

## UNIPORTERS, SYMPORTERS AND ANTIPOINTERS

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Transporters are a diverse group of membrane proteins that facilitate the movement of water-soluble solutes through the lipid bilayer of biological membranes. The least complex transporters are the uniporters (Kakuda and MacLeod, 1994). They simply facilitate the diffusion of their substrates across membranes and dissipate substrate gradients that arise as the result of other processes. Uniporters fall into two classes, channels and carriers, which mediate transmembrane solute movement by fundamentally different mechanisms. Channel proteins contain hydrophilic pores that span the lipid bilayer. Water-soluble solutes move across the membrane by diffusion through these pores. The lumen of a channel is accessible from either side of the membrane simultaneously. Carriers may also span the lipid bilayer, but their substrate binding sites are never accessible from both sides of the membrane simultaneously. Because of this difference in mechanism, carriers but not channels are able to mediate countertransport (Harold, 1986). Since carriers are much more closely related, at least mechanistically, to symporters and antiporters than to channels, they are the type of uniporter emphasized in this volume.

At the opposite end of the transporter spectrum from uniporters are the molecular devices that carry out primary active transport. Primary active transport involves conversion of energy stored in readily oxidized, reduced or hydrolyzed chemical bonds into electrochemical gradients of solutes, usually protons (Nelson, 1994) or other cations, across membranes. Primary active transport is the subject matter of many books (e.g. Harvey and Nelson, 1992). However, this book is not one of them.

The main subjects of this volume are the molecular devices that use the energy stored in the ion gradients generated by primary active transport to redistribute the actively transported ions, as well as many of the other organic and inorganic solutes of intracellular and extracellular fluids, across the membranes of cells and organelles. Because they couple the translocation of at least two substrates, these devices as a group are generally called cotransporters. One of the cotransported substrates (the driving substrate) always moves across the membrane in a direction that dissipates its electrochemical gradient, established directly or indirectly by primary active transport. The second substrate (the driven substrate) moves against its activity gradient. The energetically uphill translocation of the driven substrate has led some workers to refer to cotransport as secondary active transport. Especially when contending with this term, one must remember that the result of cotransport is always a net dissipation of the energy stored in gradients of all cotransported substrates.

The direction of transmembrane movement of the driven substrate can be either the same as (symport), or opposite to (antiport), that of the driving substrate. Simple symport systems are often just referred to as cotransporters, whereas simple antiport systems are

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Table 1. *Transporter nomenclature*

| Traditional name                                     | Gene name   | Systematic name                            |
|--|-------------|--|
| y <sup>+</sup> -type cationic amino acid transporter | <i>CAT</i>  | Cationic amino acid uniporter              |
| Na <sup>+</sup> /glucose cotransporter               | <i>SGLT</i> | Glucose–Na <sup>+</sup> symporter          |
| Na <sup>+</sup> /H <sup>+</sup> exchanger            | <i>NHE</i>  | H <sup>+</sup> /Na <sup>+</sup> antiporter |

often referred to as exchangers. In cases of cotransporters with more than two substrates (e.g. Nelson and Lill, 1994) the decision as to whether they are symporters or antiporters depends upon the direction of translocation, relative to that of the primary driving ion, of the substrate of greatest physiological importance.

One can assign a systematic name to any cotransporter by specifying the primary driven substrate, the primary driving substrate and their direction of movement with respect to one another (Table 1). However, the most studied and best characterized cotransporters have come to be commonly known by names that do not follow this convention (Bianchini and Pouysségur, 1994; Kaback *et al.* 1994; Wright *et al.* 1994).

In addition to a wealth of information on the structure and mechanism of action of individual cotransporters (for an overview, see Hediger, 1994), this chapter contains an analysis of cotransport energetics (Gerenscer and Stevens, 1994). It also contains an article in which ionic circuit analysis is applied to a transporting epithelium (Martin and Harvey, 1994). This epithelium is energized by a proton-motive ATPase that transforms the energy liberated during ATP hydrolysis into an electrochemical proton gradient. A K<sup>+</sup>/2H<sup>+</sup> antiporter then transforms the proton-motive force into an electrochemical potassium gradient that drives amino acid uptake by means of amino acid–K<sup>+</sup> symporters. Although this analysis may seem complex, it is a rather straightforward example of the ubiquitous use of cotransporters to effect the translocation of a wide variety of substrates using the energy in ion gradients generated by a very limited variety of primary active transport systems.

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