

# Raiding the sweet shop

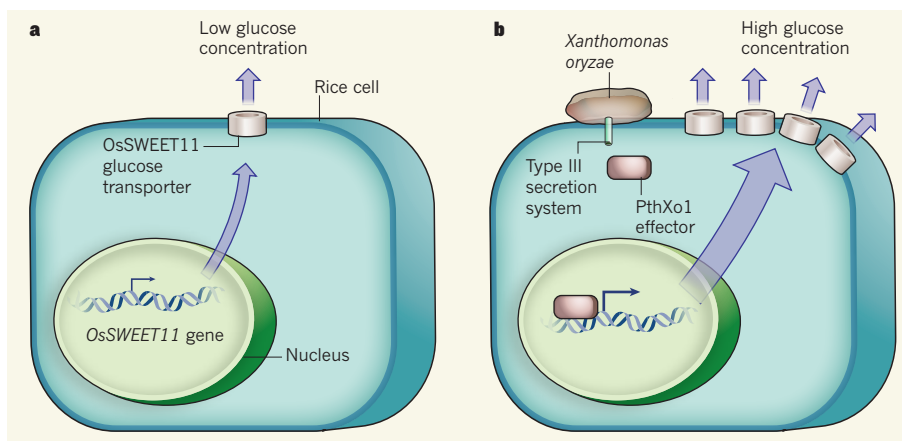
A type of sugar transporter has been discovered that exports glucose from cells. In plants, these transporters are targeted by disease-causing microbes that divert sugar production for their own use. [SEE ARTICLE P.527](#)

NICHOLAS J. TALBOT

Sweetening nectar, maintaining blood sugar levels and producing milk — these are just some of the many processes that require living cells to export sugar. It comes as a surprise, therefore, that until now the identity of the proteins responsible for sugar export has been unclear. On page 527 of this issue, Chen *et al.*<sup>1</sup> describe a family of sugar transporters, called SWEETs, that are essential for moving glucose between cells in both plants and animals. The importance of these transporters is highlighted by the fact that they are selectively targeted by pathogenic fungi and bacteria that plunder sugar from living plants.

Chen and colleagues' discovery<sup>1</sup> of SWEET transporters was aided by their use of a novel glucose nanosensor capable of measuring small changes in glucose concentration in living cells<sup>2</sup>. The authors first scanned a database of candidate membrane proteins from the model plant *Arabidopsis* to identify genes encoding potential sugar transporters. These genes were then expressed in cultured human embryonic kidney cells together with the nanosensor. Protein nanosensors work by a mechanism known as fluorescence resonance energy transfer (FRET), in which binding of a ligand — in this case, glucose — causes a conformational change in the protein that results in emission of fluorescence proportional to the amount of glucose present<sup>2–4</sup>.

Using this approach, as well as two independent methods, Chen *et al.* identified a candidate protein, AtSWEET1, that can transport sugar across plasma membranes, or between internal cellular compartments of living cells, and that defines a new type of glucose-efflux transporter. SWEET proteins contain seven helices that potentially span the cell or internal cellular membrane and that are predicted from the authors' modelling studies to form a single pore for transporting sugar across membranes. The authors find that the SWEET family is extensive in plants, with 17 members in *Arabidopsis* and 21 predicted in rice. But they also find that it occurs in animals — seven members in nematode worms and one in humans. All of the SWEETs have similar glucose-transport characteristics, implying that they have widespread roles in



**Figure 1 | Pathogen exploitation of plant SWEET genes.** These genes, identified by Chen *et al.*<sup>1</sup>, are targeted by bacteria to divert glucose into the intercellular spaces where the microorganisms grow. **a**, A rice cell in an uninfected plant has a set of SWEET-encoding genes, including *OsSWEET11*, and steady-state SWEET protein activity results in a low concentration of glucose outside the cell. **b**, The invading bacterium *Xanthomonas oryzae* uses a TAL effector protein, PthXo1, delivered by the type III secretion system, to increase *OsSWEET11* activity. Distinct SWEET-encoding genes are targeted by further TAL effectors, leading to increased extracellular glucose that fuels bacterial growth.

sugar export in both animals and plants.

What can we learn about intercellular sugar transport from the identification of the SWEET exporters? Several clues come from Chen and colleagues' investigations of the expression patterns of SWEET-encoding genes in diverse organisms, and also from their study of a range of previously reported mutant organisms whose characteristics turn out to be associated with genes now known to encode SWEET transporters. AtSWEET1, for instance, is highly expressed in *Arabidopsis* flowers, particularly in petals and stamens, suggesting that it is involved in supplying sugar to nectaries. AtSWEET8 is expressed in the tapetum — the nutritive layer of cells within the pollen sac that functions in pollen nutrition — and AtSWEET8 mutants cause male sterility, consistent with a function in pollen-tube development.

In animals, gene silencing of *CeSWEET1* in the nematode worm *Caenorhabditis elegans* causes fat accumulation, which may be a consequence of the loss of glucose efflux from cells. In mice, the *MmSWEET1* gene is highly expressed in the mammary gland during lactation, suggesting a function in glucose export to the cell's Golgi apparatus for synthesis and secretion of lactose for milk production. And

in humans, the HsSWEET1 transporter occurs predominantly within the Golgi, and is most abundantly found in the oviduct, epididymis and intestine — so raising the intriguing possibility of a hitherto unknown glucose-efflux pathway in which glucose is exported to the Golgi by a SWEET transporter to facilitate its secretion from epithelial cells to neighbouring tissue.

Accessing sugar from a host organism is, of course, also key to the survival and reproduction of microorganisms that need to invade and grow within living tissue<sup>5</sup>. Indeed, altering the expression and activity of SWEET efflux transporters would provide an elegant way of diverting glucose towards an invading pathogen. Remarkably, this ability seems to have evolved not only in bacterial plant pathogens but also in fungi. For example, Chen *et al.*<sup>1</sup> find that two plant-pathogenic fungi — the powdery mildew *Golovinomyces cichoracearum* and the grey mould *Botrytis cinerea* — induce the expression of distinct sets of SWEET genes during infection. How this is accomplished is unknown, but it may involve delivery of fungal effector proteins<sup>6</sup> into plant cells to bring about changes in host gene expression.

There is increasing evidence that fungi and other microbial pathogens can dispatch

effector proteins into plant cells to cause changes in the cells' behaviour<sup>6,7</sup>. Bacterial pathogens use the specialized type III secretion system that sends proteins directly into plant-host cells<sup>5,8</sup>, providing evidence for effector-protein-driven modulation of SWEET activity (Fig. 1). In rice, the recessive gene *xa13* has been reported to confer resistance to the bacterium *Xanthomonas oryzae*<sup>9</sup>. It is now clear that *xa13* originates from a mutation in the promoter sequence of the *OsSWEET11* transporter gene. *Xanthomonas oryzae* delivers a transcriptional-activator-like (TAL) effector protein, PthXo1, into rice cells, where it is taken up by the nucleus and targets the *OsSWEET11* promoter<sup>1</sup>. Mutation of the promoter therefore prevents the pathogen-induced increase in *OsSWEET11* expression. Thus, resistance to a bacterium develops because its ability to acquire sugar from the host plant is blocked.

Interestingly, a second glucose-efflux transporter gene, *OsSWEET14*, is activated by another *X. oryzae* TAL effector, AvrXa7, indicating that SWEETs are perhaps common

targets of bacterial effectors. This possibility is supported by Chen and colleagues' finding<sup>1</sup> that the bacterium *Pseudomonas syringae* pv. *tomato* induces expression of seven SWEET genes during infection of *Arabidopsis*. Pathogenic microorganisms are therefore able to manipulate the expression of sugar transporters and to divert the flow of glucose into the spaces between plant cells where the microorganisms can rapidly grow and reproduce. This ability may be pivotal to disease induction by microbes that proliferate in living host tissue.

The discovery of SWEETs opens up possibilities for studying the diverse roles of sugar transport in multicellular organisms, including the way in which glucose is moved from absorptive tissue to neighbouring cells in animals and its role in physiological processes such as lactation and control of blood glucose levels. In plants, the identification of SWEETs is likely to result in a far deeper knowledge of sink-source relationships in plant tissues, as well as providing insight into the biology of floral function and sexual reproduction.

Finally, understanding how pathogen effector proteins manipulate SWEET activity, and perhaps drive other forms of metabolic reprogramming in their hosts, may provide an exciting avenue for developing disease-control strategies. ■

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## COSMOLOGY

# Geometry of the Universe

**A neat way of measuring the geometry of the Universe offers a new test of the standard cosmological model. It probes, among other things, the elusive dark energy thought to be driving the Universe's expansion. SEE LETTER P.539**

ALAN HEAVENS

Twenty years ago, most cosmologists thought the Universe was dominated by a large amount of dark matter, and the idea of dark energy was no more than a curiosity. Now, as a result of exquisite observations of the radiation left over from the Big Bang, the large-scale structure of galaxies and distant supernovae, all that has changed: we have a generally accepted 'standard cosmological model', in which 23% of the energy density of the Universe is in the form of dark matter, 73% in dark energy, and only 4% in the form of the ordinary matter that we know on Earth. On page 539 of this issue, Marinoni and Buzzi<sup>1</sup> describe a new technique for testing the cosmological model that is completely independent of previous methods.

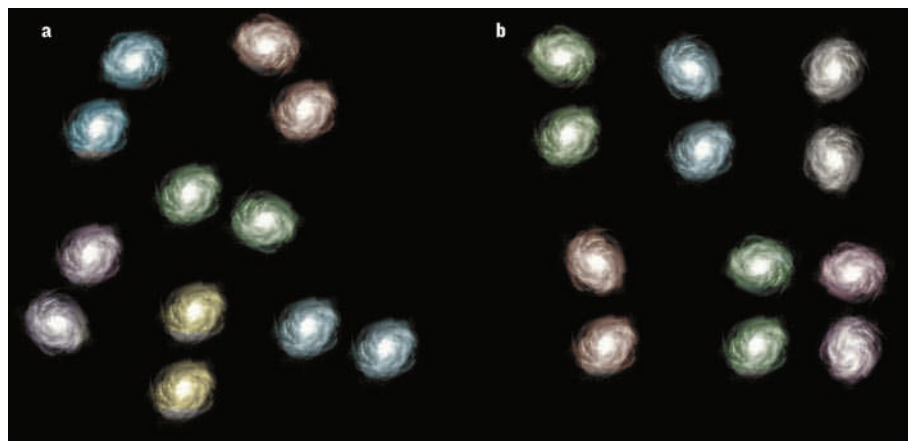
To say the finding that dark energy contributes about three-quarters of the total energy density of the Universe was unexpected would be an understatement. Gravity slows the expansion of the Universe, and yet the Universe isn't playing ball — its expansion rate is actually accelerating, and this

requires a component of the Universe with a repulsive gravity, a role thought to be played by dark energy. Not surprisingly, many cosmologists regard determining the nature of dark energy and dark matter as the most

important scientific question of the decade.

Our picture of the Universe involves putting together a number of pieces of evidence, so it is appealing to hear of Marinoni and Buzzi's novel technique<sup>1</sup> for testing the cosmological model, not least because it provides a very direct and simple measurement of the geometry of the Universe. One of Einstein's most remarkable insights was that the geometry of the Universe depends on its contents. So we can use geometrical measurements to determine the amounts of dark matter and dark energy, and the nature of the latter.

The general idea of Marinoni and Buzzi's technique goes back to Alcock and Paczyński<sup>2</sup> and, curiously, exploits the fact that we cannot directly measure distances in cosmology — there is no prospect of placing rulers between us and a distant galaxy. Instead, we rely on



**Figure 1 | The principle of Marinoni and Buzzi's cosmological technique<sup>1</sup>.** **a**, If the correct geometry and contents of the Universe are assumed, then the orientation of galaxy pairs should appear to be random. **b**, If not, then the pair orientations will show a preference for certain directions. (For clarity, the complications arising from the orbital speeds of the galaxies are not shown.)