two teams searched for other such protective mechanisms. Both groups analysed human cells grown *in vitro* to test whether any components block ferroptosis when GPX4 is not present, and they independently identified a gene encoding a protein that they name ferroptosis suppressor protein 1 (FSP1), which was previously called AIFM2.

Excitingly, the authors discovered that FSP1 replenishes a reduced form of ubiquinone, called ubiquinol, that acts protectively by combating the lipid peroxidation that drives ferroptosis. Further experiments revealed that this FSP1-dependent modification of ubiquinone, in locations other than mitochondria, acts to protect against ferroptosis. The comic-book superhero Green Lantern has a power ring that needs to be recharged once its protective energy becomes depleted, and, by analogy, FSP1's role in generating protective ubiquinol could be a similarly crucial recharging process.

The identification of this FSP1-mediated process suggests that drugs that inhibit FSP1 might be developed as anticancer treatments. Doll *et al.* and Bersuker *et al.* found that the level of resistance to ferroptosis across many human cancer cell lines grown *in vitro* correlates with the amount of FSP1 present in the cells, suggesting that modulating FSP1 might have clinical relevance. It would also be worth investigating whether treatments that boost FSP1 activity are useful as therapies for degenerative diseases driven by ferroptosis. These two latest studies clearly suggest that the mysteries of ferroptosis continue to yield important biological and therapeutic insights.

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Electrochemistry

Carbon dioxide efficiently converted to methanol

Xin-Ming Hu & Kim Daasbjerg

A molecular catalyst dispersed on carbon nanotubes has been found to catalyse the electrochemical conversion of carbon dioxide to methanol – a liquid fuel and industrially useful bulk chemical. **See p.639**

Molecular catalysts that mediate reactions with carbon dioxide often promote chemical reductions that form either carbon monoxide or formic acid (HCO_2H), but lack the activity and selectivity to reduce these compounds further to make other useful products, such as methanol, ethanol or methane. On page 639, Wu *et al.*[1] report that a molecular catalyst immobilized on carbon nanotubes can promote the electrochemical conversion of CO_2 to methanol in water. The result holds promise for advancing the search for catalysts that make highly reduced products from CO_2. Such products can then be used as fuels and as feedstock chemicals for industrial processes.

The heavy use of fossil fuels has led to excessive emissions of CO_2 into the atmosphere, and poses imminent threats to our climate system. Renewable energy sources, such as solar and wind power, are green and sustainable alternatives to fossil fuels for powering our society. Unfortunately, their intermittent nature limits their widespread use. Methods for storing the energy from these sources are therefore needed, to even out the supply.

Electrically powered methods for transforming CO_2 into fuels and other CO_2-derived chemicals are a promising strategy for tackling some of these energy issues, with the added bonus that they might help to mitigate atmospheric CO_2 levels[2]. But the development of such methods is by no means easy, because CO_2 is a stable and relatively unreactive molecule. Catalysts are therefore essential to activate CO_2 and drive its conversion into desired products.

Among the various classes of catalytic material, molecular catalysts that consist of ligand molecules bound to metal ions have certain advantages: they follow well-characterized reaction pathways, and have chemically modifiable structures that allow their activity to be tuned quite precisely. Molecular catalysts that promote the electrochemical conversion of CO_2 to carbon monoxide or, in fewer cases, to formic acid (or its formate salt) have been known for decades[3]. Attempts to reduce these compounds further to make methanol, ethanol, methane or ethylene (CH_2=CH_2) have been unsuccessful – or, at best, have provided

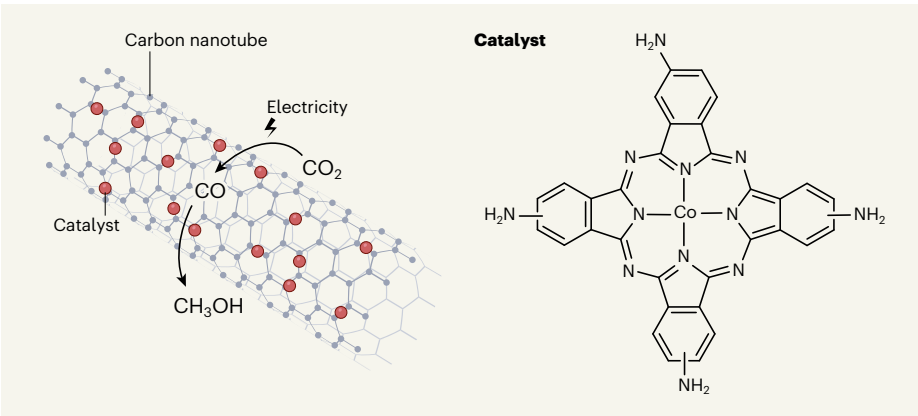

Figure 1 | Electrochemical production of methanol from carbon dioxide. Wu *et al.*[1] report that a cobalt phthalocyanine catalyst immobilized on carbon nanotubes can electrochemically reduce carbon dioxide in water. The reaction first produces carbon monoxide, which is reduced further to methanol (CH_3OH), an important liquid fuel and bulk chemical. The conversion of CO_2 to methanol using molecular catalysts has previously been ineffective. The point of attachment of three of the amino (NH_2) groups to the benzene rings in the catalyst is not known. Co, cobalt.

these products in small quantities with low selectivity[4,5] (that is, as a small component of a mixture with other products). Copper-based materials have previously been the most successful catalysts for such reactions[6].

Wu *et al.* now reveal that, when a complex called cobalt phthalocyanine is dispersed on carbon nanotubes, it has appreciable catalytic activity and selectivity for the electrochemical reduction of CO_2 to methanol (Fig. 1). More specifically, the cobalt phthalocyanine complex must be physically adsorbed to the surface of the carbon nanotubes as individual molecules. The key finding is that this mixed catalyst system not only activates CO_2 to produce carbon monoxide, but also, surprisingly, promotes further reduction to methanol when high voltages are applied in the electrochemical cell.

The researchers found that optimization of the catalytic system was difficult, because many extrinsic factors affected the activity of the molecular catalyst. These included the method used to immobilize the catalyst on the support; the specific carbon support chosen; the ratio of the concentration of the catalyst to that of the support; and the voltage used for the electrochemical reduction. The product selectivity of CO_2 reductions catalysed by cobalt phthalocyanine can be strongly affected by even a subtle variation in any of these factors[7]. However, the optimized catalyst system has significantly improved activity and selectivity compared with previous molecular-catalyst systems. Still, it is not as good as the state-of-the-art, solid-state metallic catalysts that have been reported for methanol production[8,9].

A long-standing issue associated with molecular catalysts in general is their long-term stability. Wu *et al.* found that their cobalt phthalocyanine system lost its catalytic activity over the course of five hours, and they identified the deactivation process as degradation of the phthalocyanine ligand. When they modified the ligand by appending amino (NH_2) substituents to it, they found that their system's stability was enhanced — it lasted for more than 12 hours, with only a slight loss of overall activity and selectivity. The reason for the stabilizing effect is not known. Note, however, that the catalyst would need to last for thousands of hours if the reduction process were to be implemented in an industrial setting.

The findings reveal that molecular catalysts have great prospects for use in CO_2 transformations. Future research could focus on further improving the activity, selectivity and stability of the molecular catalyst–carbon nanotube hybrid system through judicious chemical manipulations of the catalyst and the support, and of the interactions between them. Detailed mechanistic insight into the catalytic conversion of CO_2 to carbon monoxide, and further to methanol, might be gained using computational modelling and 'operando' characterization techniques, which monitor the consumption of reactants and the build-up of products during catalysis. Such efforts would lay the foundations not only for improving the performance of existing systems, but also for discovering new catalysts involving metal complexes, or structurally similar catalysts consisting of single metal atoms dispersed in carbon materials[10].

Concerns have been raised that the generally moderate activity, selectivity and stability of molecular catalysts for CO_2 reactions will prevent them from being used on an industrial scale. Moreover, the transport of CO_2 in electrochemical cells that have been used in proof-of-concept experiments is limited by the low solubility of this gas in water[11]. However, the adoption of flow technology in which a large quantity of gaseous CO_2 is fed directly to catalysts can greatly improve the outcome of CO_2 transformations[12]. With continued efforts to improve catalyst performance and the design of electrochemical cells, the industrial production of methanol from CO_2 could well be within reach.

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Microbiology

Fresh ammunition in bacterial warfare

Brent W. Anderson & Jue D. Wang

A previously unknown bacterial toxin has now been characterized. The protein is secreted into neighbouring cells, depleting them of essential energy-carrying molecules and so leading to the cells' demise. **See p.674**

To survive, bacteria must monopolize valuable resources. One way to do this is to attack and outcompete neighbouring cells — for example using the type VI secretion system, which injects neighbours with a toxin that can inhibit their growth or kill them[1]. On page 674, Ahmad *et al.*[2] describe a previously unknown toxin, Tas1, used in the type VI secretion system of the pathogen *Pseudomonas aeruginosa*. Tas1 launches a two-pronged attack on cells: not only does it rapidly deplete them of essential energy-carrying ATP molecules, but it also produces a signalling molecule that prevents the synthesis of more ATP.

Ahmad *et al.* made their discovery when studying a highly virulent strain of *P. aeruginosa*. The authors identified a region of the bacterium's genome that encodes a protein allowing *P. aeruginosa* to outcompete other bacteria. The amino-acid sequence of this toxin had no obvious similarity to any other proteins secreted by the type VI system.

The authors found that the toxin was structurally similar to a class of enzyme that synthesizes the 'alarmone' molecules guanosine tetraphosphate (ppGpp) and guanosine pentaphosphate (pppGpp), collectively referred to as (p)ppGpp. Alarmones are signalling molecules produced by bacteria and plants to help them to survive stressful conditions. Production of (p)ppGpp is a near-universal response to stresses such as nutrient starvation in bacteria. Its production causes a decrease in bacterial growth[3], preventing excessive proliferation and so allowing bacteria to survive in low-nutrient conditions.

It seems logical for a bacterial toxin to produce (p)ppGpp as a way of slowing the growth of competitor cells, so Ahmad and colleagues tested the enzymatic capabilities of the purified *P. aeruginosa* toxin. Unexpectedly, the protein did not produce (p)ppGpp. Instead, it produced the related alarmone (p)ppApp, which comprises adenosine tetraphosphate