Past-paper walk-through

Regulation of Cell Cycle ▪ 4.6

eXercise

Questions in this set

- 2021 Q1

Reading the mark scheme

- **B1** a mark that stands on its own – the point is either made or not.
- **M1** a *method* mark: the right approach, even if the number is wrong.
- **A1** an *answer* mark, and it usually needs its M mark first.
- **C1** a working mark on the way to the answer.
- // separates answers the examiner accepts equally.
- **ecf** = error carried forward: a later part is marked on your own earlier answer.
- **owtte** = "or words to that effect" – the wording need not match.

Question 1

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Polycystic kidney disease (PKD) is an inherited disease that causes water loss from the body and affects cell division in the kidneys. Because water movement across cell membranes is related to ion movement, scientists investigated the role of the Na^+/K^+ATPase (also known as the sodium/potassium pump) in this disease. Ouabain, a steroid hormone, binds to the Na^+/K^+ATPase in plasma membranes. Individuals with PKD have a genetic mutation that results in an increased binding of ouabain to the Na^+/K^+ATPase. The scientists treated normal human kidney (NHK) cells and PKD cells with increasing concentrations of ouabain and measured the number of cells (Figure 1) and the activity of the Na^+/K^+ATPase (Figure 2) after a period of time. The scientists hypothesized that a signal transduction pathway that includes the protein kinases MEK and ERK (Figure 3) may play a role in PKD symptoms.

Question 1

[Figure 1: Bar graph, "Number of Cells" (y-axis, 0 to 160) vs. "Ouabain (pM)" (x-axis: 0, 1, 10, 10^2, 10^3, 10^4, 10^5, 10^6, 10^7, 10^8, 10^9), grouped bars for NHK (grey) and PKD (white). Approximate values: at 0 pM both ~100; NHK stays roughly 100-110 across most concentrations dropping to ~30-40 at 10^6-10^9 pM; PKD rises to ~110 at 10^2 pM, ~125 at 10^3 pM, peaks ~148 at 10^4 pM, ~110 at 10^5 pM, then drops to ~35-45 at 10^6-10^9 pM. Error bars represent $\pm 2SE_{\bar{x}}$. Caption: "Figure 1. Cell number compared with the number of cells at 0 pM ouabain. Normal human kidney (NHK) cells and polycystic kidney disease (PKD) cells were treated with increasing concentrations of ouabain. Error bars represent $\pm 2SE_{\bar{x}}$."]
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pM (~80%), drop steeply through 10^5 pM (~30%), reaching near 0% by 10^7-10^9 pM. Error bars represent $\pm 2SE_{\bar{x}}$. Caption: "Figure 2. Percent Na^+/K^+ATPase activity of NHK and PKD cells treated with increasing concentrations of ouabain. Error bars represent $\pm 2SE_{\bar{x}}$."]

[Figure 3: Diagram of a signal transduction pathway. Bound Ouabain sits on the Na^+/K^+ ATPase embedded in the Plasma Membrane. An arrow leads from the receptor down to MEK, which is converted to P-MEK (phosphorylated MEK); P-MEK activates ERK, converting it to P-ERK (phosphorylated ERK). An arrow from P-ERK crosses the Nuclear Envelope to DNA (shown as a double helix), leading to "Transcription of Target Genes." Caption: "Figure 3. Signal transduction pathway hypothesized to play a role in the increased number of PKD cells."]

Question 1

(a) Describe the characteristics of the plasma membrane that prevent simple diffusion of Na^+ and K^+ across the membrane. **Explain** why ATP is required for the activity of the Na^+/K^+ATPase.

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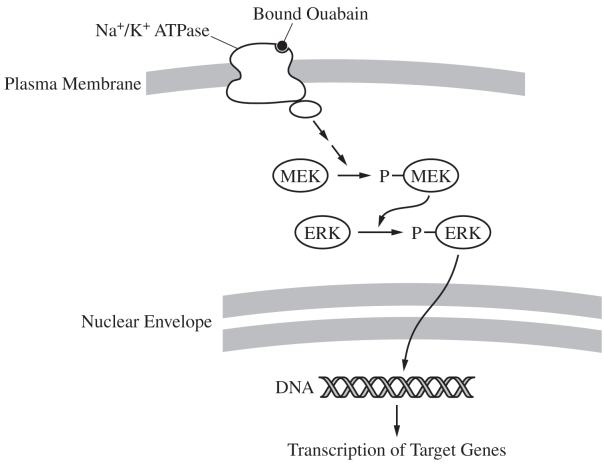
Bound Ouabain
Na+/K+ ATPase
Plasma Membrane
MEK
P–MEK
ERK
P–ERK
Nuclear Envelope
DNA
Transcription of Target Genes

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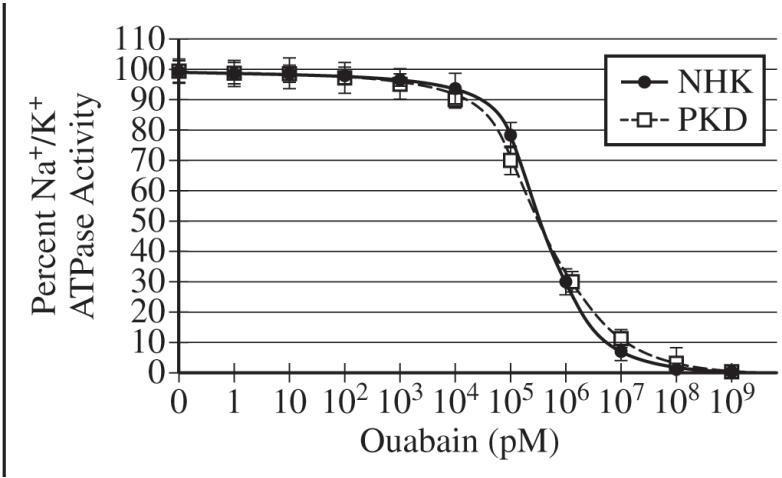
Percent Na^+/K^+ ATPase Activity
110
100
90
80
70
60
50
40
30
20
10
0
0
1
10
10^2
10^3
10^4
10^5
10^6
10^7
10^8
10^9
Ouabain (pM)
NHK
PKD

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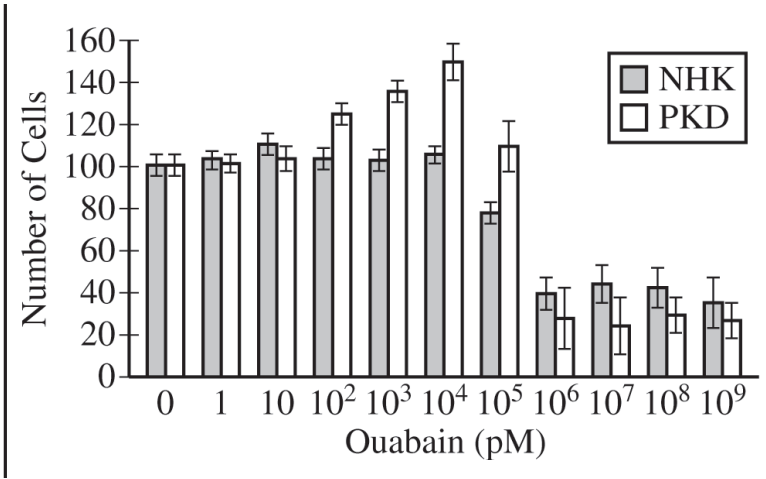
Number of Cells
160
140
120
100
80
60
40
20
0
NHK
PKD
0
1
10
10^2
10^3
10^4
10^5
10^6
10^7
10^8
10^9
Ouabain (pM)

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(b) Identify a dependent variable in the experiment represented in Figure 1. **Justify** the use of normal human kidney (NHK) cells as a control in the experiments. **Justify** the use of a range of ouabain concentrations in the experiment represented in Figure 1.

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(c) Based on the data shown in Figure 2, **describe** the relationship between the concentration of ouabain and the Na^+/K^+ATPase activity both in normal human kidney (NHK) cells AND in PKD cells. The scientists determined that Na^+/K^+ATPase activity in PKD cells treated with 1 pM ouabain is 150 units of ATP hydrolyzed/sec. **Calculate** the expected Na^+/K^+ATPase activity (units/sec) in PKD cells treated with 10^6 pM ouabain.

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(d) In a third experiment, the scientists added an inhibitor of phosphorylated MEK (pMEK) to the PKD cells exposed to 10^4 pM ouabain. Based on Figure 3, **predict** the change in the relative ratio of ERK to pERK in ouabain-treated PKD cells with the inhibitor compared with ouabain-treated PKD cells without the inhibitor. Provide reasoning to **justify** your prediction. Using the data in Figure 1 AND the signal transduction pathway represented in Figure 3, **explain** how the concentration of cyclin proteins may increase in PKD cells treated with 10^4 pM ouabain.

Solution 1

(a)

Mark scheme

- Describe (1 pt): Accept any one — the interior of the plasma membrane is hydrophobic/nonpolar; the phospholipid tails are hydrophobic/nonpolar; the exterior of the plasma membrane is hydrophilic/polar; the phospholipid heads are hydrophilic/polar. Na+ and K+ are charged ions, so they cannot cross the hydrophobic membrane interior by simple diffusion. Explain (1 pt): The Na+/K+ ATPase pumps ions (Na+ out, K+ in) against their concentration gradients; this active transport requires an input of (metabolic) energy, which ATP hydrolysis provides.

Solution 1

(b) Mark scheme

- Identify (1 pt): A dependent variable in the Figure 1 experiment is the number of cells. Justify NHK control (1 pt): Accept either — using normal human kidney (NHK) cells allows the scientists to determine the effect of PKD on the cells' responses to (various concentrations of) ouabain; or it allows them to compare the responses of PKD cells and normal cells (to ouabain). Justify range of ouabain concentrations (1 pt): Accept either — the scientists needed to determine whether different concentrations have different effects on cell numbers; or the scientists did not know at which concentration of ouabain there would be an effect.

Solution 1

(c)

Mark scheme

- Describe relationship (1 pt): Accept either — increasing concentrations of ouabain result in decreasing ATPase activity (in both types of cells); or there is an inverse relationship/negative correlation between the concentration of ouabain and the ATPase activity (in both types of cells). Calculate (1 pt): Given 150 units/sec at 1 pM ouabain, the expected Na+/K+ ATPase activity at 10^6 pM ouabain is 45 units/sec (accept between 40 and 50), read from the plateau/low end of the Figure 2 dose-response curve (~30% of the 1 pM baseline activity).

Solution 1

(d) Mark scheme

- Predict (1 pt): Accept either — Option 1: the ratio of ERK to pERK will increase in the cells with the (pMEK) inhibitor; or Option 2: the ratio of ERK to pERK will stay the same in the cells with the inhibitor. Justify (1 pt): Must indicate the pMEK inhibitor blocks further phosphorylation of ERK AND one of the following. For Option 1: the amount of pERK will not increase as it does without the inhibitor; or the amount of ERK will not decrease as it does without the inhibitor; or the cell continues to synthesize ERK; or phosphorylated ERK is being dephosphorylated to ERK. For Option 2: no additional ERK is synthesized/pERK is not being dephosphorylated. Explain cyclin increase (1 pt): Cell number (Figure 1) increases to a maximum at 10^4 pM ouabain. The ouabain-triggered signaling

Solution 1

pathway (Figure 3) stimulates transcription of genes involved in cell division; the target genes likely include those for cyclins, because cyclins regulate the cell cycle.