protect the silicon surface at a thickness of only 0.8 nanometres. Conventional solar cells use opposing electrical contacts on the top and bottom of a light-absorbing semiconductor to extract electrons and holes, which gives rise to the electric current. By contrast, some high-efficiency solar cells are designed with both types of contact separated, but on the rear of the device. Such a rear-contact cell design, coupled with the passivation layer, is key to the authors' singlet-fission solar cell.

Einzinger and colleagues show that, when the tetracene layer on top of their solar cell is excited with blue or green light, triplet excitons are formed (Fig. 1). These excitons are transferred through the hafnium oxynitride into the silicon solar cell, without the need for extra electrical contacts. The exciton yield, which is defined as the average number of excitons transferred into the solar cell per photon, is about 1.3. In addition to the yield exceeding 1, further evidence for triplet-exciton transfer lies in magnetic-field effects that have a distinctive signature for triplet excitons born from singlet fission.

After excitation of the tetracene, collisions between electrons and holes in the silicon layer lead to the emission of light. Modelling of this light shows that 76% of triplet excitons are transferred through the passivation layer, compared with 56% of singlet excitons. The singlet excitons are not beneficial because they represent only one electron–hole pair per photon. Therefore, reducing their influence on the solar cell by increasing the rate of singlet fission in the tetracene, and thus the proportion of triplets at the interface, is a major goal for the near future.

At this stage, Einzinger and colleagues' solar cell is relatively inefficient and the design is ripe for optimization. The hafnium oxynitride passivates the silicon surface, but the first few injected electrons and holes are found to initially fill imperfections at the silicon surface before moving into the solar cell. This finding indicates that the interface is still imperfect, but nevertheless shows the potential for this strategy in a working solar cell. Furthermore, the mechanism of triplet-exciton transfer, and how it can be expedited, is currently not described well by theory. Despite the need for considerable improvement, the field is now set on a route towards efficient triplet-exciton transfer into silicon that could some day make Dexter's dream a reality. ■

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TUMOUR BIOLOGY

Metabolic signal curbs cancer-cell migration

Metastasis, the migration of tumour cells from their primary site, is associated with poor prognosis. A molecule made during cell metabolism limits metastasis, revealing that this metabolite restrains cancer progression. SEE LETTER P.127

LYDIA W. S. FINLEY

Cancer becomes lethal when tumour cells spread from their primary site in the body to invade distant organs — a process termed metastasis. For this complex event to occur, the cells must invade their surrounding tissue, enter the bloodstream and colonize another location, where secondary tumours called metastases form. Several of the early steps in metastasis, including cell migration, can be induced by the abnormal activation of a normal developmental program called epithelial–mesenchymal transition (EMT), in which the epithelial cells that line body surfaces take on the characteristics of mesenchymal cells, which have migratory properties[1]. On page 127, Wang *et al.*[2] identify a previously unknown mechanism by which a molecule generated in cellular metabolism inhibits the induction of EMT and thereby restrains the metastasis of lung cancer in mice.

The molecules formed during metabolism can have a key role in supporting the survival, proliferation and metastasis of tumour cells. Cancer cells have a higher than normal level of nutrient uptake and altered metabolic pathways, and these properties ensure that tumours make the metabolites they need to grow[3]. When tumour cells migrate into the bloodstream, they experience cellular stress. This is characterized by an increase in molecules called reactive oxygen species, and metabolic alterations that counter such stress can promote metastasis[3,4]. But whether metabolic pathways affect other aspects of metastasis has been poorly understood.

To investigate this further, Wang and colleagues individually blocked the expression of 111 metabolic enzymes in human lung cancer cells that had arisen from epithelial cells. Using these cells grown *in vitro,* the authors found that inhibiting production of the enzyme UGDH impaired the migratory capacity of the

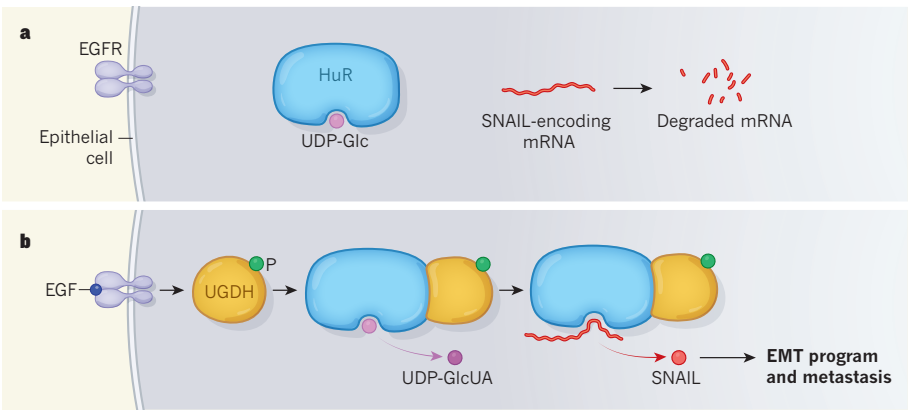

Figure 1 | A molecule formed during cellular metabolism hinders cancer-cell migration. Wang *et al.*[2] investigated how metabolism affects the migration (metastasis) of human lung cancer cells grown *in vitro* or transplanted into mice. These tumours arise from a type of cell called an epithelial cell. **a**, In epithelial cells that express the receptor EGFR, binding of the protein HuR to a UDP-glucose (UDP-Glc) molecule prevents HuR from binding to and stabilizing the messenger RNA that encodes the SNAIL protein, so that this mRNA is degraded. **b**, When signalling through EGFR is activated by the EGF protein, a phosphate group (P) is added to the enzyme UGDH, enabling UGDH to bind to HuR. UGDH catalyses the conversion of UDP-Glc to UDP-glucuronic acid (UDP-GlcUA). The authors propose that UGDH carries out this conversion on UDP-Glc bound to HuR, enabling HuR to bind to and stabilize SNAIL mRNA. This allows SNAIL to be produced, facilitating a process called epithelial–mesenchymal transition (EMT), which aids metastasis.

cells. UGDH converts UDP-glucose (UDP-Glc) to UDP-glucuronic acid (UDP-GlcUA), which is needed to make polysaccharide molecules such as hyaluronic acid, a component of the extracellular matrix material in the tissues in which epithelial cells reside. Hyaluronic acid can activate receptors on the surface of cells to initiate EMT, and its accumulation in tumours is often associated with poor clinical outcome[5].

Surprisingly, when the authors inhibited UGDH expression, cell migration was not impaired as a result of reduced levels of UDP-GlcUA or hyaluronic acid, but because of an accumulation of UDP-Glc. Because EMT in cancer cells is associated with an increase in their migration[1], the authors investigated whether UDP-Glc has an effect on the induction of EMT. They found that depletion of UGDH, and hence UDP-Glc accumulation, was accompanied by a decrease in the stability of messenger RNA that encodes a transcription-factor protein called SNAIL. This transcription factor regulates the expression of genes associated with EMT[1]. When the authors engineered cancer cells so that SNAIL was produced, the cells migrated even when UGDH was depleted. These results indicate that UGDH acts in a pathway that regulates cell migration by affecting SNAIL production (Fig. 1).

How might a metabolic enzyme such as UGDH affect mRNA stability? The authors focused on HuR, a protein that binds to and stabilizes mRNA targets[6], including the transcript that encodes SNAIL. They found that UDP-Glc binds directly to HuR, thereby preventing the protein from interacting with the mRNA that encodes SNAIL. The authors engineered a form of HuR that had mutations in the amino-acid residues predicted to coordinate its binding to UDP-Glc. Compared with cells that had wild-type HuR, those with the mutant form were found to be more likely both to form metastases in mice and to migrate *in vitro* across a membrane in a culture dish.

This suggests that an interaction between UDP-Glc and HuR prevents HuR from acting in a pathway to induce cellular programs that promote metastasis. When the authors injected tumour cells into mice and gave UDP-Glc to some of them, those that received UDP-Glc had fewer metastases than the animals that did not receive it.

There are intriguing hints that the authors' findings might have relevance for human cancer. In lung cancer, the receptor EGFR is commonly activated by mutations[7], and the authors found that an increase in signalling through this receptor is associated with increased stability of SNAIL-encoding mRNA in human lung cancer cells grown *in vitro*. They observed that EGFR activation triggers the phosphorylation (the addition of a phosphate group) of the amino-acid residue tyrosine 473 (Y473) in UGDH, inducing a physical interaction between HuR and UGDH.

Wang and colleagues speculate that phosphorylated UGDH bound to HuR causes the local conversion of UDP-Glc to UDP-GlcUA, thereby alleviating UDP-Glc's inhibition of the interaction between HuR and SNAIL-encoding mRNA and promoting SNAIL accumulation (Fig. 1). The authors engineered human lung cancer cells to express UGDH lacking a tyrosine residue at position 473, and found that such cells formed fewer metastases in mice than did cells that had wild-type UGDH. Wang *et al.* also noted that, in people with lung cancer, phosphorylation of Y473 in UGDH was more common in metastases than in primary tumours, and that this phosphorylation was associated with a poor clinical prognosis.

The authors' findings add to growing evidence that metabolites can affect gene-expression programs[8]. The best-known examples of this are cases in which metabolites provide substrates for enzymes that regulate gene expression by modifying chemical groups attached to DNA or to the histone proteins that bind to DNA. However, UDP-Glc instead affects gene expression by physically preventing the interaction between a protein and mRNA. How UDP-Glc specifically affects HuR's interaction with SNAIL-encoding mRNA, without impairing its interaction with other mRNAs, is an open question. Given the links between SNAIL expression, EMT and the extracellular matrix, it is tempting to speculate that coupling the production of SNAIL to the metabolites that generate hyaluronic acid might be an efficient way to coordinate the changes in both metabolism and protein production that are needed to promote metastasis.

Thus, in contrast to the metabolites that accumulate through cancer-associated mutations in metabolic enzymes and promote tumour progression[8], UDP-Glc limits progression. This discovery widens our horizons regarding the ways in which metabolites can influence cancer. Although it has long been recognized that the metabolic profiles of cancer cells differ from those of normal cells, we are only beginning to appreciate the complexity of the metabolic alterations involved in tumour growth. ■

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NEUROSCIENCE

The minds of two worms

Understanding how the brain's functions emerge from the workings of neural circuits is a central pursuit of neuroscience. New wiring diagrams of the nervous system in both sexes of a worm mark important progress. SEE ARTICLE P.63

DOUGLAS S. PORTMAN

Across biology, function follows form. The structure of a wing provides insight into flight; the anatomy of the lung suggests mechanisms for gas exchange. When applied to the brain, however, this approach falters. The uniform, gelatinous consistency of the mammalian brain belies an almost inconceivable cellular complexity: billions of nerve cells (neurons), interacting through trillions of connections (synapses), form circuits that perceive stimuli, store memories and generate emotions. What if we had a complete map of these connections? Would this help us to understand how the brain works? This is the premise of 'connectomics', the systematic identification of all connections in a nervous system. On page 63, Cook *et al.*[1] report the complete connectomes of both sexes of a tiny roundworm — a major step towards understanding how a brain's function emerges from its form.

Long before the word connectomics was first uttered, the ideas behind it were apparent to the late Sydney Brenner, who, in the 1960s, famously sought to 'tame' a creature whose nervous system might be completely mapped[2]. Brenner settled on the millimetre-long nematode *Caenorhabditis elegans*, affectionately known to those who study it as 'the worm'. The worm's nervous system comprises just a few hundred neurons, whose position and overall structure are identical between individuals.