Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Übung 9

Vorlesung Bio-Engineering

Frühlingssemester 2021

Part 1. Cell Signaling

Signaling Some Questions:

Q1. Why do signaling responses that involve changes in proteins already present in the cell occur in milliseconds to seconds, whereas responses that require changes in gene expression require minutes to hours?

Q2. How is it that different cells can respond in different ways to exactly the same signaling molecule even when they have identical receptors?

Q3. Choose if the following statement are right or wrong:

	Right	Wrong
Signal molecules have to be hydrophobic to be able to cross the plasma membrane		
Hydrophilic molecules can bind to cell surface receptors as well as intracellular receptors located in the cytosol or nucleus.		
Paracrine signaling acts over far distances		
Most signaling molecules are used in paracrine, endocrine and synaptic signaling. The crucial difference is the speed and the selectivity of the signals		
Endocrine cells mostly use the same molecule for signaling, while nerve cells have to uses different neurotransmitters		

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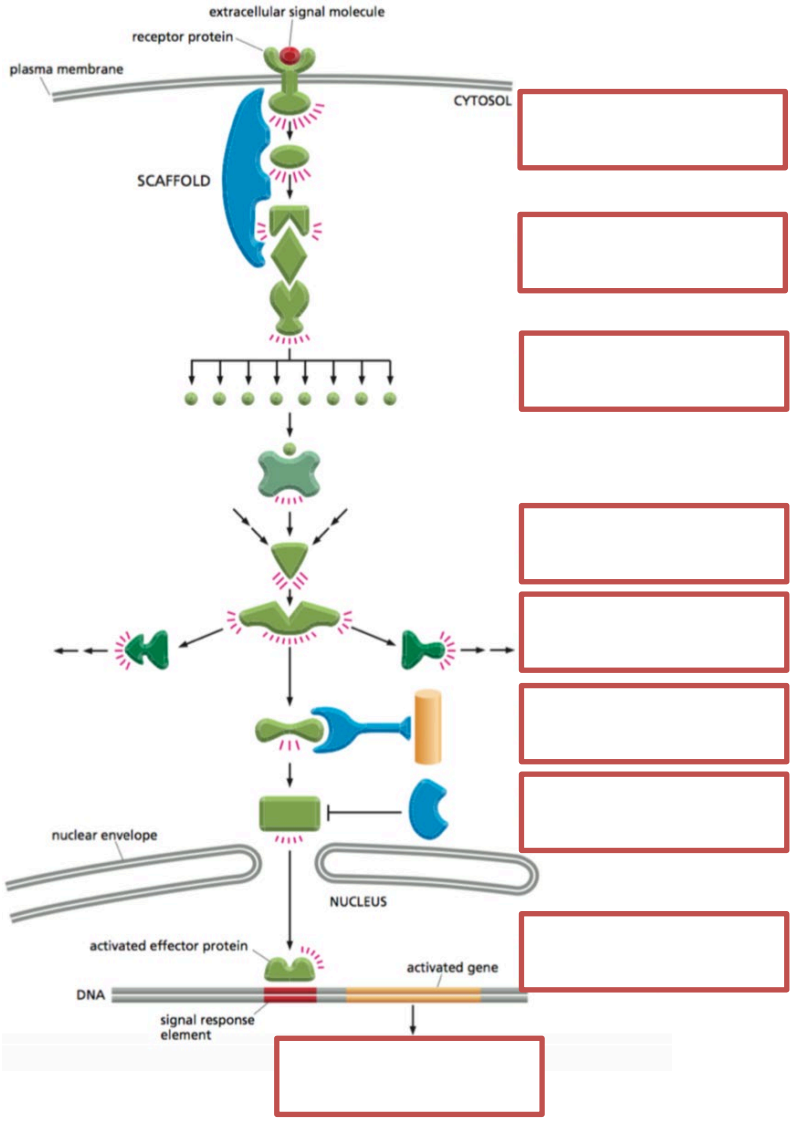
Q4. Label the steps of the hypothetical intracellular pathway using the following terms:

- spread
- anchor
- effector protein activation
- relay
- primary transduction
- integrate
- gene transcription
- transduce and amplify
- modulate



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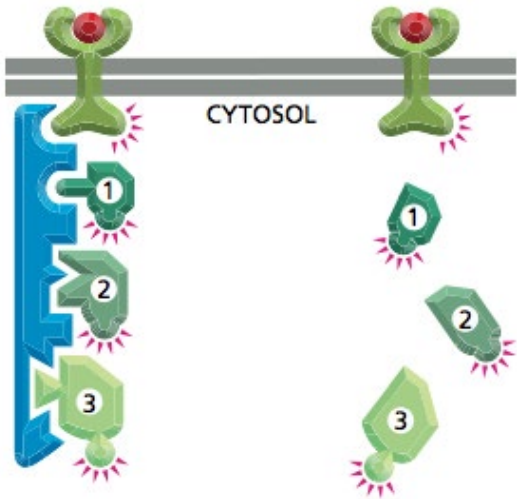
Q5. Consider a signaling pathway that proceeds through three protein kinases that are sequentially activated by phosphorylation. In one case, the kinases are held in a signaling complex by a scaffolding protein; in the other, the kinases are freely diffusible (see fig). Discuss the properties of these two types of organization in terms of signal amplification, speed, and potential for cross-talk between signaling pathways.



Q6. Cells communicate in ways that resemble human communication. Decide which of the following forms of human communication are analogous to autocrine, paracrine, endocrine, and synaptic signaling by cells.

A. A telephone conversation
B. Talking to people at a cocktail party
C. A radio announcement
D. Talking to yourself

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Q7. Proteins play a variety of roles in signaling pathways. Match the following list of signaling proteins with the best description of their functions. Each description should be matched with only one protein.

A. Amplifier proteins	1. Bind multiple signaling proteins together in a functional complex
B. Anchoring proteins	2. Combine signals from two or more pathways before passing it onward
C. Integrator proteins	3. Convert the signal to a different form
D. Modulator proteins	4. Greatly increase the signal they receive
E. Relay proteins	5. Maintain specific signaling proteins at a precise location in the cell
F. Scaffold proteins	6. Modify the activity of signaling proteins to regulate signal strength
G. Transducer proteins	7. Pass the message to the next signaling component in the pathway

Q8. Extracellular Matrix - TRUE/FALSE (Decide whether each of these statements is true or false, and then explain why.)

a) The extracellular matrix is a relatively inert scaffolding that stabilizes the structure of tissues.
b) One of the main chemical differences between proteoglycans and other glycoproteins lies in the structure of their carbohydrate side chains: proteoglycans mostly contain long, unbranched polysaccharide side chains, whereas other glycoproteins contain much shorter, highly branched oligosaccharides.
c) Integrins can convert mechanical signals into molecular signals.
d) Various types of integrins connect extracellular binding sites to all the different kinds of cytoskeletal elements, including actin, microtubules, and intermediate filaments.
e) Integrins are thought to be rigid rods that span the membrane and link binding sites outside the cell to those inside the cell.

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Q9. Extracellular Matrix - General - It is not an easy matter to assign particular functions to specific components of the extracellular matrix, since the overall structure is a complicated composite material with both mechanical and signaling properties. Nidogen, for example. cross-links two central components of the basal lamina by binding to the laminin-γl chain and to type IV collagen. Given such a key role, it was surprising that mice with a homozygous knockout of the gene for nidogen-l were entirely healthy, with no abnormal phenotype. Similarly, mice homozygous for a knockout of the gene for nidogen-2 also appeared completely normal.

By contrast. mice that were homozygous for a defined mutation in the gene for laminin-γl, which eliminated just the binding site for nidogen, died at birth with severe defects in lung and kidney formation. The mutant portion of the laminin-γl chain is thought to have no other function than to bind nidogen, and does not affect laminin structure or its ability to assemble into basal lamina.

How would you explain these genetic observations, which are summarized in Table Q9? What would you predict would be the phenotype of a mouse that was homozygous for knockouts of both nidogen genes?

Table Q9: Phenotypes of mice with genetic defects in components of the basal lamina

PROTEIN	GENETIC DEFECT	PHENOTYPE
nidogen-1	gene knockout (–/–)	none
nidogen-2	gene knockout (–/–)	none
laminin-γ1	nidogen binding-site deletion (+/–)	none
laminin-γ1	nidogen binding-site deletion (–/–)	dead at birth

+/– stands for heterozygous, –/– stands for homozygous.