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This Week's Citation Classic

Post R L, Merrill C R, Kinsolving C R & Albright C D. Membrane adenosine triphosphatase as a participant in the active transport of sodium and potassium in the human erythrocyte. *J. Biol. Chem.* **235**:1796-802, 1960.
[Dept. Physiology, Vanderbilt Medical School, Nashville, TN]

A correspondence between the kinetics of energy-dependent transport of sodium and potassium ions across intact human erythrocyte membranes and that of sodium plus potassium ion-dependent adenosine triphosphatase activity of fragments of the same membranes suggests that a single entity performs both transport and hydrolase functions. [The *SCI*® indicates that this paper has been cited over 865 times since 1961.]

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"In 1954 when I started on the kinetics of active sodium and potassium transport in human erythrocytes, I began as an observer. The transports of the two ions turned out to be linked so that transport of each required transport of the other. There was one pump for both. Then in 1957 Jens Skou published his now classic paper[1] on an ATPase activity in particles derived from crab nerves. This ATPase activity required both sodium and potassium ions simultaneously. Skou wrote, 'Characteristics of the system suggest that the ATPase studied here may be involved in the active extrusion of sodium from the nerve fiber.'

"Skou was, and still is, at the University of Aarhus in Denmark. I had become acquainted with him in 1953 when he visited the United States. In Vienna in 1958 at the International Biochemical Congress we met again and compared notes. As I listened to him, I became convinced that he had the pumping enzyme. In turn I told him about linkage in transport and about the cardioactive steroid inhibitors, which are specific or this pump. I began to appreciate that work on the erythrocyte could identify a sodium plus potassium ATPase activity and active transport of sodium and potassium as distinct functions of a single system. I began work on the ATPase in erythrocytes when I got back home.

"I am pleased to learn that this paper became a *Citation Classic*. I believe this happened for two reasons. The first reason was practical. The paper provided a method for identifying a transport system in a preparation of broken membranes. This made it easy to search for this system in tissues in which transport studies were difficult. The second reason was conceptual. The paper built a bridge between the then mysterious process of active transport and familiar concepts of enzymology. It confirmed to transportologists that ATP was a direct source of energy for an ion pump and it showed enzymologists that ions which might have been considered only as catalysts could in fact be substrates for translocation. Also the sodium and potassium ion pump of the erythrocyte turned out to be representative of a unique transport system found in almost all animal cells.

"The paper initiated an abbreviation with the expression (Na^+ + K^+)-dependent ATPase.' Nowadays some authors keep the parentheses, (Na,K)ATPase, and others keep the hyphen, Na,K-ATPase.

"My collaborators were students. Cullen Merritt and Charlie Albright are now practicing internal medicine, the former in Nashville and the latter in Tyler, Texas. Richard Kinsolving is director of research at Pennwalt Pharmaceutical Co., Rochester, NY. An account of our adventures has been published.[2]

"Of many recent reviews on the (Na,K) ATPase[3] perhaps the broadest is that of Hobbs and Albers."[4]

1. **Skou J C.** The influence of some cations on an adenosine triphosphatase from peripheral nerves. *Biochim. Biophys. Acta* **23**:394-401, 1957.
2. **Post R L.** A reminiscence abut sodium, potassium-ATpase. *Ann. NY Acad. Sci.* **242**:6-11, 1974.
3. ..... A perspective on sodium and potassium ion transport adenosine triphosphatase. (Mukohata Y & Packer L, eds.) *Cation flux across biomembranes.* New York: Academic Press, 1979. p. 3-19.
4. **Hobbs A S & Albers R W.** The structure of proteins involved in active membrance transport. *Annu. Rev. Biophys. Bioeng.* **9**:259-91, 1980.