

Overview of Cell Signaling

local regulators:

~ paracrine: on site release and response of signal molecules

~ synaptic: neurons use ACH

~ cell to cell joining

~ long distance regulators: carry communication factor to tissue group far from source

~ endocrine: pituitary gland

~ animals: hormones / HGH

~ plants: ethylene CH₂ = CH₂

~ ex: one bad apple ruins the bunch

Cell Communication

Paracrine: target cells lie near the secreting cell

Juxtacrine: a ligand on one cell surface binds to a receptor on the other

Autocrine: the secreted molecules act on the secreting cell itself

Endocrine: secrete specific hormones into the bloodstream

Tyrosine-Kinase Steps

1) Tyrosine Kinase is separate when inactive

2) Ligand attaches to a receptor

3) Tyrosine Kinase comes together (dimer)

4) Tyrosine Kinase is phosphorylated with a (P) from ATP

5) The activated Tyrosine will activate relay proteins

Transduction Pathways

regulation

specificity

amplification

termination

C. Elegans (Apoptosis)

nematodes

apoptosis occurs when specific proteins that accelerate apoptosis override the proteins that "put the brakes" on apoptosis

Why Should a Cell Program its Death?

needed for proper development:

~ metamorphosis

~ removes fetal webbing between fingers / toes

~ menstruation

~ synapse formation

~ eliminates T cells that cause autoimmune

destroy cells that pose a threat:

~ infected with virus

~ DNA damage

~ cancer cells

Fever

when the phagocytes are overwhelmed:

~ release a signal to the hypothalamus

~ body temperature increases

~ increase in metabolism

Inflammatory Response

"chemical alarm"

redness, swelling, heat, pain

mast cells release histamine:

~ vasodilation occurs

~ increase temp = increase in metabolic rate

~ attracts phagocytes

Cell Cycle

life cycle of the cell

functions: reproduction, growth, repair

Interphase:

1) G1: first gap / growth

2) S: DNA synthesis / DNA is copied

3) G2: second gap / preparation of cell contents for division

mitotic division:

4) the m phase: cell division

~ prophase

~ metaphase

~ anaphase

~ telophase

5) cytokinesis: completes division of cytoplasmic contents

G1 Checkpoint

checks for:

~ cell size

~ nutrients

~ growth factors

~ DNA damage



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Internal Controls

CDKs: cyclin dependent kinases (proteins)

cyclins: regulatory proteins (must be present)

~ increases as the cell goes through interphase

MPF: mitosis promoting factors in G2

~ cyclin + CDK

APC-Anaphase promoting complex

~ kinetochore fiber connection

Causes of Cancer

mutations

carcinogenic chemicals

UV light

viruses

oncogenes

p53 genes

What Causes Uncontrolled Cell Growth?

defects in proteins that control the cell cycle

mutations that knock out key genes

Basic Types of Cancer

carcinoma: arises from body's outer coverings and inner linings

sarcoma: arises from body's supporting structures

lymphoma: arises from lymph system

leukemia: arises from red marrow in bone, spleen

Proto-oncogenes

initiate each phase of the cell cycle

active when conditions are appropriate for growth

mutations cause growth to occur at all times

oncogenes promote cancer development

Steps of Cell Signaling

1) signal reception

~ a cell detects a signaling molecule

2) signal transduction

~ a series of chemical reactions that creates a response

3) signal response

~ the signal triggers a cell response

G-Protein Steps

1) Ligand attaches to receptor

2) Activates the G-protein

3) G-protein moves across membrane

4) G-protein interacts with another protein in the cell membrane

Ion Channel Steps

1) the ion channel is closed

2) ligand attaches to a receptor

3) the ion channel opens

4) ions pass through

Cell Response to Signal

regulation of activities or transcription

initiation = signals sent to turn on a gene

ex: testosterone enters directly into the cell

elaborate pathways amplify and specify responses to signals

Apoptotic Pathways and Signals that Trigger them

caspases are the main proteases (enzymes that cut up proteins) that carry out apoptosis

apoptosis can be triggered by external or internal factors

Apoptotic Pathways and Signals that Trigger them (cont)

examples:

~ an extracellular death-signaling ligand

~ DNA damage in the nucleus

~ protein misfolding in the ER

Positive and Negative Feedback

homeostasis: maintaining stable internal conditions

negative feedback:

~ shuts off original stimulus

~ ex: thermostat

positive feedback:

~ speeds up the original stimulus

~ ex: gossip

Chemical Signals and Cells (Phagocytes)

neutrophils:

~ engulf a pathogen and self-destruct

macrophages:

~ grabs pathogens with cytoplasmic extensions

~ engulfs pathogen

~ digests pathogen

~ removes pathogen through exocytosis

natural killer cells:

~ kills cells infected with a class 1 MHC protein

when a cell is infected:

~ the cell stops making MHC

~ NK cells poke the infected cell with enzymes

~ triggers apoptosis



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Mitosis

Interphase: 46 chromosomes

Prophase: 92 chromosomes

Prometaphase: nucleus dissolves and microtubules attach to centromeres

Metaphase: chromosomes align in the middle of the cell

Anaphase: separated chromosomes pulled apart by spindle fibers

Telophase: microtubules disappear and cell division begins

Cytokinesis: two daughter cells formed

Spindle Fibers

centrosome

kinetichore fibers:

~ attach to chromosomes

~ movements

nonkinetichore fibers:

~ attach pole to pole

~ support

G2 Checkpoint

checks for:

~ DNA damage

~ DNA replication completeness

M (mitosis) Checkpoint

the spindle checkpoint

checks for:

~ chromosome attachment to spindle at metaphase plate

~ 92 spindle fibers

~ 46 chromosomes

External Factors

chemical factors:

~ nutrients

~ PDGF

physical factors:

~ density dependent

~ anchorage

Disrupt Cell Cycle and Trigger Cancer

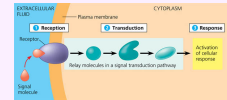
genes that stop or slow the cell cycle

~ ex: tumor suppressor genes

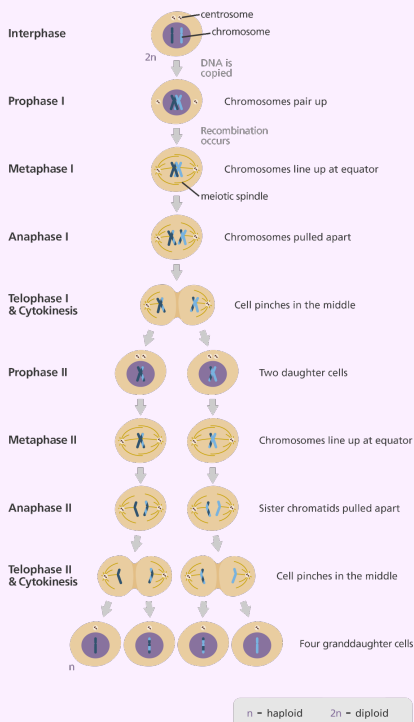
genes that trigger cell growth and division by initiating different stages of the cell cycle

~ ex: proto-oncogenes

Steps of Cell Signaling Image



Meiosis Image



EpiPen (Cell Signaling)

epinephrine (adrenaline) is released

hormone / neurotransmitter

endocrine / nervous system

initiates a flight or fight response

triggered by stressors

secreted from adrenal gland

Secondary Messengers

small molecules and ions are key signaling components

cyclic AMP /adenyl cyclase / phosphodiesterase

calcium ion and inositol triphosphates IP3

Apoptosis

programmed cell death

"cell suicide"

evolved early

Apoptosis Cell Death (ways cells die)

injury: ~ mechanical damage

~ toxic chemicals

suicide: ~ shrink, bleb, fragment

~ chromatin degrades

~ mitochondria breaks down

~ "find me" / "engulf me" signal

Innate (nonspecific) Immune System

physical and chemical barriers that protect the body

1st line of defense:

~ skin (physical barrier)

~ mucous membranes (chemical and physical barrier; enzymes and defensins)

2nd line of defense:

~ fever

~ chemical signals

~ inflammation

Humoral Response

identification of specific antigens in body fluid

antigen:

~ bacteria

~ virus

~ fungus

~ toxin

~ diseased cell

Antibodies

protein receptors on the surface of B cells

some antibodies travel freely

antibodies connect with a complementary antigen

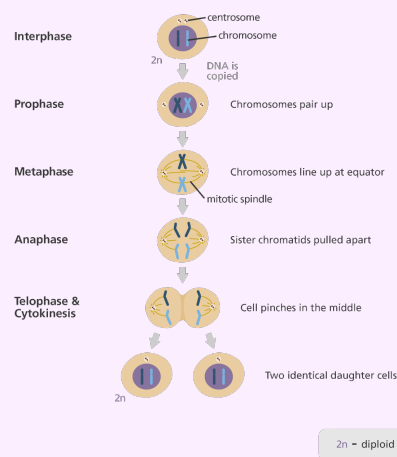
Cytokinesis

animal cells: cleavage furrow

~ contractile ring of actin involved

plant cells: cell plate

Mitosis Image



Cell Cycle Control

cells should only divide when needed

internal and external controls

cell cycle control systems (internal control):

~ series of checkpoints

~ must pass all checkpoints to divide

example: cellular inspection station

S (synthesis) Checkpoint

checks for:

~ DNA damage

~ prevents reduplication of DNA

Cell Cycle Image



Cancer

definitions of cancer:

~ neoplasm of proliferating cells (new tissue growing out of control)

~ cell division out of control

~ cells produced are useless

~ compete with healthy cells for nutrients and oxygen

benign (not moving) versus malignant (moving)

~ benign is a sedentary mass of cancerous cells

~ malignant is a moving mass of cancerous cells - metastasis

Tumor-Suppressor Genes

p53 (guardian of the genome)

~ p53 protein increases in cells exposed to UV radiation

p53 mode of action"

1) DNA damage

2) p53 increases

3) p53 bind to DNA (not at damage site)

4) transcription of genes that stop cell cycle or lead to cell death



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