Dr. Herbert and Nicole Wertheim Leadership in Healthcare and Medicine Lectureship

Gas Channels

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Date: March 21, 2014
Time: 10:00 am - 11:00 am
Venue: AHC2 655
Refreshments will be provided

Biography: Dr. Boron is the David N. & Inez Myers/Antonio Scarpa Professor & Chairman of the Department of Physiology & Biophysics at Case Western Reserve University. He earned his AB in chemistry at Saint Louis University, & his MD and PhD (Physiology & Biophysics) at Washington University in St. Louis. Boron joined Yale University as a postdoctoral fellow with Emile Boulpaep in 1978, & remained there for the next 29 years, serving as Chairman of the Department of Cellular & Molecular Physiology for three 3-year terms (1989-1998). In 2007 he returned to his hometown of Cleveland. Boron is the former President of the American Physiological Society (APS) & is currently Secretary-General of the International Union of Physiological Sciences (IUPS). He is the former editor-in-chief of Physiological Reviews & former editor-in-chief of Physiology. He & Emile Boulpaep co-edit the textbook Medical Physiology. Boron developed his life-long interest in acid-base transport & intracellular-pH regulation with PhD mentor Albert Roos as well as Paul De Weer, & his complementary interest in renal HCO_3^- transport with Boulpaep. His group currently focuses on three related areas: the molecular physiology of the Na^+-coupled HCO_3^- transporters, molecular CO_2/HCO_3^- sensors, & gas channels. Among Boron's previous honors are a Young Investigator Award (American Society of Nephrology/American Heart Association, 1986), the Robert F. Pitts Award (IUPS, 1993), the Gottschalk Award (APS, 1998), an NIH MERIT Award (2002), the Homer Smith Award (ASN, 2005), and the Sharpey-Schafer Award (The Physiological Society, 2008), & The Palade Gold Medal (shared with William Catterall & Richard Tsien, Wayne State University, 2010).

Abstract

The traditional view—stemming mainly from the pioneering work of Overton over a century ago—has been that all gases cross all membranes simply by dissolving in the membrane lipid. Two observations from our group are (I hope) slowly changing that perception. First, Waisbren et al (Nature, 1994) discovered the first membranes with negligible gas permeability. Second, Nakhoul (Am J Physiol 1998) demonstrated the first gas channel—which is in fact the water channel aquaporin 1 (AQP1)—by finding that the heterologous expression of human AQP1 in Xenopus oocytes accelerates the fall of intracellular pH (pH_i) elicited by exposing the cell to CO_2. We have now introduced a new approach for assessing the movements of gases that affect pH: we use a microelectrode to monitor the pH on the surface of an oocyte (pH_s). The influx of CO_2 (which causes a sustained fall in pH_i) causes a transient rise in pH_s, the magnitude of which is proportional to CO_2 influx. Similarly, the influx of the weak base NH_3 causes a transient fall in pH_s. We used this approach to study the CO_2-vs-NH_3 selectivity of several AQPs as well as members of the Rh family. We find that each channel has a characteristic selectivity for CO_2 vs NH_3—the first example of gas selectivity. Inhibitor studies suggest that CO_2 moves—predominantly or exclusively, depending up on the channel—through the central pore that is at the middle of AQP4 tetramers or Rh trimers. In terms of physiological significance, renal proximal tubules reabsorb ~80% of all filtered HCO_3^- by moving CO_2 across the apical membrane and then HCO_3^- across the basolateral membrane. Apical AQP1 appears to be responsible for ~60% of the CO_2 uptake from lumen to cell. Moreover, we and other have shown that AQP1 and the Rh complex account for ~90% of all CO_2 permeability in RBCs. Our most recent work indicates that the majority of O_2 transport across RBC membranes occurs through channels. Thus, at least in certain cells that perform gas transport at high rates, gas channels appear to play important physiological roles.

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