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

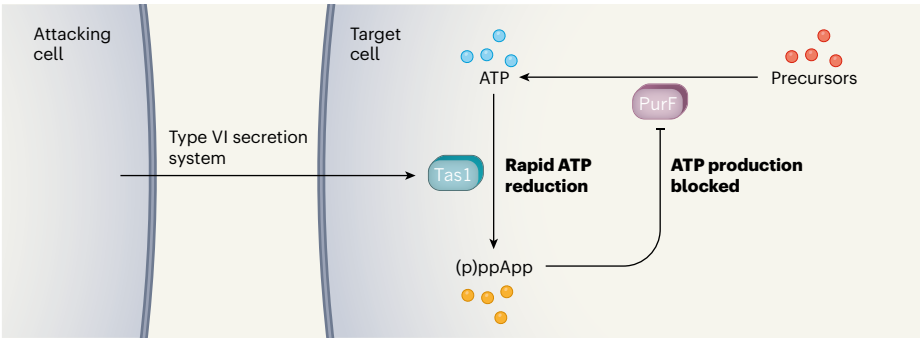

Figure 1 | A two-pronged attack system. Bacteria can attack target cells using cellular machinery called the type VI secretion system. Ahmad *et al.*[2] find that the type VI system of one bacterium, *Pseudomonas aeruginosa*, secretes a previously unknown toxin, which the authors name Tas1. Tas1 uses energy-carrying ATP molecules to produce the signalling molecule (p)ppApp, rapidly reducing ATP levels. In turn, (p)ppApp blocks production of ATP by inhibiting the first enzyme in the ATP-synthesis pathway, PurF. This two-pronged attack depletes target cells of essential ATP within minutes, causing death.

(ppApp) and adenosine pentaphosphate (pppApp) molecules. The authors therefore named the toxin type VI secretion effector (p)ppApp synthetase 1, or Tas1 for short. This is the first example of an alarmone-producing enzyme being transported between bacteria — a remarkable fact, given that these enzymes are found in nearly all bacteria.

Type VI systems often secrete enzymes that destroy essential cellular structures, such as the cell wall, the cell membrane or the genome itself[4]. But Ahmad *et al.* found that the toxicity of Tas1 is linked to its synthesis of (p)ppApp from ATP (Fig. 1). ATP is crucial for almost every cellular process, from DNA replication to the production of proteins and maintenance of the cell's structural integrity. Tas1 synthesizes (p)ppApp from ATP strikingly quickly — one molecule of toxin produces 180,000 (p)ppApp molecules per minute. At such a rate, the toxin depletes the target cell of ATP within minutes, simultaneously disrupting several essential metabolic pathways. Of note, *P. aeruginosa* secretes other toxins alongside Tas1, some of which attack cellular structures that require ATP for their synthesis, including the cell wall and membrane. Tas1 activity might therefore compound the effects of these other toxins.

Ahmad and colleagues went on to highlight the toxic role of (p)ppApp in influencing bacterial physiology. Little has been reported about how (p)ppApp is produced and what it does in bacteria[5]. The authors found that (p)ppApp blocks ATP synthesis in the target cell by binding and inhibiting PurF, a key enzyme in the synthesizing process. Thus, (p)ppApp probably prevents the cell from regenerating ATP and so escaping the death spiral induced by the alarmone's own production. More work is needed to delineate how much this role for (p)ppApp contributes to the overall toxicity of Tas1 in target cells.

Alarmone production is highly regulated to ensure that the molecules are synthesized only when needed, and degraded when stress has passed. Tas1 production of (p)ppApp overrides these rules — (p)ppApp is synthesized with abandon and, as the authors show, there are unlikely to be any enzymes that can degrade (p)ppApp quickly enough to avoid cell death. Nonetheless, this newfound understanding of (p)ppApp can augment our knowledge of other alarmones. (p)ppGpp, which is structurally similar to (p)ppApp, controls cell growth in part by inhibiting proteins involved in the synthesis of energy-carrying molecules such as ATP and GTP[3,6–8], including PurF. The fact that both (p)ppApp and (p)ppGpp inhibit this protein, along with the structural similarity between the two alarmones, led Ahmad *et al.* to hypothesize that the molecules could have many overlapping targets.

Tas1 is the only dedicated (p)ppApp-synthesizing enzyme found so far. However, (p)ppApp has been detected in some bacteria, in which its physiological role has yet to be determined[8]. Clearly, it is unlikely to act as a toxin in these cells. Ahmad and colleagues' discovery that (p)ppApp inhibits PurF is the first step towards mapping the network of targets regulated by this alarmone in healthy cells. Doing so should help us to gain a broader understanding of how alarmone regulatory pathways rewire bacterial physiology.

Type VI secretion systems provide bacteria with weapons against competitors, increasing their ability to thrive in a range of environments — from plants to the human intestinal tract to hospitals[9,10]. The discovery of a toxin that so irreversibly suppresses competitor metabolism opens a new chapter in our understanding of the ammunition used in interbacterial warfare. It will be exciting to see whether other examples of this toxin are found across the bacterial domain, or perhaps even in bacterium–host interactions.

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Solid-state physics

Surface polarization feels the heat

Gustau Catalan & Beatriz Noheda

A crystal's surface has been found to behave as a distinct material that has temperature-dependent electrical polarization — despite the rest of the crystal being non-polar.

When crystals of certain materials are squeezed, the compression causes a separation of internal charge — a polarization — that generates a voltage. This phenomenon is known as piezoelectricity. Some piezoelectric materials also exhibit spontaneous polarization that changes in magnitude with increasing temperature. These materials are said to be pyroelectric, and are useful in heat sensors and for solid-state cooling (because pyroelectrics change temperature in an applied electric field)[1]. Pyroelectrics have thus been intensively investigated, with research naturally focusing on electrically