AP Bio FRQ Fridays

2021 #1
Membrane Transport, Cell Signaling, & Inhibition

NOTES

FRQ Friday #18

2021 #1

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.

FRQ Friday #18

2021 #1

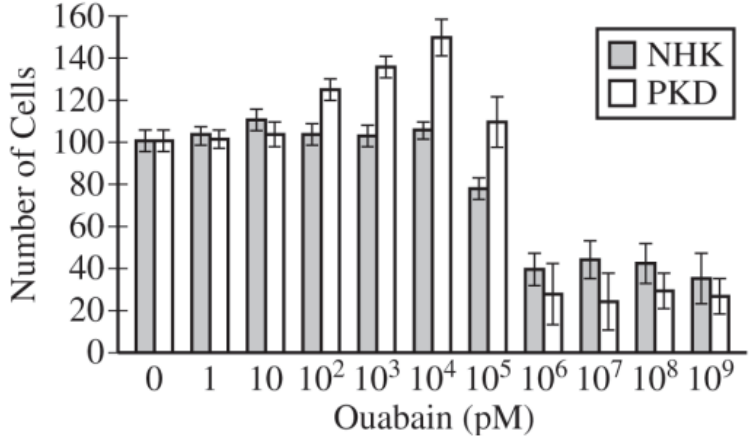


Figure 1. Cell number compared with the number of cells at 0 pM ouabain. Normal human kidney (NHK) cells and polycystic kidney disease (PKD) cells were treated with increasing concentrations of ouabain. Error bars represent $\pm 2SE_{\bar{x}}$.

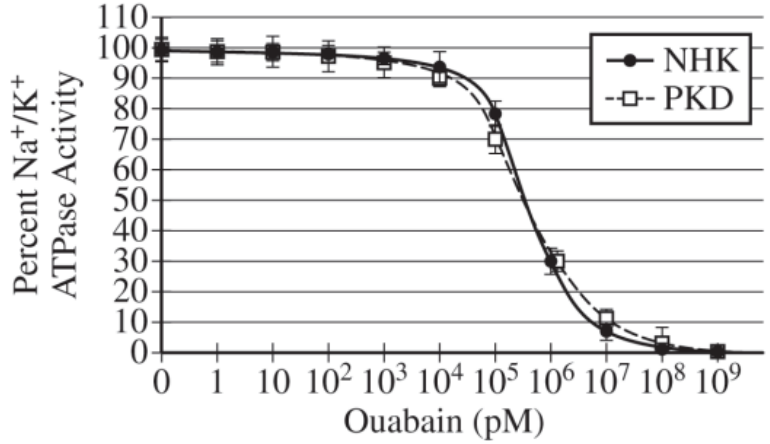
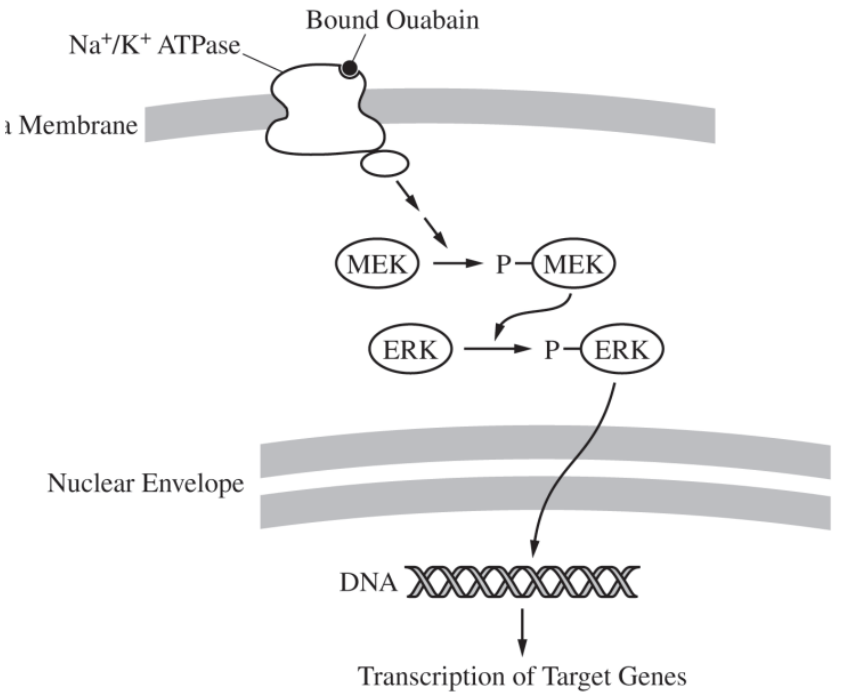


Figure 2. Percent Na^+/K^+ATPase activity of NHK and PKD cells treated with increasing concentrations of ouabain. Error bars represent $\pm 2SE_{\bar{x}}$.



nsduction pathway hypothesized to play a role in the increased number of PK

FRQ Friday #18

2021 #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.

Accept one of the following:

- 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.

- The Na^+/K^+ ATPase pumps ions against their concentration gradients. This requires an input of (metabolic) energy.

FRQ Friday #18

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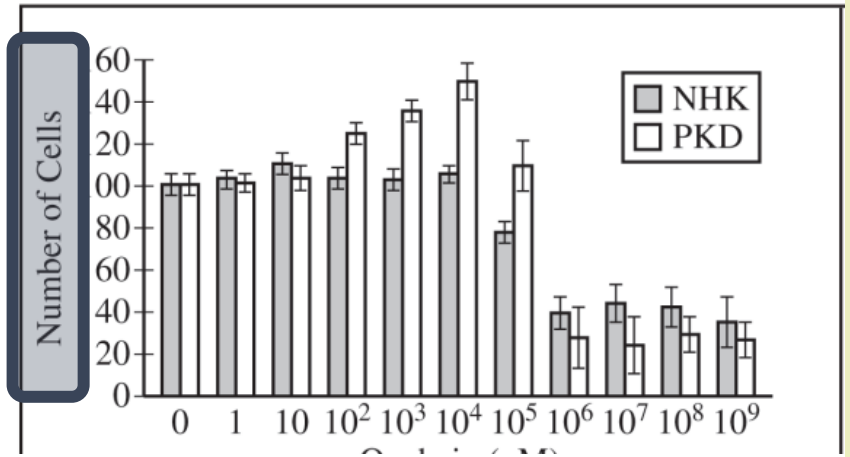
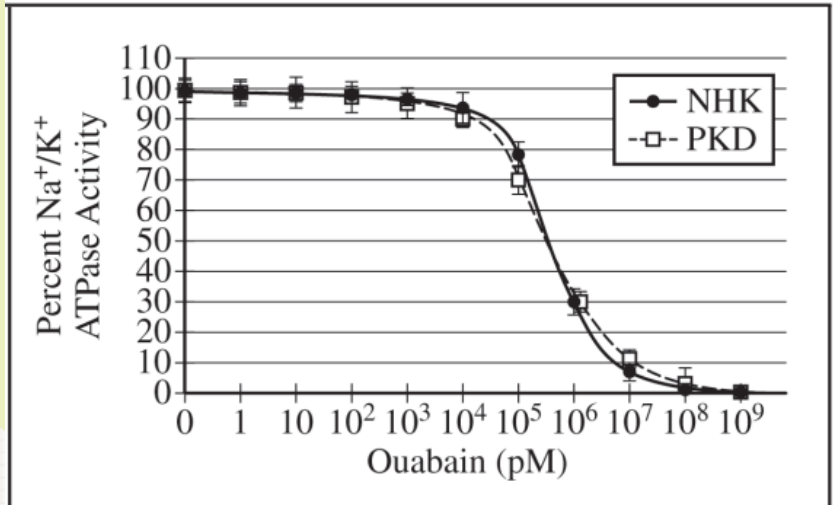
The plasma membrane is composed of phospholipids, which have a hydrophilic phosphate head and inward facing hydrophobic fatty acid tails. This plasma membrane is semipermeable, meaning that only nonpolar, small substances can undergo simple diffusion through this membrane. Since Na^+ and K^+ are ions (they have an electric charge) they must enter the cell through transpot proteins since can't diffuse through membrane. Because cells create a gradient of K^+ ions within the cell, ATP is required for the transport protein Na^+/K^+ ATPase. Since the cell is bringing in more K^+ ions against their concentration gradient and pumping out Na^+ ions against their concentration gradient, energy in the form of ATP ~~is~~ is necessary for this protein to work.

FRQ Friday #18

2021 #1

(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.





- The number of cells

Accept one of the following:

- It allows the scientists to determine the effect of PKD on the cells' responses to (various concentrations of) ouabain.
- It allows the scientists to compare the responses of PKD cells and normal cells (to ouabain).

Accept one of the following:

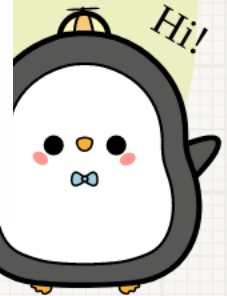
- The scientists need to determine whether different concentrations have different effects on the cell numbers.
- The scientists did not know at which concentration of ouabain there would be an effect.

FRQ Friday #18

2021 #1

(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.

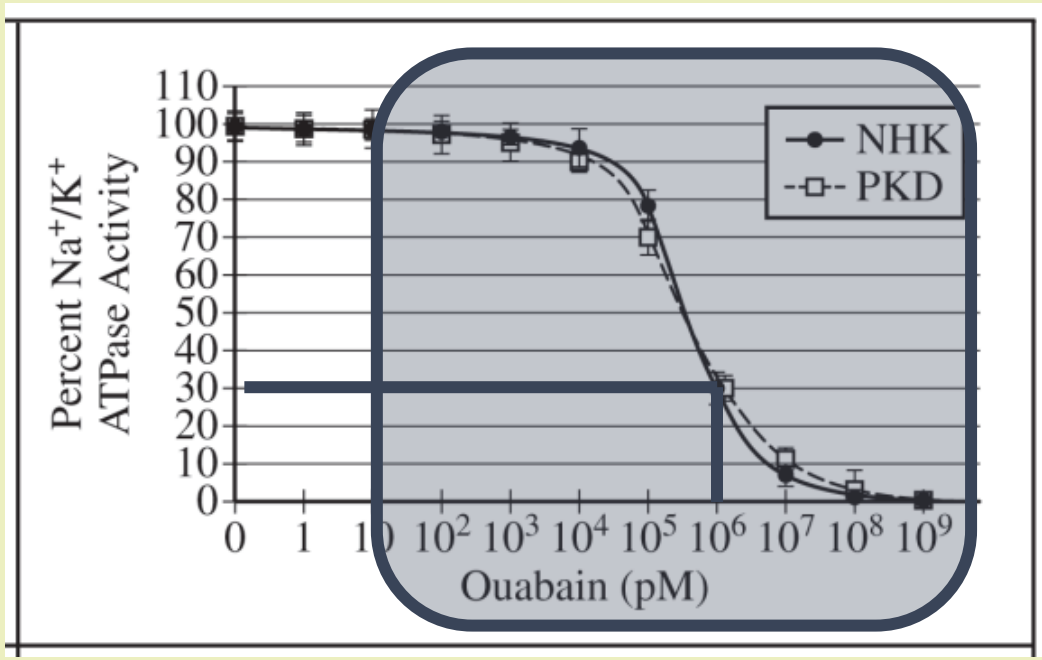
Dependent variable is the number of resulting NHK and PKD cells following different levels of ouabain concentrations. NHK cells serve as a model to compare the cellular changes caused by ouabain in PKD cells, since the values collected would be insignificant without a relavent comparison. Using a range of ouabain concentrations allowed the researchers to observe the changes that occur in cells in multiple conditions, since a very small amount of ouabain may have a very different effect on kidney cells compared to a very high amount.



FRQ Friday #18

2021 #1

(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.



Accept one of the following:

- Increasing concentrations of ouabain result in decreasing ATPase activity (in both types of cells).
- There is an inverse relationship/negative correlation between the concentration of ouabain and the ATPase activity (in both types of cells).

150 * 30% = 45

- 45 (Accept between 40 and 50)

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In both ~~normal~~ normal kidney cells and PKD cells, as concentration of ouabain increases past 10^4 pM, a drastic decrease in Na^+/K^+ ATPase occurs. So there is a negative relationship between ouabain and Na^+/K^+ ATPase activity. In PKD cells treated at with 10^6 pM ouabain, Na^+/K^+ ATPase activity is 45 units of ATP hydrolyzed per second.

FRQ Friday #18

2021 #1

(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.

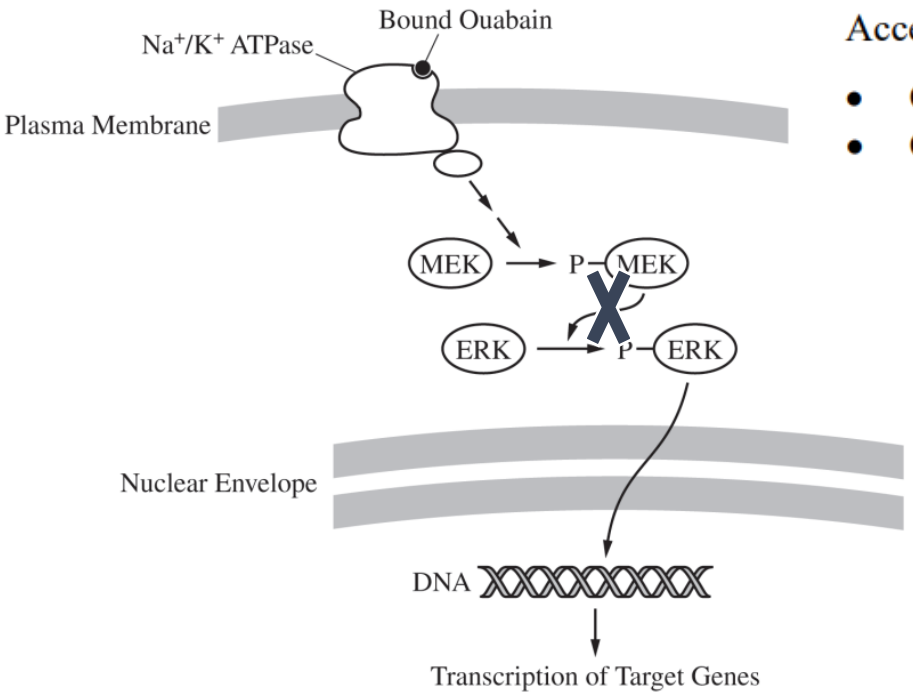

Figure 3. Signal transduction pathway hypothesized to play a role in the increased number of PKD cells

Accept one of the following:

- Option 1: The ratio of ERK to pERK will increase in the cells with the inhibitor.
- Option 2: The ratio of ERK to pERK will stay the same in the cells with the inhibitor.

Option 1:

- The amount of pERK will not increase as it does in cells without the inhibitor.
- The amount of ERK will not decrease as it does in cells without the inhibitor.
- The cell continues to synthesize ERK.
- Phosphorylated ERK is being dephosphorylated to ERK.

Option 2:

- No additional ERK is synthesized/pERK is not being dephosphorylated.

FRQ Friday #18

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Option 2:

- No additional ERK is synthesized/pERK is not being dephosphorylated.

The relative ratio of ERK to pERK will increase ~~decrease~~ in cells treated with the inhibiter compared to cells not treated with the inhibitor. Since pMEK signals the transfer of ERK to pERK, if this ~~pET~~ pMEK is inhibited, it won't allow for the phosphorylation of ERK to pERK and the amount of ERK will increase relative to pERK, causing an increase in ratio.

FRQ Friday #18

2021 #1

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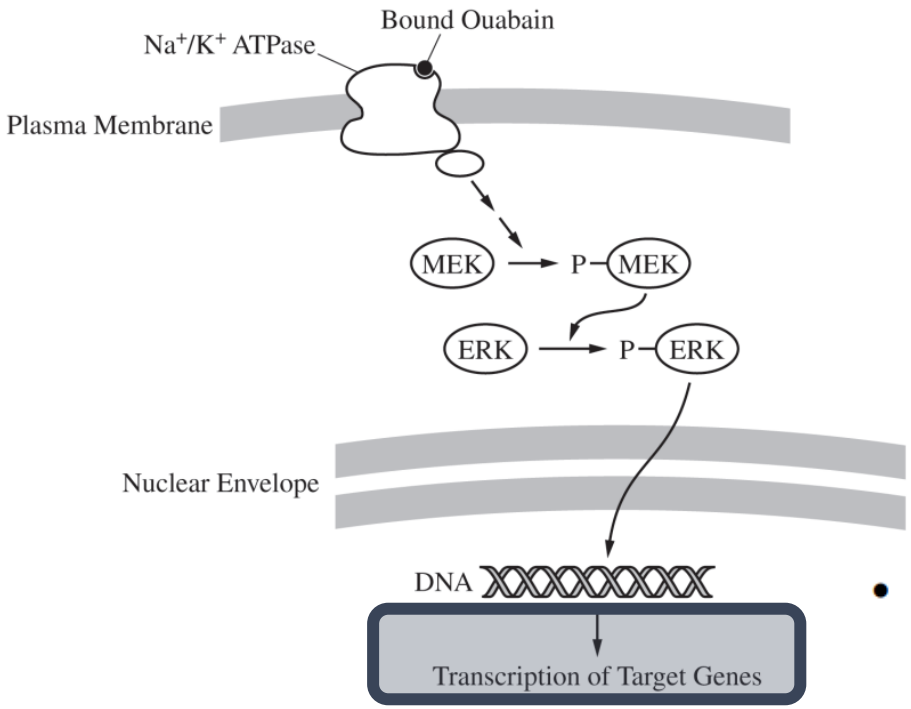
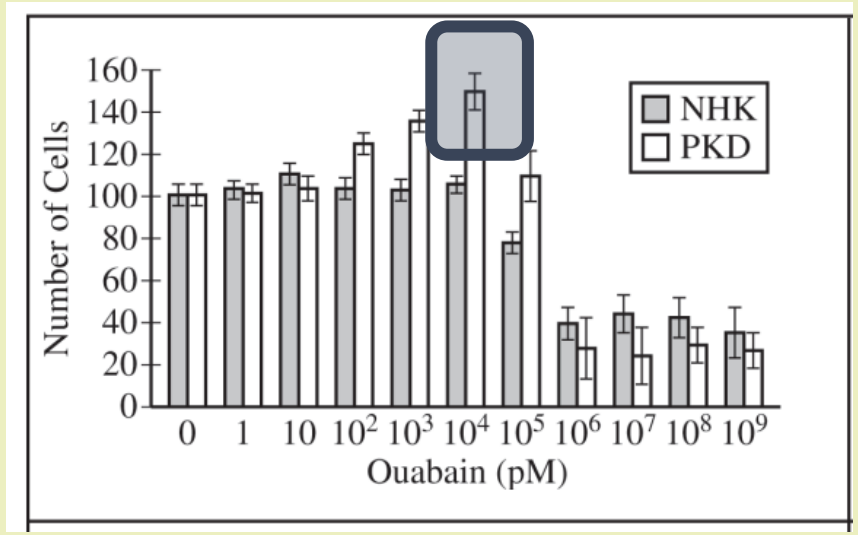
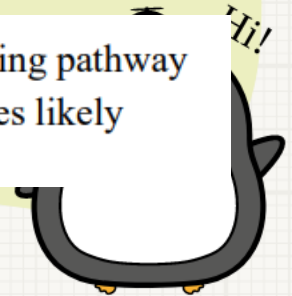




- The cell number increases to a maximum at 10^4 pM ouabain. The signaling pathway stimulates transcription of genes involved in cell division. The target genes likely include those for cyclins because cyclins regulate the cell cycle.

Figure 3. Signal transduction pathway hypothesized to play a role in the increased number of PKD cells



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Ouabain is a signaling molecule that causes the transcription of target genes in ~~PKD~~ they cells. Since PKD cells have increased binding of ouabain, and cells in a concentration of 10^4 ouabain have significantly higher levels of cells; it can be inferred that ouabain increases transcription of cyclin genes, which promote cell growth + divison, as shown in figure 1.