DEGRADATION

1. Compare and contrast the functions of protein degradation versus RNA degradation.
2. Diagram the main protein degradation pathways (ubiquitin, calpain, caspase, and lysosomal-mediated) in the cell, and be able to identify which of them is the most quantitatively important.
3. Diagram and explain the steps and proteins involved in:
 - a. Ubiquitin-dependent protein degradation
 - b. Protein degradation of NF-kappaB
 - c. IGF-I regulation of protein degradation
4. Describe the ways IGF-I influences protein content in the cell, and predict how changes in IGF-I influence overall cell growth.

Part II Topic Goals**Cytoskeletal Elements**

1. Describe the purpose of the cytoskeleton.
2. Compare and contrast the cytoskeletal filaments (actin, intermediate, microtubules) in terms of:
 - a. Protein composition/structure
 - b. Size (diameter)
 - c. Distribution within the cell
 - d. Functions (structural, movement)
 - e. Stability
 - f. Polarity
 - g. Assembly & regulation
3. Diagram the steps, proteins, and structures involved in:
 - a. Cytoskeletal filament assembly (actin, intermediate, microtubule)
 - b. Cell migration
 - c. Chemotaxis
 - d. Cross-bridge cycling
 - e. Calcium activation of skeletal muscle contraction
 - f. Smooth muscle relaxation
 - g. Ciliary/flagellar movement
 - h. Separation of sister chromatids during mitosis
 - i. Microtubule “walking”
 - j. Organelle movement/axonal transport
4. Given a scenario, identify the factors or poisons affecting (or not affecting) cytoskeletal filament assembly/disassembly and stability.
5. Describe what structures the microtubule organizing structures (MTOC) (centrosome, spindle poles, MTOC, basal body) are critical for.
6. Compare and contrast the various motor proteins (myosin, kinesin, dynein) in terms of structure, subunit composition, type of motor (processive, non-processive), directionality (anterograde, retrograde), and function.
7. Describe the main components of the mitotic spindle apparatus.
8. Compare and contrast cilia and flagella in terms of location, structure, and function.

Muscle Contraction

1. Compare and contrast the different types of muscles cells (skeletal, cardiac, smooth) in terms of function, size, and organization of cytoskeleton.
2. Describe the main units and subunits of a sarcomere (thin filaments – actin, troponin, tropomyosin, thick filaments - myosin, Z disk, A band) and their functions.
3. Diagram the sliding filament model during relaxed and contracted muscle states.
4. Compare and contrast skeletal/cardiac vs. smooth muscle contraction in terms of speed, initiation signal, calcium activation of thick or thin filament, and inactivation signal.

Extracellular Matrix and Mechanical Signaling

1. Describe the purpose of the extracellular matrix.
2. Compare and contrast the structure and function of the main components of the extracellular matrix (collagens, proteoglycans, multiadhesive proteins).
3. Given a scenario, identify the cause of fibrosis.
4. Compare and contrast the types of specialized extracellular matrix (bone, cartilage, tendon) in terms of the cell type that produces them, what they consist of, and their function.
5. Describe the main components and functions of cell-matrix adhesions.
6. Compare and contrast the types of cell-matrix adhesions (integrin-mediated, dystroglycan-mediated attachments) in terms of what they link and the proteins involved in each.
7. Diagram the steps and proteins involved in integrin-mediated mechanical signaling.

Mutations

1. Predict the functional significance of a mutation to the following proteins:
 - a. Proteins involved in cell migration
 - b. Thick and thin filaments
 - c. Ciliary and flagellar proteins
 - d. Cell matrix adhesion proteins
 - e. Cytoskeletal filaments (actin, intermediate, microtubules)
 - f. Proteins involved in chromatid separation

Energetics

Predict the effects of the following on mitochondrial biogenesis and/or ATP production: mitochondrial diseases, exercise training, hypoxia, and changes in temperature.

Mitochondria

1. Identify examples of cellular mechanisms that require energy.
2. Describe the key features of mitochondria.
3. Compare and contrast the main steps of oxidative phosphorylation (glycolysis, citric acid cycle, electron transport chain, synthesis of ATP) in terms of where and when they occur, the input and output molecules, and their primary functions.
4. Describe the processes turned on/off by AMP kinase to restore energy balance (catabolism vs. anabolism).
5. Describe the steps and major proteins involved in mitochondrial biogenesis, and explain how biogenesis can be altered.
6. Given symptoms of a myopathy, determine what type of mitochondrial disorder and/or mutation exists, and vice versa.
7. Explain the effect of heteroplasmy on mitochondrial diseases.
8. Compare and contrast nuclear vs. mitochondrial gene mutations in terms of what processes they affect, how they are inherited and passed, types of symptoms, and when they manifest.

Lipids

For a given scenario:

1. Identify the lipoprotein complex involved in lipid transport (chylomicrons, VLDL, LDL, or HDL) including what the complex transports and where.
2. Predict which gene(s) influence lipid transport.
3. Identify the lipid import pathway that has been activated (transport protein-mediated uptake or lipoprotein-mediated endocytosis) including which step(s) and/or protein(s) were affected.
4. Determine how hormones and/or adipokines influence fatty acid mobilization, fat utilization, and food intake.
5. Predict how leptin levels would be influenced by altered food intake (e.g., obesity, starvation.)

Atherosclerosis

1. Define atherosclerosis and list the steps involved in its progression.

Hypoxia

1. List the environmental and disease states characterized by hypoxia.
2. Given a scenario, identify which specific step of ATP synthesis is affected by hypoxia.
3. Describe the main cellular responses of hypoxia including the speed and the physiological effects of the gene(s) and/or protein(s) involved.
4. Explain how activation of Hif-1alpha influences oxygen delivery to the cell.
5. Describe how hypoxia can be used to improve endurance exercise performance.

Heat and Cold

1. Describe the effects of temperature on cellular functions.
2. Explain how shivering and metabolic uncoupling increase body temperature.
3. Explain how thyroid hormones influence basal metabolic rate and metabolic uncoupling.
4. Diagram the steps involved in activation of heat shock proteins (HSPs).

Part III**Epithelial Transport and Glucose Uptake**

1. Describe the main functions of epithelial cells.
2. Explain what is meant when it is said that epithelial cells are polarized.
3. Compare and contrast the types of cell-cell adhesions in epithelial cells (tight junctions, adherens junctions, desmosomes) in terms of their location, their function, the cytoskeletal systems they connect to, and the proteins that comprise them.
4. Given a scenario, predict the effects of a mutation to one of the cell-cell adhesion proteins.
5. Describe the main types of transepithelial transport (paracellular pathway, transcellular pathway) and give examples of each.
6. Describe the factors that can increase tight junction leakiness and therefore paracellular transport (physiological signaling, genetic defects, bacterial toxins, snake and insect venom).
7. Describe the types of transcellular transport across epithelia (transcytosis, transporter-mediated) and give examples of each.
8. Describe the types of transporters (uniporters, cotransporters) and types of cotransporters (symporters, antiporters) found in epithelial cells.
9. Given the starting conditions, design a method for transporting a substance across an epithelial cell barrier.
10. Describe the steps and key players involved in glucose transport across the gut epithelium.
11. Describe the factors contributing to the differential distribution of proteins on the apical and basolateral membranes.
12. Describe the steps involved in glucose transport into muscle and explain the role of insulin in this process.
13. Describe the types of diabetes (Type I/Juvenile onset, Type II/Adult onset), and explain the effects of diabetes or exercise on glucose uptake.
14. Predict the effects of mutations to proteins involved in glucose uptake on blood insulin and glucose levels.

Pumps, Channels, and Membrane Potential

1. Categorize the different membrane proteins (transporters, cotransporters, membrane pumps, ion channels) as to whether they participate in active transport, facilitated diffusion, or secondary active transport.
2. Identify ANY AND ALL channels discussed in terms of whether they are non-gated, voltage gated, or ion channel gated.
3. Describe the main functions of membrane pumps.
4. Describe the main types and functions of ion channels (non-gated, voltage gated, ligand gated) and give examples of each.
5. Describe the function of the different segments of the voltage gated ion channel (P segment, voltage-sensing alpha helix, channel-inactivating segment) and explain how they influence ion channel function.
6. Describe the structure of the membrane and its different segments during the closed, open, and inactive states.

7. List 4 ions that are differentially distributed across the cell membrane and explain what the function of this differential distribution is.
8. Describe the factors contributing to resting membrane potential.
9. Explain how changes in membrane potential are important for muscle contraction, hormonal secretion, neural communication.
10. Diagram the steps involved in insulin secretion.
11. Diagram the different phases of the action potential (depolarization, repolarization, hyperpolarization), and explain how these phases correspond with the opening and closing of ion channels.

Synaptic Transmission

1. Diagram the steps involved in synaptic transmission.
2. Compare and contrast excitatory vs. inhibitory postsynaptic potentials in terms of which channels they open and their effect on the postsynaptic membrane.
3. Define threshold potential and describe the types of summation that can allow a neuron to reach it.
4. Describe the main methods for terminating synaptic transmission.
5. Distinguish how drugs (Prozac, cocaine, Ritalin) and poisons (insecticides) affect termination of synaptic transmission.
6. Distinguish between learning and memory.
7. Distinguish how short-term memory and long-term memory differ with respect to synaptic changes.
8. Diagram the steps and proteins involved in the habituation and long-term potentiation.
9. Predict the consequences, both cellular and on learning and memory, of mutations to the proteins involved in habituation or long-term potentiation.
10. Design a process by which short-term potentiation or long-term habituation might occur.

Signaling Pathways

1. Describe the types and subtypes of cell-cell signaling found in multicellular organisms, give examples of each, and explain what they are important for.
2. Given a scenario, predict whether a novel factor is hormonal vs. autocrine/paracrine and lipophilic vs. hydrophilic.
3. Explain how synaptic signaling is similar to or different from other forms of paracrine signaling.
4. Diagram the steps involved in lipophilic factor signaling.
5. Given a scenario, predict whether something acts as an agonist or antagonist.
6. Compare and contrast the functional classes of cell surface receptors (ion channel-linked, catalytic, G-protein linked) in terms of function, and give examples of each.
7. Diagram the steps involved in G-protein activation and inactivation.
8. Predict the effects of mutations to G-protein linked receptors or subunits on G-protein activation and signaling.
9. Compare and contrast the main types of second messengers (cAMP, cGMP, IP3 and DAG, CA²⁺) in terms of the intracellular proteins they activate and their effector.

10. Explain how protein kinases and phosphatases change the activity of other proteins to produce the desired cellular response.
11. Evaluate the ramifications of amplification and termination with respect to cell signaling.
12. Describe the mechanisms involved in signal termination.

G-protein receptor mediated-signaling & autonomic nervous system

1. Compare and contrast the sympathetic and parasympathetic nervous systems in terms of the hormones they use, their receptors, and their effects on fat/glycogen storage, bronchioles, blood vessels, and heart rate.
2. Categorize all the examples of G protein signaling in terms of whether they are:
 - a. Adenylate cyclase activating
 - b. Phospholipase C activating
 - c. Ion channel activating
 - d. β 1 adrenergic
 - e. M2 muscarinic
 - f. M3 muscarinic
3. Explain the function of the enzymes involved in glycogen storage (glycogen synthase) and degradation (glycogen phosphorylase).
4. Diagram the steps and proteins involved in:
 - a. Epinephrine (β 1)-induced glycogen breakdown
 - b. Acetylcholine (M3)-induced bronchial smooth muscle contraction
 - c. Acetylcholine (M3)-induced blood vessel endothelium smooth muscle relaxation
 - d. Acetylcholine (M2)-induced regulation of heart rate
5. Explain why M3 muscarinic signaling has differing effects on smooth muscles in the bronchi vs. smooth muscles in the blood vessels.
6. Explain how the pacemaker potential drift determines heart rate.
7. Compare and contrast the adrenergic (β 1) and acetylcholine receptors (M2 muscarinic, M3 muscarinic, and nicotinic) in terms of their location, receptor type, and mechanism of action, and give examples of each.
8. Predict the effects of agonists and antagonists to the β 1 adrenergic, M2 muscarinic, and M3 muscarinic pathways on function of the heart, blood vessels, and bronchioles.

Catalytic receptors and the regulation of cell growth and proliferation

1. Diagram the steps and proteins involved in cell growth and proliferation:
 - a. General model of catalytic receptor action
 - b. Growth hormone-JAK-STAT pathway
 - c. TGF-beta signaling
 - d. Growth factor signaling
2. Predict the effects of mutations to genes involved in cell growth and proliferation.
3. Compare and contrast the catalytic receptors (associated kinase activity, intrinsic receptor kinase) in terms of how they activate cell signaling, and give examples of each.
4. Describe the mechanisms of inactivation of the JAK/STAT pathway.
5. Compare and contrast the 3 types of TGF-beta receptors in terms of intrinsic kinase activity.
6. Compare and contrast the functions of the MAP kinase signaling pathways (ERK, JNK, p38).

Part IV**Cell Cycle**

1. Given an example of a type of cell, predict whether it is likely to be in G₀ or in the cell cycle.
2. For each phase (interphase, mitosis) and sub-phase (G₀, G₁, S, G₂, prophase, metaphase, anaphase, telophase) of the cell cycle, identify the following:
 - a. Function(s) of the phase
 - b. Events that take place within each phase
 - c. Checkpoints
 - d. Restriction points
3. Explain how changes in mitotic cyclin/cyclin-dependent kinase (CDK) expression and activity influence entry, transition, exit, and termination of the different phases of the cell cycle. Be sure to include a discussion of:
 - a. Increased/decreased expression of cyclin and CDKs
 - b. Binding of CDKs to cyclin
 - c. Phosphorylation/dephosphorylation of cyclin/CDK complex
 - d. Increased/decreased expression of cyclin inhibitory protein (CIPs) and kinase inhibitory protein (KIPs)
 - e. Phosphorylation/dephosphorylation of CIPs and KIPs
4. Diagram the steps and proteins involved in:
 - a. Separation of sister chromatids during anaphase
 - b. Cyclin D and passage through the restriction point
 - c. G₁ to S phase transition
 - d. Degradation of mitotic cyclin/CDKs at the end of M phase
 - e. p53 cell cycle inhibition
5. Predict the effects of drugs, diseases, or mutations on the cell cycle, and identify which phase of the cell cycle would most likely be affected.
6. Given a modification to a step, signal, or phase involved in the cell cycle, identify the mutation that may have occurred to cause this change.

Stem Cells & Cellular Development

1. Given a set of cells, predict the relative level of potency (totipotent, pluripotent, unipotent).
2. Given a scenario of a mutation or change to the layers of the gastrula (ectoderm, mesoderm, endoderm), identify which tissue(s) would be affected.
3. Explain how stem cells know the location of the tissues they are supposed to form. Be sure to include a discussion of:
 - a. Cell-cell signaling (notch and delta)
 - b. Morphogen gradients (fibroblast growth factors 4 and 8, Wnt7a, sonic hedgehog, retinoic acid)
 - c. Master transcription factors involved in patterning (Hox gene, master regulatory genes)
 - d. DNA Methylation

4. Predict the effects of mutations to the factors involved in cell fate restriction during development.
5. Given a scenario involving a change to normal cellular development, predict the defect/mutation/change in gene expression that may have occurred to cell patterning.
6. Given a description of the morphogen concentrations experienced by a cell, predict where on the limb a cell is.
7. Conversely, given a location on the limb, determine the morphogen(s) that led to the patterning.
8. Compare and contrast the mechanisms of stem cell determination and differentiation in terms of:
 - a. Processes
 - b. Myogenic regulatory factors (MyoD, myf-5, Myogenin, MRF4)
 - c. Signals
 - d. Purpose of each mechanism
9. Diagram the key events and proteins involved in skeletal muscle (myogenesis), bone, and neuronal determination and differentiation.
10. Given a scenario in which stem cell differentiation and/or determination are altered, predict the gene and cell type involved.
11. Conversely, if given a scenario involving a change to a gene involved in cell determination or differentiation, predict the outcome.
12. Given a scenario, predict whether a stem cell in a particular tissue is continuously active, quiescent, limited, or there will be no stem cell replacement.
13. Compare and contrast the advantages and disadvantages of using embryonic vs. adult stem cells for organ replacement in a human.

Cell Death & Aging

1. Compare and contrast apoptosis (regulated, programmed cell death) and necrosis (accidental cell death) in terms of how they eliminate unneeded or damaged cells, their requirements, and their role in inflammation; and be able to give examples of each.
2. Diagram the various steps and proteins involved in activation and inhibition of apoptosis.
3. Identify disease(s) that occur due to excessive or insufficient apoptosis.
4. Conversely, predict the likely outcome of disruptions to apoptosis (e.g., mutations to various pro- and anti-apoptotic genes, removal of tropic factors) on developmental processes and the likelihood of the cell undergoing apoptosis.
5. Describe the factors that contribute to aging:
 - a. Decreased secretion of growth factors and hormones (growth hormone/IGF-1, leptin)
 - b. Decreased proliferative capacity of cells (telomere length)
 - c. Increased somatic cell DNA changes (reactive oxygen species, mutations)
6. Identify what types of cells would have longer or shorter telomeres.
7. Define sarcopenia, and describe the factors contributing to this phenomenon.
8. Discuss the pros and cons of exercise in elderly populations.

Cancer

1. Explain the sources of DNA changes during cell proliferation (inherited, DNA copying errors, DNA damaging agents).
2. Provide examples of gain-of-function and loss-of-function mutations, and explain the likelihood of that mutation in developing cancer.
3. Given a scenario in which the quantity and/or activity of a protein changes, determine the type of mutation (gain-of-function vs. loss-of-function) and genes affected (proto-oncogenes vs. tumor suppressor genes).
4. Compare and contrast benign vs. malignant tumors in terms of:
 - a. Ability to metastasize
 - b. Level of harm
 - c. Capability to perform angiogenesis
 - d. Methods of removal
5. Summarize the 6 factors involved in formation of malignant cancer. Be sure to include a discussion of the genes and types of mutations (gain-of-function vs. loss-of-function) involved in each process.
 - a. Evasion of apoptosis
 - b. Limitless replicative potential (immortalization)
 - c. Sustained angiogenesis
 - d. Hypoxia resistance
 - e. Tissue invasion and metastasis
 - f. Self-sufficiency in growth signals (hyperproliferative)
6. Identify whether a mutation is homozygous or heterozygous to cause cancer.
7. Describe the various roles of p53 (tumor suppressor gene) in preventing cancer.
8. Discuss the mechanisms and pros/cons of the various cancer treatments (surgery, radiation therapy, chemotherapy, immunotherapy, cancer gene therapy).