LmrA, a surprising and versatile multidrug transporter from Lactococcus lactis.

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The lactic acid bacterium Lactococcus lactis possesses at least two broad substrate specificity multidrug resistance transporters for cations. One transporter LmrP belongs to the Major Super Family of proton motive force driven efflux systems, the second LmrA to the ABC- family of efflux. Both transporters have strongly overlapping substrate specificities and can excrete a variety of antibiotics. LmrA has strong functional and structural homology with the human MDR P-glycoprotein. Biochemical and modeling studies revealed that its substrates are picked up from the inner leaflet of the membrane and excreted directly into the external medium. LmrA functions as a dimer and has multiple substrate binding sites (1). Site-directed mutagenesis and photoaffinity labeling in combination with structural modeling of LmrA has revealed that two substrate binding sites are at the interphase of the monomers in dimeric LmrA. The transmembrane helices 3 and 5 of one monomer together with transmembrane helix 6 of the second monomer contribute tot a binding site. The interaction of substrate with these helices changes during catalysis (2). The results are consistent with a two cylinder engine mechanism of LmrA.

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