Essentials of cell physiology

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Abstract

Cell physiology investigates how cells function and interact with their environment. Cells are exposed to a range of distinct stimuli in response to which they need to initiate appropriate responses to ensure their own survival as well as that of the organism as a whole. Responding to stimuli is only possible if cells express receptors capable of sensing the presence of these stimuli. An important role in this process is played by receptors that are inserted in the membrane surrounding and protecting cells, as they permit cells to sense stimuli without directly exposing their intracellular milieu to them. Receptors can detect a number of distinct stimuli: chemical, mechanical, thermal and electrical. The response triggered in a cell following receptor stimulation depends on the type of receptor and down-stream signalling molecules present in the cell as well as the presence or absence of other stimuli. A good understanding of cell physiology is of high importance to surgeons as it helps understand, predict and improve clinical outcome and devise treatment strategies.

Keywords Cell membrane; enzyme-linked kinases; G protein-coupled receptors; ion channels; microenvironment; second messengers; signalling; transporters

Introduction

Cell physiology is concerned with how cells, the building blocks of tissues and organs, function, and how they interact with each other and their environment. In complex, multicellular organisms such as mammals, an interaction between cells and their surroundings is essential for the survival of the organism. All mammalian cells have the same general organization and organelles (see Box 1 for a quick guide to organelles and their functions), yet different cells within the body have to fulfil distinct roles. This is achieved through differences in cell shape including specializations such as dendrites or cilia, and cell-specific expression of proteins that convey distinct properties to the cells that express them. Of particular importance here are proteins embedded in the membrane, as they represent a link between extra- and intracellular environment and determine how cells respond to external stimuli.

Microenvironment

Cells do not exist and function in isolation but they are surrounded by other cells, which they may be physically connected to (in tissues) or not (e.g. immune cells). They are also surrounded by interstitial fluid, which contains ions and other chemicals. The sum of all the cells and chemicals that surround a cell as well as prevailing physical factors, such as temperature, impacting on cells is called the microenvironment of that cell. Crucially, cells can sense changes in their microenvironment, whether these changes are chemical, mechanical, electrical or thermal. This ability to detect changes in their environment is the fundamental basis that allows cells to respond appropriately to externally generated stimuli, such as starting or stopping to proliferate or releasing chemicals, and to communicate with other cells.

Cells in different tissues have different cellular neighbours, and the interstitial fluids of distinct tissues differ in their composition. Importantly, the interstitial fluid composition can change in a cell and tissue activity dependent manner. Hence, cells alter and shape their own microenvironment and that of neighbouring cells. Whether or not changes in the cellular microenvironment are picked up by a cell depends on the presence of sensors, or receptors, for the parameter that has changed, and on the ability of the stimulus to reach that receptor.

Cell membrane

All eukaryotic cells are surrounded by a cell, or plasma, membrane, a lipid bilayer made up of hundreds to thousands of distinct lipids. It acts as a diffusion barrier that controls which chemicals can cross into and out of cells. Very small and hydrophobic chemicals as well as gases can diffuse through the plasma membrane unaided. All other chemicals, including ions, need to be transported across with the help of specialized proteins that are inserted in the membrane, channel and carrier proteins. This selective permeability of membranes to chemicals and in particular to ions results in the generation of a membrane potential across the membrane that, in turn, influences transport processes and allows cells to create and respond to electrical signals.

Not all chemical or other stimuli can or need to cross the membrane to have an effect. The plasma membrane offers a surface for insertion of sensors/receptors that can detect changes in virtually all aspects of the cellular microenvironment. Intriguingly, distribution of receptors across the membrane is not uniform. The membrane presents a scaffold to enable creation of niches of specialized activity. This is achieved via lipid rafts: specialized membrane microdomains that enable cells to compartmentalize cellular processes by serving as organizing centres for specific signalling events. Lipid rafts consist of membrane lipids and receptor proteins and may differ in structure and function depending on their composition.

This non-uniformity is not limited to proteins but also applies to the lipids that make up the membrane, and stimulus-driven hydrolysis of membrane lipids can lead to the generation of extra- and intracellular signalling molecules.

Cell membrane receptors

Activation of cell surface receptors by chemical, mechanical, electrical or thermal stimuli invariably results in conformational changes of the receptor protein, which in turn cause knock-on effects intracellularly and affect intracellular signalling cascades, culminating in altered intracellular processes. In this way,

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Organelles and their functions

Nucleus
- Contains all genetic material in form of chromosomes made up of DNA
- Proteins in nucleus control which genes are transcribed into RNA and when (including selection of gene allele to be transcribed)
- Surrounded by two membranes separated by a layer of nucleoplasm; transport into/out of nucleus is heavily regulated

Ribosomes
- Machinery required for translation of RNA into protein
- Consists of large and small subunit composed of ribosomal RNA and protein
- Free in cytosol or bound to endoplasmic reticulum (ER)
- Also found in mitochondria (resemble bacterial ribosomes)

Endoplasmic reticulum
- Made up of stacks of membrane-bound vesicles and sheets that extend out from the nucleus (is in part continuous/in contact with outer membrane of nucleus) into the cytoplasm
- Rough ER has ribosomes attached and is the site of protein synthesis
- Main lipid biosynthesis organelle
- Sends proteins and lipids on to Golgi apparatus for further modifications
- Intracellular Ca^{2+} store that can release Ca^{2+} into the cytoplasm via opening of Ca^{2+}-permeable ion channels

Golgi apparatus
- Made up of a series of membrane sacks called cisternae
- Receives proteins, lipids and some carbohydrates and modifies them to enable correct trafficking and targeting
- Also organelle for de novo lipid synthesis

Lysosomes
- Large membrane-bound vesicles with acidic intraluminal pH (pH5)
- Break down foreign macromolecules, bacteria and viruses taken up by endo- and phagocytosis and expired proteins from within the cell
- Involved in apoptosis (programmed cell death)
- Intracellular Ca^{2+} store that can release Ca^{2+} into the cytoplasm via opening of Ca^{2+}-permeable ion channels

Mitochondria
- Surrounded by two membranes
- Contain their own circular DNA and (small) ribosomes (‘cells within cells’)
- Only passed on from mother to child
- Oxidative phosphorylation, in which glucose is turned into CO_2 and ATP, the generic energy unit utilized by all living organisms
- Trigger apoptosis (programmed cell death)
- Synthesis of steroids (in cells that produce them)
- Lipid synthesis and modification
- Heat generation (body thermoregulation in mammals)
- Intracellular Ca^{2+} store that can release Ca^{2+} into the cytoplasm via opening of Ca^{2+}-permeable ion channels

Peroxysomes
- Membrane-bound vesicles that break down molecules using O_2, including β-oxidation of fatty acids
- Produce some phospholipids and cholesterol, as well as bile acids in liver cells

Cytoskeleton
- Complex network of interacting microfilaments and -tubules
- Provides cell shape, mechanical resistance to deformation, tethering site for proteins, transport route, chromosome anchoring site during cell division

Box 1

extracellular changes are transduced intracellularly. Importantly, a cell is unaware of changes in its environment if it does not express the appropriate receptors that allow it to sense these changes. The different stimulus modalities (chemical, mechanical, electrical, thermal) are sensed by receptors that specialize in picking up these stimuli.

Chemical stimuli directly bind to their receptor and include a range of distinct compounds, such as break down products of complex molecules that indicate cell damage or pathogen invasion, or hormones. Significantly, receptors may also sense the absence of molecules that would normally be present, in which case the unbinding of a usually present chemical and subsequent termination of a normally ongoing signalling cascade is meaningful to the cell.

Mechanical stimuli include changes in pressure on the cell membrane, which can be brought about through cell shrinking or