Solute Carrier (SLC) transporters mediate the translocation of substrates across membranes and after GPCRs represent the second-largest fraction of the human membrane proteome. SLC transporters are critical to cell homeostasis, which is reflected in the fact that more than a quarter of them are associated with Mendelian disease. Despite a few exceptions, however, they have been under-utilized as drug targets and mechanistic understanding has been hampered due to technical difficulties in working with them. Here, I will present our multidisciplinary approach that has revealed important mechanistic themes of two SLC transporters that are key for our cells to utilize sugar as an energy source and for cells to fine-tune cytoplasmic and organellar pH.

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