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Oxender D L & Christensen H N. Distinct mediating systems for the transport of neutral amino acids by the Ehrlich cell. *J. Biol. Chem.* **238**:3686-99, 1963.

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This paper developed a strategy for discriminating distinct transport systems. Based on the sensitivity of the transport activity to alkali metal ion, pH, and competitive interactions, two distinct but overlapping systems (A and L) for the neutral amino acids were described for the Ehrlich cell. [The SCI® indicates that this paper has been cited in over 580 publications since 1963.]

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"At a recent national meeting of biochemists, someone came up to me after listening to my presentation on the genetics and cloning of transport in bacteria and said, 'It is nice that you stayed in the same transport research field that your father was in. He was using more classical approaches with animal cells in the 1963 *Journal of Biological Chemistry* paper and you are now applying recombinant DNA techniques to study transport in bacteria.'¹ I had to tell him I was somewhat older than he thought and bore responsibility for both approaches.

"I was just finishing my postdoctoral training with Christensen when the research for the 1963 paper on the A and L transport systems was carried out. The main view in the transport field for animal cells prior to 1963 was that a broad specificity system served for essentially all of the neutral amino acids, even though looking back at results from our laboratory and others, heterogeneity in the systems was already evident. The main contribution of our 1963 effort was to develop a comprehensive characterization involving kinetics, competitive interactions, and

NA⁺-dependence, and to provide simple letter names for reference. The letters A and L were chosen at the time to denote alanine-preferring and leucine-preferring, respectively. We considered more descriptive names such as sodium dependent and sodium independent, and pH sensitive and pH insensitive, which describe one or more of the properties of the A and L transport systems. We abandoned these terms since we could not anticipate how many systems might later turn up and what their properties might be. As we have learned more about the systems, we stopped referring to A and L as alanine- and leucine-preferring since each system represents a broad specificity transport system and it is possible to find or prepare amino acid solutes for which each system shows more distinct preference.^{2,3} The letters A and L should be considered as simple names for identification and not as indications of their specificity.

"Since that time, other systems for the neutral amino acids such as the ASC system have been distinguished.⁴ We used the Ehrlich cell for the initial studies because it is convenient to propagate and has high levels of transport activity. By comparing transport activities in a variety of cells and tissues, we have found that the Ehrlich cell as well as other transformed cell types generally has increased System A activity while more normal cells have lower levels of System A and high levels of ASC (see references 2 and 3). Starvation of normal cells for amino acids results in increased System A activity.

"Some of the reasons the 1963 paper has been cited as much as it has may lie in the simple letter names for transport systems showing detailed characteristics, as well as describing in one place a comprehensive statement of the strategy of discriminating the several systems kinetically and by use of analogues, pH, and alkali-ion specificities."

1. Landick R C & Oxender D L. Bacterial periplasmic binding proteins in membranes and transport 1981: a critical review. (Martonosi A, ed.) *Membranes and transport*. New York: Plenum Press, 1982. p. 81-8.
2. Christensen H N. Exploiting amino acid structure to learn about membrane transport. *Advan. Enzymol. Relat. Areas Mol. Biol.* **49**:41-101, 1979.
3. Shotwell M A, Kilberg M S & Oxender D L. The regulation of neutral amino acid transport in mammalian cells. *Biochim. Biophys. Acta* **737**:267-84, 1983.
4. Christensen H N, Liang M & Archer E G. A distinct Na⁺-requiring transport system for alanine, serine, cysteine and similar amino acids. *J. Biol. Chem.* **242**:5237-46, 1967. (Cited 140 times.)