

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.

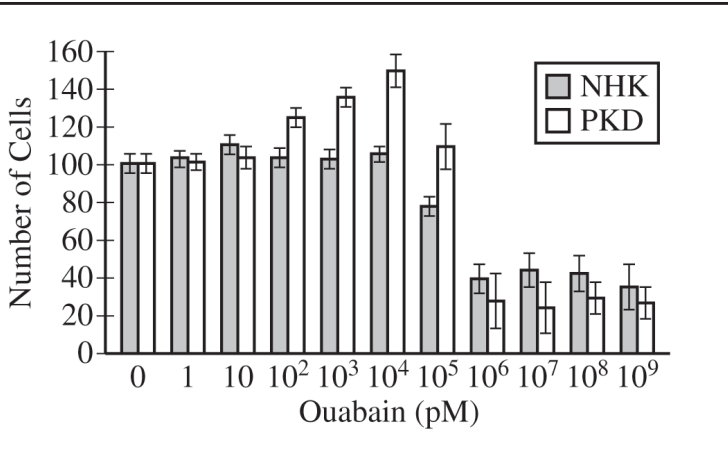


Figure 1. Cell number compared with the number of cells at 0 pM ouabain. Normal human kidney (NHK) cells and polycystic kidney disease (PKD) cells were treated with increasing concentrations of ouabain. Error bars represent $\pm 2\text{SE}_{\bar{x}}$.

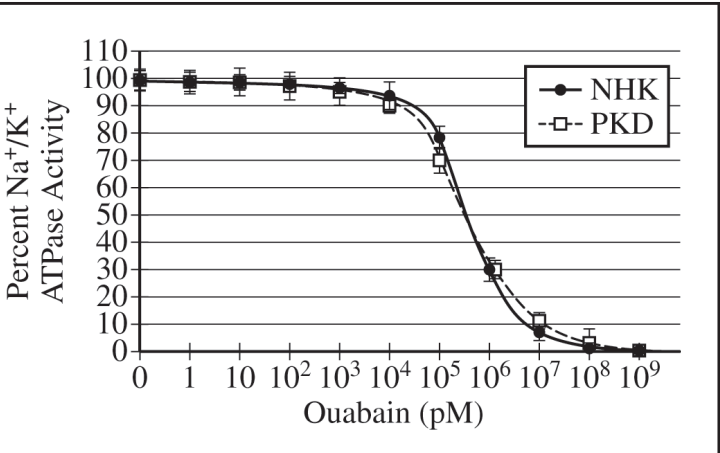


Figure 2. Percent Na^+/K^+ ATPase activity of NHK and PKD cells treated with increasing concentrations of ouabain. Error bars represent $\pm 2\text{SE}_{\bar{x}}$.

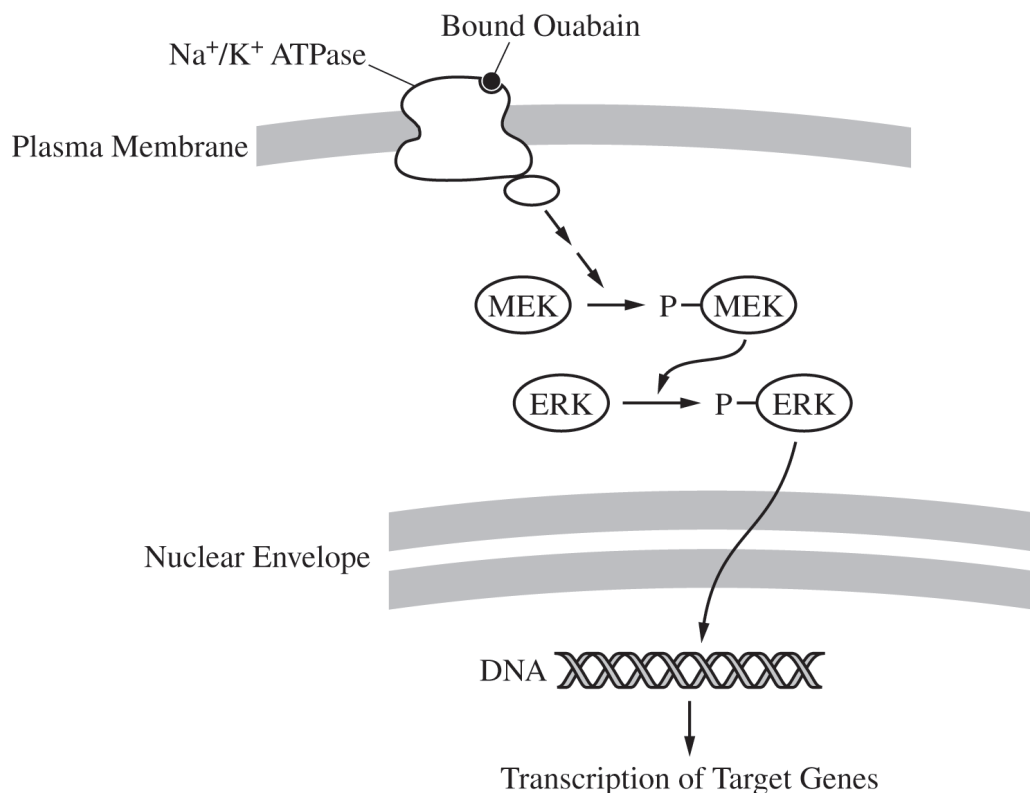


Figure 3. Signal transduction pathway hypothesized to play a role in the increased number of PKD cells

- (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.
- (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.
- (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 10⁶ pM ouabain.
- (d) In a third experiment, the scientists added an inhibitor of phosphorylated MEK (pMEK) to the PKD cells exposed to 10⁴ 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 10⁴ pM ouabain.

Write your responses to this question only on the designated pages in the separate Free Response booklet.