Kinetic comparisons of heart and kidney Na^+,K^+-ATPases

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Researchers working on the mechanism of the Na^+,K^+-ATPase can be broadly divided into two categories: 1) Those working on purified enzyme, and 2) Those working on the enzyme in intact cells. There are few research groups working in both areas. Those working on purified enzyme mostly isolate it from kidney, because this tissue yields a very high purity of the protein. Those in the second category generally work on the Na^+,K^+-ATPase naturally present within cardiac myocytes or they express the protein in oocytes. However, results obtained by researchers in these two categories are not necessarily directly comparable. The kidney and heart are known to express different isoforms of the Na^+,K^+-ATPase. In the kidney the enzyme exists virtually exclusively in the $\alpha_1\beta_1$ form, whereas in the heart there is a significant degree of expression of the α_2 isoform of the catalytic subunit. These differences in expression are likely to lead to differences in function. Unfortunately there is no partial reaction kinetic data available on purified heart muscle Na^+,K^+-ATPase or on the enzyme *in situ* in kidney cells. Therefore, direct comparisons between kinetic behavior of the same isoform of the Na^+,K^+-ATPase in both purified form and within native cells are currently not possible.

Fortunately, sufficient partial reaction data has now been obtained on purified mammalian kidney Na^+,K^+-ATPase that kinetic modeling allows the enzyme's expected steady-state and transient behaviour in intact kidney cells to be reconstructed and predicted. We have used a kinetic model to give the expected voltage dependence of the kidney enzyme. Comparisons with patch-clamp data obtained on cardiac myocytes indicate that the activity of the heart enzyme has significantly greater voltage dependence than that of the kidney enzyme. This has important physiological consequences for heart muscle function, where the membrane voltage undergoes frequent large fluctuations.