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Cells need safety valves

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In *Escherichia coli*, the role of *lacA*, the third gene of the lactose operon, has remained an enigma. I suggest that its role is the consequence of the need for cells to have safety valves that protect them from the osmotic effect created by their permeases. Safety valves allow them to cope with the buildup of osmotic pressure under accidental transient conditions. Multidrug resistance (MDR) efflux, thus named because of our anthropocentrism, is ubiquitous. Yet, the formation of simple leaks would result in futile influx/efflux cycles. Versatile modification enzymes with low sensitivity solve the problem if the modified metabolite is the one exported by MDR permeases. This may account for the pervasive presence of acetyl transferases, such as *LacA*, associated to acetyl metabolite exporters. This scenario of constraints imposed by efficient influx of metabolites provides us with a model that should be followed when constructing synthetic cells.