Cells to Systems: Lecture 11

PRINCIPLES OF CELL COMMUNICATION

Dr Laura Dooley
Email: laura.dooley@unimelb.edu.au

Intended Learning Outcomes:

- Define the terms autocrine, paracrine, endocrine and synaptic signalling and explain why these different types of signalling processes exist
- Describe the anatomical and functional arrangement of the Hypothalamo-Pituitary axis and how this axis regulates the release of pituitary hormones
- List the hormones produced by the anterior and posterior pituitary and describe their main functions

Introduction

Cells need to communicate with each other to coordinate the diverse activities required to maintain homeostasis, growth and development. Cell communication involves the sending and receiving of information (signals) between cells. While some signalling molecules can cross a cell membrane and enter a cell, others require the signal to interact with a specific receptor on the cell membrane and transmit that signal to the interior of the cell. In this case the signalling molecule is the ligand.

Depending upon the type of signal, once inside the cell, the signal may travel and react within membrane, organelle, cytosol or nuclear components. Signalling within a cell is extremely complex with cells often receiving multiple signals simultaneously which in turn activate different signalling pathways. This cross talk (that occurs at multiple steps within the signalling pathway) helps to regulate and control the signalling pathways so that an appropriate response is initiated. Combinations of signalling molecules are required to regulate cell behaviour control cell survival, cell differentiation, cell division and even cell death (apoptosis).

Cell communication mechanisms

Cells can communicate through direct contact (gap junctions and cell-cell recognition) or through chemical messengers.

Gap junctions

- Gap junctions are aqueous pores or channels that link the interior of adjacent cells
- These allow for quick signals that enable rapidly coordinated functions
- Metabolites and ions (<1200 Da) such as cAMP, glucose -6-phosphate and Ca2+ can move directly between the cells, giving direct electrical and chemical communication

Cell-to-cell (direct) signalling

- Direct contact through cell surface molecules on the surface of both cells (or via contact with extracellular matrix components
- The signalling molecule is bound to the cell surface, not secreted

- Binding to the target cell surface receptor initiates signalling transduction
- Examples of this type of signalling are:
    - Antigen presentation by dendritic cells to T lymphocytes, leading to an immune response
    - Attachment of leukocytes to endothelial cell walls of blood vessels, allowing leukocytes to move from blood to adjacent tissues (diapedesis)

Cell-to-cell signalling through chemical messengers

The most common method of cellular communication is through extra cellular chemical messengers. There are five types of signalling processes.

- **Autocrine signalling** - Cell releases a signalling molecule that binds to receptors on its own surface
    - Example: Cytokine binds to receptors on the same cell from which it was secreted.
- **Paracrine signalling** – Secreted molecules diffuse locally and trigger a response in the local area. This is important in localized signalling such as inflammation and angiogenesis
    - Signalling molecules diffuse through the extracellular fluid and act on neighbouring cells, which can create a signal concentration gradient
    - The signalling molecule is rapidly taken up by cells or broken down by extracellular enzymes
        - An example is nitric oxide (NO) released by endothelial cells results in smooth muscle relaxation and vasodilation
- **Endocrine signalling**
    - Secreted hormones are long-distance chemical messengers that travel in the bloodstream
    - Signalling molecules exert their effect on target cells in distant sites
    - Only the target cells of a hormone have the specific membrane receptors for that hormone
    - Non-target cells are not influenced by hormones that contact them
- **Synaptic Signalling**
    - Neurons communicate with cells they innervate (target cells) by releasing neurotransmitters
    - Neurotransmitters are short-range chemical messengers released in response to electrical signals

- **Neuroendocrine signalling**
    - Neurohormones are released into the bloodstream by neurosecretory neurons to act at distant sites
    - Neurosecretory neurons respond to an electrical signal

ROLE OF HYPOTHALAMUS AND PITUITARY IN ENDOCRINE SYSTEM

The endocrine system, via secretion of hormones, mediates its actions via specific receptor binding, and normally controls activities that require longer duration rather than speed; e.g. maintaining glucose levels in blood.

Some hormones affect large numbers of cells and tissues (e.g. insulin that affects glucose

uptake by a number of cells), while others mediate their effect on single organs (e.g. thyroid stimulating hormone, TSH, only acts on the thyroid).

Hypothalamus

- Part of the central nervous system located within the diencephalon region of the brain
- Located below the thalamus and above the pituitary gland
- Composed of anatomically distinct nuclei that possess extensive synaptic connections with other regions of the nervous system
- It controls a number of metabolic functions as well as being one of the main regulators of the autonomic nervous system through direct connections with autonomic nuclei in the brainstem and spinal cord
- Important link between the nervous system & endocrine system, regulating many homeostatic functions
- Hypothalamic hormones are secreted in response to neural inputs from other areas of the CNS. These include sensory nerve excitation, stress (emotional or physical,) chemical changes e.g. metabolites, ions, glucose, rhythms, changes in levels of circulating hormones (feedback inhibition)

Hypothalamus-pituitary axis

- The pituitary gland is composed of two distinct lobes
    1. posterior pituitary
    2. anterior pituitary.
- It is connected to the hypothalamus via the pituitary stalk (infundibulum) that contains vascular and neural connections
- Posterior pituitary:
    - Large neurons (magnocellular neurons) in hypothalamus synthesize and release two hormones, oxytocin (OCT) and antidiuretic hormone (ADH). Once released they travel down the axons of the neurons to the **posterior pituitary** where the hormones are stored in the nerve terminals until released into blood capillaries following the appropriate stimuli
    - Release is by exocytosis when the nerve terminals are depolarized
- Anterior Pituitary:
    - Small bodied neurons in various regions of the hypothalamus (arcuate, paraventricular and preoptic nuclei) secrete releasing or inhibitory hormones into a specialized circulatory system - the hypothalamo-hypophyseal portal veins (portal veins are special veins that connect two capillary beds)
    - Releasing & inhibiting hormones bind to specific endocrine cells within the **anterior pituitary**, regulating their production and secretion of hormones into the general circulation

    - Anterior pituitary contains five types of endocrine cells which secrete 6 peptide hormones into the systemic circulation:
        - Thyroid stimulating hormone (TSH) produced by thyrotropes of anterior pituitary regulate the secretion of thyroid hormones (T3 and T4) by the thyroid gland
        - Adrenocorticotropic hormone (ACTH) produced by corticotrophs
            - Regulate the secretion of cortisol and corticosterone from the adrenal cortex
        - Prolactin (PRL) produced by lactrotrophs

        - Stimulates and sustains milk production from mammary gland
    - Luteinizing hormone (LH) produced by gonadotrophs
        - Females: stimulates egg formation (growth & development of ovarian follicles) in ovaries
        - Males: helps stimulate sperm formation in testes
    - Follicle stimulating hormone (FSH) produced by gonadotrophs
        - Females: stimulates egg formation (growth & development of ovarian follicles)
        - Males: helps stimulate sperm formation
    - Growth hormone (GH) produced by somatotrophs
        - Stimulates postnatal somatic growth & development (IGF-I & II)
        - Mobilizes fat stores, stimulates protein synthesis, inhibits insulin

Further Reading

- Hall JE: *Guyton and Hall Textbook of Medical Physiology*, Elsevier, 2021.Ebook. Chapters 1&2.
- Klein BG: *Cunningham's textbook of veterinary physiology*. Elsevier, 2020. Available in BioMed and Werribee libraries.