BENG 100 Frontiers of Biomedical Engineering
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Chapter 6

SUMMARY

In this chapter, cell signaling was presented within the context of three physiological systems that utilize communication extensively: the nervous system, endocrine system, and immune system.

- The nervous and endocrine systems are the main control systems of the body, helping to maintain homeostasis.
- The immune system constantly monitors for the presence of foreign invaders and acts to rid them from our bodies.
- Cells are capable of executing controlled responses to internal and external changes in the environment through intricate signal transduction pathways.
- Cells communicate with each other via signaling ligands which interact with receptors located on the surface or inside the target cell.
- Receptor-ligand binding can activate different signal transduction pathways depending on the type of ligand, receptor, and target cell.
- Although the signal transduction pathways and responses may differ, all cellular communication proceeds in a cascade fashion: a ligand binds to receptor; enzymes and 2_{nd} messengers transduce and amplify the signal inside the cell; the cell responds to the signal.
- The consequences of signal transduction pathways (or cellular response) vary, ranging from opening or closing of an ion channel to activating transcription of target genes. Many diseases are the result of failures or alterations in signal transduction. Any component of a signaling pathway can be affected. Understanding these pathways has also enabled development of therapeutic drugs that can inhibit or enhance the biological responses. Biomedical engineers can use the knowledge of receptor-ligand interactions in the design of new therapeutics, diagnostic methods, and biosensors.

KEY CONCEPTS AND DEFINITIONS

action potential – electrical signal or nerve impulse

affinity – strength of binding of one molecule to another at a single site

agonist – molecule which can bind to a receptor and activates a receptor

amplifier – a device that increases the magnitude of an input

antagonist – a molecule that competes with a ligand and inhibits receptor activation

antigen presenting cells – cells that display peptide fragments from antigens on their surface along with other molecules required for the activation of T cells

apoptosis – an active process of programmed cell death, characterized by cleavage of chromosomal DNA, chromatin condensation, and fragmentation of both the nucleus and the cell; also referred to a cell suicide

autocrine signaling – a type of cell signaling in which a cell secretes a molecule to which it also responds

axon - long process extending from the cell body of a neuron that conducts an electric impulse (action potential) away from the neuron

CD4 – co-receptor protein on helper T cells which recognizes antigens bound to MHC class II molecules

CD8 – co-receptor protein on cytotoxic T cells which recognizes antigens bound to MHC class I molecules

cell-mediated immunity – adaptive immune response in which antigen-specific T cells have the main role

clonal expansion – proliferation of antigen-specific lymphocytes in response to antigenic stimulation, an important step in adaptive immunity

complement system – a set of proteins activated by the innate immune system which facilitate uptake and de

connexins - a group of homologous proteins which form the intermembrane channels of gap junctions

cytokine – any of numerous secreted, small proteins (e.g., interferons, interleukins) that bind to cell-surface receptors on certain cells to trigger their differentiation or proliferation

cytotoxic T cell – a type of T cell which kills other cells when it recognizes a peptide fragment on MHC class I proteins with its CD8 receptor

dendrite - process extending from the cell body of a neuron that is relatively short and typically branched and receives signals from axons of other neurons

depolarization - a change in the membrane potential in the positive direction, from its normal negative level.

dimerization – process in which two polypeptide chains bind to each other.
endocrine signaling – a type of cell signaling in which cells secrete molecules that are carried by
the circulation to distant target cells.

effector – proteins located inside the cell which carry out the action of the original signal of a ligand binding to a receptor.

equilibrium association constant (K_a) – the ratio of the concentration of the bound receptor [*RL]* to the concentrations unbound receptor [*R]* and ligand [*L*]; the inverse of the equilibrium dissociation constant; the higher the K_a, the tighter the binding between the receptor and ligand

equilibrium dissociation constant (K_D) – the equilibrium constant for the dissociation of a complex of two or more biomolecules into its components; the ratio of the concentrations of the unbound receptor [*R*] and ligand [*L*] to the bound receptor [*RL*]. (See Chapter 2)

gap junctions - a site of electrical connection between the membranes of two cells, that uses connexins to bridge the gap between the insides of the two cells and allow small molecules such as ions to cross directly from one cell to the other

glial cell - cell that provides support to nerve cells, but does not participate directly in synaptic interactions and electrical signaling.

helper T cell – a type of T cell that stimulates other lymphocytes when it recognizes a peptide fragment on MHC class II proteins with its CD4 receptor

heterodimer – a protein consisting of two different polypeptide chains

homeostasis - the body's ability to maintain a stable internal environment in response to a changing external environment or internal malfunction

homodimer – a protein consisting of two of the same polypeptide chains

hormone **-** a ligand that induces specific responses in target cells especially in the endocrine system; hormones regulate the growth, differentiation, and metabolic activities of various cells, tissues, and organs.

humoral immunity – adaptive immune response in which antibodies produced by B cells cause the destruction of extracellular microorganisms and prevent the spread of intracellular infections

hydrophilic - polar or charged molecules that dissolve readily in water (see Chapter 2)

hydrophobic - nonpolar molecules that are insoluble in water (see Chapter 2)

hyperpolarization – a change in the membrane potential, making the cell more negative than its resting membrane potential

ion channels - a membrane protein that forms an aqueous pore through which charged ions can cross the membrane

kinase – an enzyme that catalyzes the phosphorylation of certain molecules using ATP as a phosphate source

ligand - any molecule, other than an enzyme substrate, that binds tightly and specifically to a macromolecule, usually a protein, forming a macromolecule-ligand complex.

lysis – the breaking of a cell's membrane which results in the death of the cell
MAP Kinases - *mi*togen-*ac*tivated *p*rotein kinases which are activated in response to a variety of growth factors and other signaling molecules. MAP kinases phosphorylate serine or threonine residues in their substrates.

MHC class I molecules – receptors which present peptides generated in the cytosol to CD8 T cytoxic cells

MHC class II molecules – receptors which present peptides degraded in intracellular vesicles to CD4 T helper cells.

monomer – a protein consisting of one polypeptide chain

myelin – protein and lipid material produced by glial cells which insulates regions of an axon

nernst potential – the potential across a semipermeable membrane caused by a difference in concentration of an ion on each side of the membrane. The Nernst potential occurs when the concentration gradient is equal to the voltage gradient.

neurotransmitter - a small, hydrophilic molecule that carries a signal from a stimulated neuron to a target cell at a synapse

Nodes of Ranvier – unmyelinated regions of an axon which are exposed to the extracellular space and contain the Na_+ channels for the propagation of action potentials

oligodendrocyte - a type of glial cell which produces myelin in the central nervous system

oncoprotein – a product of an oncogene(s) which can induce one or more characteristics of cancer cells, such as proliferation.

opsonization – process by which specialized proteins of the complement system or antibodies bind to pathogens and facilitate phagocytosis of the pathogen by macrophages or neutrophils.

paracrine signaling – a type of cell signaling in which a molecule secreted by one cell acts on a neighboring target cell

phagocytosis – the uptake of large particles by a cell; particles are taken up in vesicles which fuse to the lysosome

phosphatase – an enzyme that catalyzes the removal of a phosphate group from a protein phosphorylation – covalent addition of phosphate group to a protein

proteolysis – hydrolysis of proteins into peptides and amino acids by cleavage of their peptide bonds

receptor – specialized protein on a cell's surface, but anchored in the cell membrane, which binds to a specific ligand and transmits an appropriate signal refractory period – period after a neuron fires during which a stimulus will not evoke a response

repolarization – a change in membrane potential in the negative direction, making the cell interior more negative and returning it to the resting membrane potential saltatory

conduction - rapid, efficient propagation of action potentials due to myelinated axons

Schwann cell - a type of glial cell which produces myelin in the peripheral nervous

system signal transduction pathway – a series of events initiated by the binding of a ligand to its receptor that allows a cell to communicate with and respond to other cells or its extracellular environment

synapse – specialized junction which allows two nerve cells to communicate either through chemical or electrical signals

synaptic cleft – extracellular space between two adjacent nerve cells into which neurotransmitters are released by the pre-synaptic cell

transducer – a device that converts a signal from one form to another transfer function - a mathematical expression of the relationship between the input signal and output signal of a system

tumor suppressor proteins – products of tumor suppressor genes which normally function to suppress tumors so when they are inactivated in some types of cancers, they promote tumor development

QUESTIONS

1. Describe each of the following diseases. What components of the nervous system are affected? How do these abnormalities result in impaired function?

   a. Epilepsy
   b. Schizophrenia
   c. Alzheimer's Disease
   d. Parkinson's Disease
   e. Multiple sclerosis (MS)
   f. Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig's Disease)
   g. Huntington's Disease
   h. Myasthenia Gravis
   i. Stroke

2. Action potential propagation is unidirectional. What ensures that the action potential is passed along the length of the axon in only one direction from the dendrites to the axon terminal? Also, what structural features of the synapse contribute to the one-way information transfer from the presynaptic neuron to the postsynaptic neuron?

3. Juvenile Diabetes (Type I) is an autoimmune disease. What does this mean and how does this lead to high blood glucose levels?

4. Human immunodeficiency virus (HIV) infects T cells expressing CD4. How does this infection lead to acquired immunodeficiency syndrome (AIDS)?

5. One of the transducers in many growth factor signaling cascades is *ras*. How can mutations in *ras* (found in some types of cancers) contribute to transforming a normal cell into a tumor cell?

6. Find a receptor which utilizes the MAP kinase cascade. Sketch a diagram showing the proteins and enzymes involved in the cascade and describe the steps.

7. Why is it important to characterize the MHC type of an individual before bone marrow or organ transplantation?

8. Immunosuppressive drugs such as cyclosporin A and tacrolimus are used in organ transplant recipients. What makes these drugs immunosuppressive (i.e., their mode of action)? What are the side effects related to taking immunosuppressive drugs?