ENGINEERING

Flying with ionic wind

Aeroplanes use propellers and turbines, and are typically powered by fossil-fuel combustion. An alternative method of propelling planes has been demonstrated that does not require moving parts or combustion. SEE LETTER P.532

FRANCK PLOURABOUÉ

Small, lightweight devices called lifters can propel themselves into the air without combustion or moving parts, and have become a popular topic of discussion with technology buffs on social media in the past few years. And yet the physical mechanism behind lifters has been known for more than a century[1]. When charged molecules in the air are subjected to an electric field, they are accelerated. And when these charged molecules collide with neutral ones, they transfer part of their momentum, leading to air movement known as an ionic wind. On page 532, Xu *et al.*[2] demonstrate that an aeroplane with a 5-metre wingspan can sustain steady-level flight using ionic-wind propulsion. Improvements are required, but the authors' proof-of-concept demonstration could pave the way for the development of enhanced propulsion systems.

In Xu and colleagues' plane, an electric field is applied to the region that surrounds a fine wire called the emitter (Fig. 1a). The field is strong enough to induce a chain reaction: free electrons in the region collide heavily enough with air molecules to ionize them, producing more electrons that then ionize more molecules. These electron cascades give rise to charged air molecules in the vicinity of the emitter — a phenomenon called a corona discharge. Finally, the charged molecules drift away from the emitter and generate a propulsive ionic wind as they are accelerated by the electric field towards a device called the collector (Fig. 1b). This process occurs only in gases, and not in liquids, justifying the authors' use of the term 'electroaerodynamics'.

Previous experiments suggested that ionic-wind propulsion could enable the steady-level flight of an aircraft, but that the feasibility of achieving this lies at the limit of what is currently technologically possible[3]. Xu *et al.* therefore needed to systematically search through all of the possible aeroplane designs for a feasible option. They used a technique called geometric programming to find the optimum set of design variables that would also minimize the aircraft's wingspan and, in turn, its weight, electrical-power requirements and cost.

The optimization technique found a feasible design at a wingspan of 5 metres, with a mass of 2.5 kilograms, a flight velocity of 4.8 metres per second and a power requirement of 600 watts. The authors built a full-scale plane based on this design (see Fig. 1b of the paper[2]). They flew the aircraft ten times, and showed that it achieved steady-level flight.

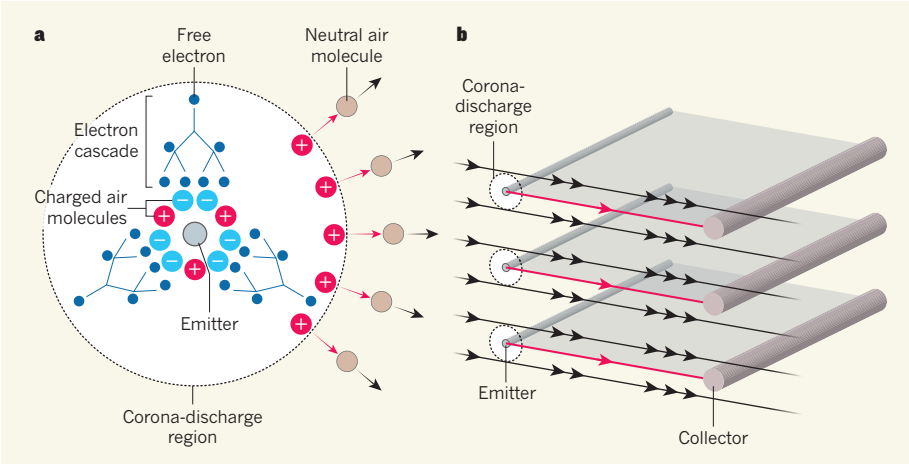

Figure 1 | Ionic-wind propulsion. Xu *et al.*[2] demonstrate that an aeroplane can sustain steady-level flight using air movement known as an ionic wind. **a**, In the authors' aircraft, an electric field (not shown) is applied to the region surrounding a fine wire called the emitter (shown in cross-section). The field induces electron cascades, whereby free electrons collide with air molecules (not shown in the cascades) and consequently free up more electrons. This process produces charged air molecules in the vicinity of the emitter — a corona discharge. Depending on the electric field, negatively or positively charged molecules drift away (red arrows) from the emitter. These molecules collide with neutral air molecules, generating an ionic wind (black arrows). **b**, The aircraft uses a series of emitters and devices called collectors, the longitudinal directions of which are perpendicular to the ionic wind. The flow of charged air molecules occurs mainly along the directions (red arrows) joining emitters and collectors. Consequently, the ionic wind is accelerated (black arrows) predominantly in these regions.

In the 1960s, various studies[4,5] seemed to sound the death knell for propulsion based on ionic wind. They demonstrated that only about 1% of the input electrical energy was used in propulsion — not far from the 2.6% reported by Xu and colleagues. However, at least three factors make the approach appealing for aircraft.

First, it is now known that the energy efficiency improves substantially when the aircraft velocity is increased. For example, if the velocity reaches 300 m s^{-1}, the efficiency[2,6] can be as high as 50%. Second, many studies have shown that ionic wind can enhance the aerodynamics of plane wings[7]. Third, the technique could facilitate what is known as distributed propulsion[8], which is considered a major direction for improvement in aviation.

Aircraft propulsion is quantified by the freestream mass-flow rate — the total mass of air that passes through a given area in a given time. This rate is directly proportional to the cross-sectional area of the propulsion system, and to the increase in air velocity provided by the system. In distributed propulsion, an array of propulsion systems is spread along the length of the aircraft. This increases the total cross-sectional area and, in turn, the freestream mass-flow rate. But it also enhances the aerodynamic drag (the frictional force between the aircraft and the air). Using fine wires as the propulsion system, as Xu *et al.* did, could allow the total cross-sectional area to be greatly increased, while having almost no impact on the aerodynamic drag.

The scalability of the authors' propulsion system remains to be seen. Can ionic-wind propulsion fly an aircraft of several tonnes? This practical issue is still open, but predictions suggest that aircraft such as the solar-powered plane Solar Impulse 2 could sustain steady-level flight using only ionic wind[9]. An advantage of

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ionic-wind propulsion systems, as opposed to propellers, is that they can be interfaced directly with batteries — the energy-storage devices of future planes — without affecting the rate of energy conversion. In the decades to come, drones or aircraft that use ionic wind might include secondary ionic-wind propulsion systems dedicated to energy saving and potentially coupled with solar panels.

These technological developments should provide a better understanding of the coupled physics of charged-molecule production and the resulting ionic wind that is central to such propulsion systems. The force generated by ionic wind is directly proportional to the electric current that flows in the system[2,10]. Because this current is strongly dependent on the configuration of emitters and collectors, research into the conception and optimization of ionic-wind propulsion can now begin, thanks to the breakthrough by Xu and colleagues. ■

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NEURODEGENERATION

Disease protein muscles out of the nucleus

Protein aggregation is a characteristic of several neurodegenerative diseases. But disease-associated aggregates of the protein TDP-43 have now been shown to have a beneficial role in healthy muscle. SEE ARTICLE P.508

LINDSAY A. BECKER & AARON D. GITLER

Most neurodegenerative disorders are characterized by the build-up of clumps of proteins in the brain[1]. A prevailing view in the field is that these large protein assemblies are inherently abnormal and are toxic to cells. Vogler *et al.*[2] challenge this canon by reporting on page 508 that muscle cells can contain physiological, reversible protein aggregates that have features similar to the aggregates seen in neurodegenerative disease, but that actually seem to be beneficial.

The protein TDP-43 forms aggregates in nerve cells in nearly all cases of the neurodegenerative disorder amyotrophic lateral sclerosis (ALS, also known as motor neuron disease)[3]. TDP-43 aggregation is also seen in other diseases, including frontotemporal dementia (FTD)[4] and inclusion body myopathy (IBM)[5], in which neurons and muscle cells, respectively, degenerate. FTD and IBM share genetic risk factors with ALS, indicating that the three have common disease mechanisms. In each disease, aggregates of TDP-43 are specifically found in the cytoplasm of dying cells. TDP-43 also has a normal job in the nucleus of healthy cells, where it acts as an RNA-binding protein[4].

Vogler *et al.* set out to investigate the behaviour of TDP-43 in healthy muscle. In doing so, they made a surprising observation. As expected, TDP-43 was located in the nucleus of muscle stem cells. But when the authors coaxed these cells to differentiate into young muscle fibres called myotubes, or if they used a chemical to injure a mouse's leg muscle to stimulate muscle regeneration, TDP-43 accumulated in the cytoplasm. There, it formed transient granular structures, which the researchers dubbed myo-granules, before moving back to the nucleus a few days later, as the myotubes became mature muscle fibres (Fig. 1). These data suggest that cytoplasmic TDP-43 myo-granules could have a role in muscle formation and regeneration.

Do myo-granules resemble the TDP-43 aggregates associated with neurodegenerative diseases? Disease aggregates are typically held together by strong bonds that are resistant to even heavy-duty detergents. Likewise, Vogler and colleagues found that TDP-43 myo-granules were resistant to such detergents. Another key feature of many neurodegenerative-disease proteins (although not all disease-associated TDP-43 aggregates) is that they can adopt a specific conformation, known as amyloid. Amyloids are long fibres made up of building blocks of the misfolded disease proteins arranged in a highly organized manner[6]. Using an array of analytical methods — including an antibody to specifically detect amyloid-like material, and high-resolution microscopy and X-ray diffraction techniques to enable examination of the myo-granule's structure — the authors demonstrated that TDP-43 myo-granules have amyloid-like properties.

Next, Vogler *et al.* investigated differences between TDP-43 in cytoplasmic myo-granules and in the nucleus, by examining the RNAs to which the protein binds in the two settings. They found that the types of messenger RNA that bind to TDP-43 changed markedly as muscle precursors differentiated into muscles. The mRNAs found associated with aggregated TDP-43 included those that encode proteins associated with the sarcomere — a unit of muscle structure that causes muscle contraction. These data suggest that TDP-43 myo-granules might control the development of sarcomeres.

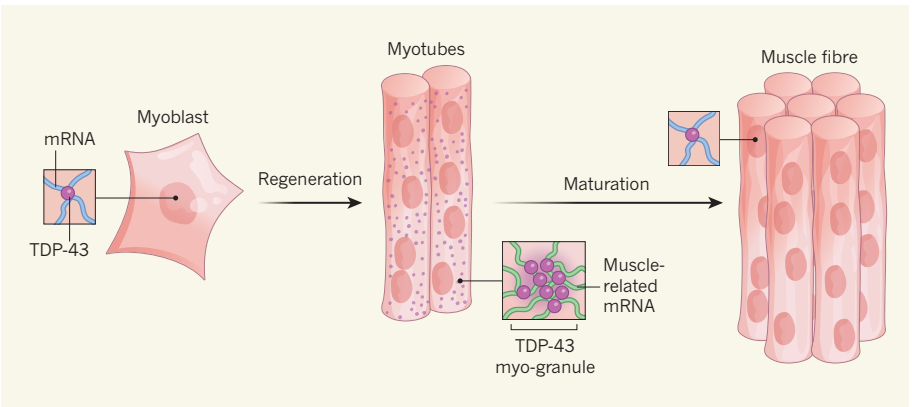

Figure 1 | A functional aggregate forms during muscle regeneration. In muscle precursor cells called myoblasts, the protein TDP-43, which binds messenger RNA, is located in the nucleus. Following muscle injury, myoblasts fuse into multi-nucleated fibres called myotubes that mature into muscle. Vogler *et al.*[2] show that TDP-43 transiently leaves the nucleus and assembles into large aggregate structures dubbed myo-granules, in which the protein binds to, and so might regulate, a distinct set of mRNA molecules involved in muscle formation. After recovery from injury, as the muscle matures, the myo-granules disassemble and TDP-43 returns to the nucleus.

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To confirm a role for TDP-43 in muscle formation, the authors generated mice whose muscle stem cells lacked one of two copies of the gene that encodes the protein. Lowering the level of TDP-43 in this way led to a decrease in the diameter of the muscle fibres generated in response to injury, indicating that TDP-43 is important for full muscle regeneration — probably because it somehow regulates the expression of muscle mRNAs. However, this experiment does not prove that myo-granule formation is necessary for TDP-43 function in muscle regeneration; reducing TDP-43 levels causes cellular dysfunction in many cell types, but Vogler *et al.* report myo-granules only in myotubes.

Regardless of the physiological function of TDP-43 myo-granules, the authors' data beg the question of whether these structures can eventually turn into disease aggregates. To investigate this possibility, the group turned to mice carrying a mutated form of the gene *VCP* that can cause ALS, FTD and IBM in humans[7]. The mutant mice, in which muscle, brain and bone tissue degenerates[5], had many more myotubes harbouring TDP-43 myo-granules than did wild-type mice. This suggests that *VCP* mutations might increase the risk of tissue degeneration by increasing the prevalence of myo-granules. In this scenario, perhaps small seeds of TDP-43 from myo-granules could be transported to the nerves that innervate muscle, where they might initiate a cascade of TDP-43 aggregation. Indeed, the earliest signs of neurodegeneration in ALS seem to originate at the nerve terminals adjacent to muscle, resulting in a 'dying-back' phenomenon that eventually reaches the main body of the neuron, which houses the nucleus[8].

The differences between TDP-43 disease aggregates and myo-granules are as interesting as the similarities. Unlike myo-granules, most TDP-43 disease aggregates seem to have an amorphous structure, although some do have amyloid-like characteristics[9]. Moreover, the disease aggregates seem to be irreversible, whereas myo-granules disassemble as muscle cells mature. Because of this, myo-granules could provide an opportunity to investigate how strongly bound aggregate structures are disassembled. Factors that promote the disassembly of myo-granules might also be effective at clearing disease-associated aggregates.

Vogler and colleagues' findings raise an intriguing question. Strenuous exercise and weight training stimulate repeated rounds of muscle growth and repair — could this activity increase the production of TDP-43 myo-granules, increasing the propensity of TDP-43 to aggregate and so leading to diseases such as ALS? Indeed, there is some evidence for increased prevalence of ALS in elite athletes[10,11]. However, much more evidence for the role of myo-granules and more human data will be needed before such a link can be assumed.

This paper sets the stage for future work characterizing the physiological function and regulation of TDP-43 myo-granules, and for investigating how these complexes might contribute to disease. There are other examples of amyloid-like protein complexes that form in healthy cells[12,13], but Vogler *et al.* describe the first that are made up of a protein that can also aggregate in disease. The race is on to search for more of these kinds of functional granule in other cell types. The idea that amyloid-like structures might have beneficial roles, rather than simply being associated with disease, represents a change in our understanding of these protein aggregates. Myo-granules provide a unique opportunity to unravel the differences between a safe and a dangerous aggregate. ■

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THERAPEUTIC RESISTANCE

A new road to cancer-drug resistance

The discovery of a mechanism that leads to cancer-therapy resistance highlights the many ways that tumour cells can adapt to survive — and reveals the limitations of categorizing patients by their gene mutations. SEE ARTICLE P.522

KATHARINA SCHLACHER

The development of resistance to cancer therapy is a major predictor of patient mortality. Therefore, understanding resistance mechanisms is key to improving therapeutic outcomes. On page 522, He *et al.*[1] report their discovery of a resistance mechanism in ovarian-cancer cells that contain a mutant version of the *BRCA1* gene.

Mutations in *BRCA1* and *BRCA2* genes can cause breast and ovarian cancer by inactivating either of two major biological pathways that ensure genome stability. One of the pathways repairs DNA double-strand breaks through a process called homologous recombination[2] (HR). The other process is called fork protection[3,4], and safeguards newly synthesized DNA at structures called stalled forks that arise during DNA replication.

In HR repair, an essential bottleneck step is the processing (resection) of double-strand breaks by nuclease enzymes to produce single-stranded (ss) DNA. BRCA1 acts as a key regulator protein that coordinates the recruitment of the nucleases, which include the MRE11–RAD50–NBS1 protein complex. BRCA1 also has a second role in HR repair: it recruits BRCA2, which in turn loads the RAD51 protein onto the ssDNA. RAD51 then assists in the binding of the ssDNA to a complementary strand that serves as a template for error-free repair.

Cancer cells that have certain *BRCA1* or *BRCA2* mutations cannot repair double-strand breaks caused by anticancer drugs currently used in the clinic, and so die when treated. Such drugs include cisplatin and PARP inhibitors (PARPi, drugs that specifically target BRCA-mutant tumours by taking advantage of their break-repair defects[5]). However, cancer cells can acquire strategies to circumvent the drugs' actions, causing resistance and limiting the use of these initially effective drugs.

In their rigorous study, He *et al.* used a gene-editing screening method[6] to identify resistance mechanisms in *BRCA1*-mutant ovarian-cancer cells. A known resistance pathway in both *BRCA1*-mutant and *BRCA2*-mutant cells is the restoration of BRCA function by re-mutating the original *BRCA* mutation (see ref. 7, for example; Fig. 1a). A second mechanism is drug avoidance, in which a membrane protein pumps the drug out of the cell or reduces its uptake[8]. He and colleagues' screen correctly identified a membrane protein implicated in the uptake of cisplatin by tumour cells as a contributor to resistance, verifying

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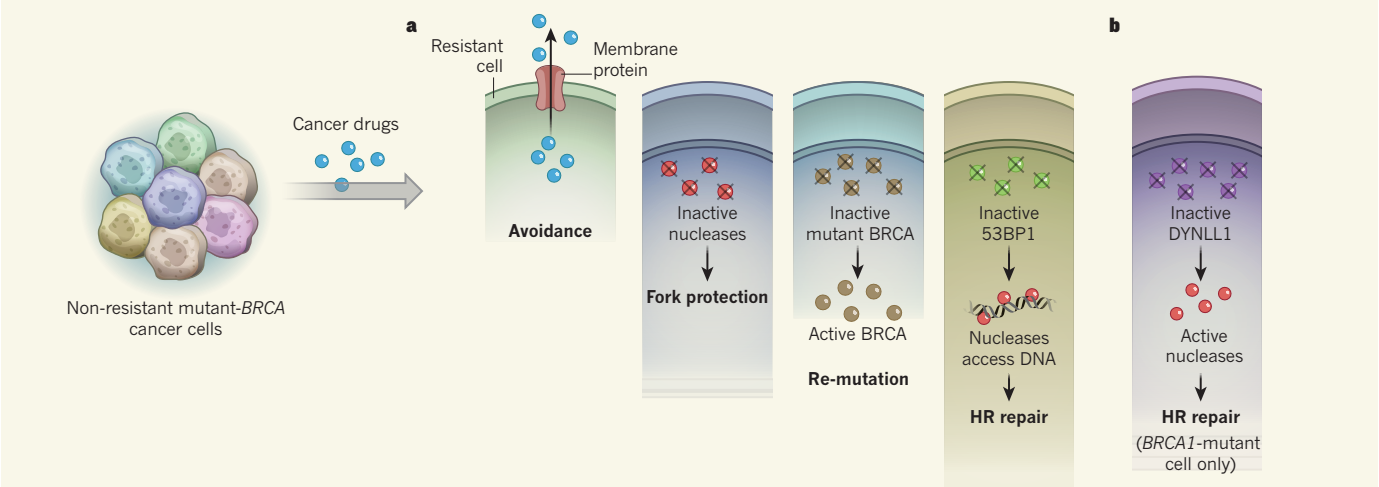

Figure 1 | Mechanisms of drug resistance in cancer cells that contain *BRCA* mutations. Many cancer cells have mutations in the *BRCA1* or *BRCA2* genes. These mutations inactivate a DNA-repair pathway that involves a process called homologous recombination (HR), or a process known as fork protection that is involved in DNA replication. **a**, *BRCA*-mutated cancer cells have developed many different paths to resist being killed by cancer drugs, including: drug avoidance by pumping drugs out of the cell through a membrane protein; restoration of fork protection by inactivating nuclease enzymes; re-mutating the original *BRCA* mutation to restore the functions of the BRCA proteins; and restoration of HR repair, for example by inactivating the 53BP1 protein in *BRCA1*-mutant cells to allow nucleases to access DNA. Here, the resistant cells are derived from non-resistant cells of the same colour. **b**, He *et al.*[1] report that in *BRCA1*-mutant cells, but not in *BRCA2*-mutant cancer cells, inactivation of the DYNLL1 protein activates nucleases and thus restores HR repair.

the suitability of the authors' approach.

Importantly, one of the top gene 'hits' identified by the screen as causing resistance to both cisplatin and PARPi was *DYNLL1*. The DYNLL1 protein acts in many cellular processes[9], including intracellular transport and motility, and also inhibits the enzyme nitric oxide synthase (which produces the cell-signalling molecule nitric oxide), but had not been previously implicated in cancer-drug resistance. Deciphering how its inactivation leads to resistance therefore seemed a daunting task.

The authors robustly established that DYNLL1 acts as a negative protein regulator of DNA-end-processing nucleases — it directly interacts with MRE11 and thereby keeps its nuclease activity in check. Inactivation of DYNLL1, therefore, unleashes the nuclease activity of MRE11, even when BRCA1 is not there to help guide it to breaks, and so restores the first of the two HR-repair functions normally carried out by BRCA1 (Fig. 1b).

Conceptually, drug resistance associated with DYNLL1 inactivation is analogous to that caused by inactivation of 53BP1 — another protein that inhibits DNA-end resection, in this case by blocking the access of nucleases to DNA. Inactivation of 53BP1 has been reported to restore resection and therefore resistance in *BRCA1*-mutant cells, but not in *BRCA2*-mutant cells[10,11]. Moreover, DYNLL1 is known[12] to interact with 53BP1. Yet, unexpectedly, He *et al.* show that resistance associated with DYNLL1 inactivation does not occur through loss of the 53BP1–DYNLL1 interaction.

He and colleagues' study highlights the intricacy of distinct gene functions in cancer-drug resistance, and the importance of defining biological mechanisms and activities to predict whether tumour cells will be killed. In this case, DYNLL1 inactivation reactivates resection, which is ablated in *BRCA1*-mutant cells, but not in *BRCA2*-mutant tumour cells. DYNLL1 inactivation, therefore, results in resistance in *BRCA1*-mutant cells, but not in *BRCA2*-mutant cells.

Another resistance mechanism that separates BRCA1 and BRCA2 functions has been reported in *BRCA2*-mutant ovarian-cancer cells[13], where inhibition of the EZH2 enzyme reduces the recruitment of the MUS81 nuclease to replication forks. Notably, this does not restore HR repair, but instead restores fork protection and the survival of *BRCA2*-mutant cells, and not of *BRCA1*-mutant cells. By contrast, EZH2 inhibition increases the sensitivity of *BRCA1*-mutant breast cancers to PARPi (ref. 14). Yet restoration of fork protection by inhibition of MRE11 results in resistance to PARPi and cisplatin in both *BRCA1*- and *BRCA2*-mutant cells, even when HR repair remains defective[15]. Thus, it is tempting to suggest that tumour-cell heterogeneity[16] — the existence of tumour-cell subtypes that stem from the same mutation, but which have mutated further to form distinct subpopulations — could partly arise as a result of cells making individual 'decisions' about which survival mechanisms to use, including HR repair, fork protection or both.

Although BRCA1 promotes resection during HR repair, it can also prevent the degradation of newly synthesized DNA by nucleases during fork protection, through an unknown mechanism. These dual, and seemingly opposing, modes of action raise the possibility that restoration of HR repair could promote tumour-cell survival even when fork protection is dysfunctional. Similarly, DYNLL1 inactivation might in fact cause defects in fork protection by promoting excessive MRE11 activity at replication forks, irrespective of *BRCA* mutations. Future studies will be crucial to dissect the apparently opposing nuclease processes at breaks and forks, and their effects on tumour-cell survival, as a possible nexus point for therapeutic intervention.

The emergence of diverse mechanisms for cancer-drug resistance demonstrates that cancer cells respond distinctively to individual defects of molecular function — rather than to an overall genetic defect — to rebalance the cellular homeostasis that ensures their survival. He *et al.* identified DYNLL1 inactivation as a resistance mechanism to cisplatin and PARPi; although both drugs cause double-strand breaks, their mode of action differs. In addition, other commonly used anticancer drugs, including gemcitabine, 5-fluorouracil and hydroxyurea, mainly disrupt replication reactions. Researchers, therefore, should expect to identify many different ways in which resistance can develop. These roads to resistance might require the restoration of replication processes, repair processes or both. The sequential use of different cancer therapies when an initial treatment is not successful is routine practice, but could lead to the development of multiple resistance mechanisms, and ultimately to resistance to any of the therapies.

People with cancer who have *BRCA1* and *BRCA2* mutations are currently grouped together in many genome studies and when considering treatment options, despite increased understanding of the molecular and genetic distinctions. He and co-workers' study suggests that molecular function, rather than genotype function — in this case, the specific

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role of BRCA1 in resection, rather than its overall role in HR repair or in fork protection — dictates the cellular outcomes. More broadly, these results suggest that personalized-medicine strategies should be considered that take into account molecular functions in individuals, rather than categorizing people solely by genotype. ■

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OPTOELECTRONICS

Efficiency breakthrough for radical LEDs

A strategy for using organic free radicals to make light-emitting diodes circumvents the constraints that limit the efficiency with which other organic LEDs convert electric current into light. SEE LETTER P.536

TETSURO KUSAMOTO & HIROSHI NISHIHARA

Light-emitting devices made from organic materials have the potential to be thin, flexible and lightweight, and might therefore be used in a variety of applications — including foldable display screens, 'smart' wallpaper incorporating digital devices, and windows that could be converted into illuminated panels at the flick of a switch. On page 536, Ai *et al.*[1] report the development of organic light-emitting diodes (OLEDs) that use free radicals as the emitter and convert electrons into light with high efficiency. The efficiencies of other types of OLED are generally limited by quantum-mechanical effects, but radical-based OLEDs (ROLEDs) don't have this constraint, owing to the electronic state of the radicals. The authors' ROLEDs have the highest emission efficiency obtained so far among LEDs that emit light in the deep-red and infrared regions of the electromagnetic spectrum.

Several types of LED are being actively developed because they are expected to produce displays that have higher brightness, colour purity, contrast and resolution than conventional lighting devices, while using less energy. OLEDs, in particular, have become familiar in the past decade, because they are used in the displays of mobile phones and televisions. Such displays perform better in several respects (such as contrast and colour reproducibility) than do liquid-crystal displays, which are currently used in many electronic devices.

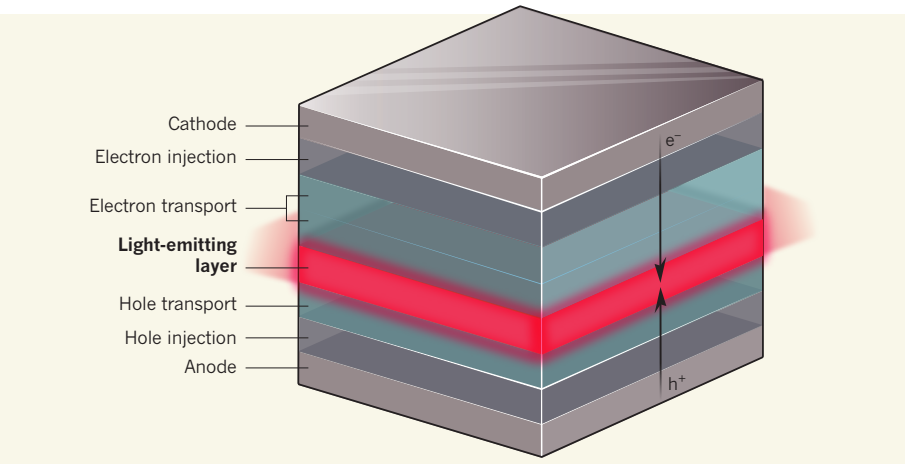

Figure 1 | An efficient radical-based organic light-emitting diode (ROLED). Ai *et al.*[1] report two organic free radicals that can be used in multilayered light-emitting diodes. Electrons (e^-) and holes (h^+; quasiparticles formed by the absence of electrons in an atomic lattice), which are produced by a cathode and an anode, respectively, pass through injection layers and transport layers before merging (recombining) on radical molecules in the light-emitting layer. This recombination produces light in the deep-red and infrared regions of the electromagnetic spectrum. Photons are produced from electrons in the light-emitting layer with almost 100% efficiency. The maximum external quantum efficiency of the device (the ratio of the number of photons that leave the LED to the number of electrons injected into it) is 27%, the highest such efficiency of any LED that emits deep-red and infrared light.

OLEDs were first reported[2] in 1987, and typically have a multilayered structure: a layer of material that contains light-emitting molecules is sandwiched between layers that transport electrons and holes (positively charged quasiparticles formed by the absence of electrons in atomic lattices), which, in turn, are sandwiched by electrodes as the outermost layers (Fig. 1). Additional layers that enable efficient injection of holes and electrons from the electrodes into the transport layers are also sometimes used. When an electric field is applied between the two electrodes, holes and electrons are injected and merge (recombine) on emitter molecules in the light-emitting layer to generate photons. The structure of the emitter molecule determines the colour of the emission.

One problem that still needs to be overcome for OLEDs is their low efficiency, which is quantified by the external quantum efficiency (EQE) — the ratio of the number of photons that leave the device to the number of electrons injected into it on the application of an electric field. The EQE is, in turn, proportional to two factors: the internal quantum efficiency (IQE), which is the efficiency with which photons are generated in the light-emitting layer from injected electrons; and the light outcoupling efficiency, which is the ratio of the number of photons that exit the device to the number generated within it. The value of the outcoupling efficiency is typically 20–30% (ref. 3). Quantum mechanics dictates that the IQE of conventional OLEDs based on fluorescent molecules is limited to 25% (ref. 4). The remaining 75% of efficiency is lost through recombination pathways that don't result in light emission. The EQEs of such OLEDs are therefore 5–6% at best.

Several groundbreaking methods have been established to solve the efficiency problem. For example, the IQE of OLEDs has been increased to nearly 100% by using phosphorescence (rather than fluorescence) as the light-emitting process[5], or by using a heat-activated

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light-emitting mechanism known as delayed fluorescence[6]. These strategies overcome the problem for devices based on conventional fluorescent molecules, but Ai *et al.* now report an innovative alternative method: they use organic radical molecules that exploit a different light-emitting mechanism, thereby enabling an IQE of almost 100%.

So what are organic radicals? Most organic molecules have an even number of electrons, in which each electron pairs up with another one, forming what is known as a closed-shell state. Organic radicals, however, have an odd number of electrons, and have one or more unpaired electrons in 'open-shell' states. Such radicals are highly reactive and therefore chemically unstable, and are typically generated transiently during chemical reactions. But the reactivity of radicals can be suppressed by modifying their molecular structures, and some are stable enough to be handled under air at room temperature.

In the context of light emission, it has long been thought that almost all stable radicals are non-emissive and inhibit emission from other sources. Nevertheless, stable light-emitting radicals have been available[7,8] since 2006, raising the possibility that they could be used in lighting materials and devices. Importantly, it was proposed[9] that ROLEDs would have high IQEs because, owing to the radicals' open-shell electronic states, they don't exhibit the energy-loss pathways that cause problems in conventional OLEDs.

The first ROLED was reported[10] in 2015 by researchers from one of the groups that contributed to the current paper, and it had an EQE of 2.4%. A year later, the same group showed experimentally[3] that it should be possible for ROLEDs to achieve an IQE of 100% — a milestone in the history of this LED class. Ai *et al.* now report another key step in the evolution of ROLEDs: they have developed two stable radicals that emit brightly in the deep-red and infrared regions of the spectrum, and they use them in devices that not only achieve almost 100% IQE, but also have an excellent EQE of 27%. This is the highest EQE among all LEDs that emit similar colours, and is largely a consequence of the efficiency with which electrons are converted into light on the radicals.

The high efficiency of Ai and colleagues' device is impressive, but ROLEDs in general currently emit light in only a limited range of colours. This is because just a small number of stable light-emitting radicals have been reported, and only those that have a particular type of chemical structure (known as an electron-donating group) deliver high EQEs when used in ROLEDs. Moreover, the electronic characteristics of light-emitting radicals suggest that these molecules will not be good at emitting blue (high-energy) light. A crucial next step will be to establish molecular design principles that enable organic radicals to be tuned to produce a wide range of colours — Ai and co-workers' radicals are not the first to emit deep-red and infrared light, and so have not extended the colour range.

Nonetheless, Ai and co-workers have demonstrated an innovative method for increasing the EQE of OLEDs, which could not have been achieved through simple developments of conventional fluorescent OLEDs. The authors' method also increases the number of radicals that can be used in ROLEDs. Given that they were discovered only a few years ago, there is probably plenty of potential for even further improvement — a challenge that offers great opportunities for materials scientists. In this field, radical progress truly promises a bright future. ■

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BIOPHYSICS

Membranes stick to one dimension

A nanometre-scale mechanism has been proposed to explain how bacteria improve their grip on human cells. The findings have implications for drug discovery, and might inspire biomimetic applications such as adhesives.

JOHN R. DUTCHER

Biological membranes serve as the barrier between cells and their surrounding environment, and regulate the transfer of ions and small molecules into and out of cells. Because of their central role in proper cellular operation, membranes are a target for many disease-causing microorganisms[1]. Writing in *Nature Communications*, Charles-Orszag *et al.*[2] propose a previously unknown mechanism by which one such pathogenic bacterium, *Neisseria meningitidis* (also known as meningococcus), rearranges the outer plasma membrane of host cells to improve its adhesion to the cells. Achieving improved cell adhesion is a key step in host infection, which in humans can lead to septic shock and meningitis[3].

A key challenge for *N. meningitidis* is how to stick to and colonize the endothelial cells that line blood vessels without being swept away by flowing blood. The interaction between the bacterial and endothelial-cell surfaces is not strong enough to withstand the forces exerted by blood flow[4], and so *N. meningitidis* uses extremely thin (6-nanometre-diameter) protein filaments called type IV pili (T4P) to increase its grip on the cell membrane. T4P can be extended and retracted through the cell wall in a variety of bacteria, and have crucial roles in the microbes' life cycle, allowing them to stick to and move across surfaces and to infect or damage other cells[5].

The interaction between *N. meningitidis* cells and endothelial cells results in the formation of protrusions on the endothelial-cell membrane[4], and it has been shown that proteins in T4P are essential for protrusion formation[6], and that they interact with specific receptors in the endothelial cells[7]. However, the molecular mechanism underlying the interaction of T4P with host cells was not understood. Charles-Orszag and co-workers now shed light on this mechanism by combining *in vivo* and *in vitro* studies with a simple theoretical model.

The theoretical model is one of the strengths of the new study, and describes a previously unknown mechanism for wetting (the spreading of a deformable substance such as a liquid on the surface of another substance[8]). Wetting is key to many aspects of everyday life, from the spreading of ink on paper to the beading of water droplets on spider webs or freshly waxed cars, and it typically occurs in two dimensions. However, in the case of a very thin fibre in contact with a soft membrane, the membrane cannot wrap around (wet) the fibre, because too much energy is required to accommodate the large curvature around the fibre's cross-section.

Charles-Orszag *et al.* use their model to show that it can be energetically more favourable for a narrow tube to be drawn out from the membrane, along the fibre, than wrapped around it (Fig. 1). This mechanism

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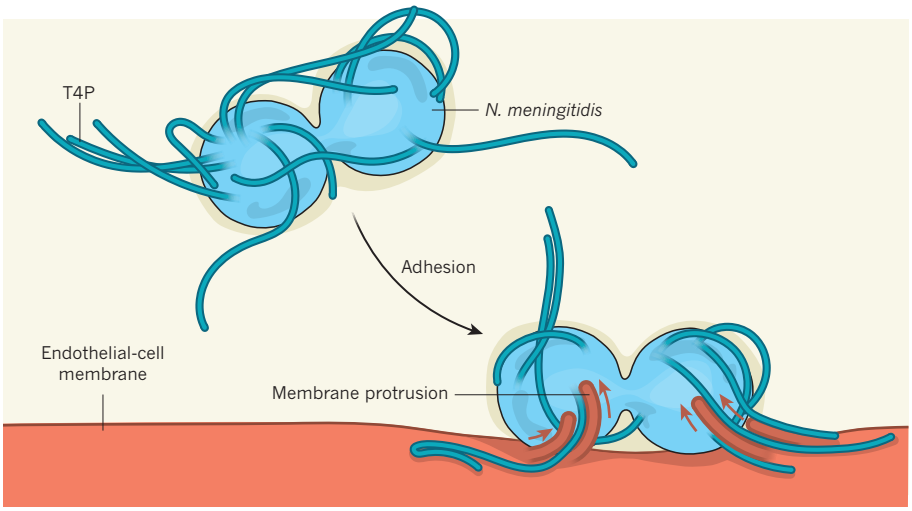

Figure 1 | Enhancing adhesion between a bacterium and an endothelial cell. The bacterium *Neisseria meningitidis* attaches itself to the endothelial cells that line blood vessels in host organisms. The bacterium uses fibres known as type IV pili (T4P) to induce the formation of protrusions from endothelial-cell membranes. These protrusions strengthen the bacterium's hold on the membrane, helping it to colonize cells without being swept away by the surrounding blood flow. Charles-Orszag *et al.*[2] propose that the adhesion of T4P to the membrane drives a process called one-dimensional wetting, in which the protrusions are drawn along the T4P fibres (red arrows). (Adapted from Fig. 5 of ref. 2.)

for forming membrane protrusions, which the authors call one-dimensional wetting, is driven by adhesion between the membrane and the fibre. The membrane protrusions could help to anchor a bacterium to a host cell as its T4P extend and retract, without breaking the adhesive interactions between the T4P and the membrane — thus maintaining the dynamic nature of the fibres.

Because the remodelling of endothelial-cell membranes by *N. meningitidis* had previously been observed only for cultured cells, the researchers studied blood vessels in human skin grafted onto mice to confirm that remodelling also occurs *in vivo*. They then complemented those experiments with *in vitro* studies to explore the mechanism involved. Unfortunately, the *in vitro* experiments did not examine the interaction of isolated T4P with model membranes, because this would have required the appropriate receptor proteins to be introduced into the membranes. Instead, Charles-Orszag *et al.* studied two model systems: artificial cells (known as giant unilamellar vesicles) interacting with filaments of a protein called actin through adhesion between the filaments and molecules attached to the cells; and endothelial-cell membranes interacting with mimics of the fibres found in the extracellular matrix around cells.

The authors show that 1D wetting does indeed occur in these systems, and that it can be understood quantitatively using their model. Their *in vitro* observations highlight the essential feature of this phenomenon: the presence of adhesion between a deformable membrane and a nanoscale fibre. Their observations also suggest that 1D wetting could occur more generally for physiologically important interactions of human cells with other biological nanofibres, and that it could have a major role in cell migration.

Further work is needed to understand 1D wetting in more detail. Systematic studies in which the fibre radius, strength of the adhesive interaction and surface tension of the membrane are varied would improve our understanding. In addition, further developments in microscopy will lead to better visualization of the structure and dynamics of the protrusions involved in 1D wetting.

Charles-Orszag and co-workers' results reveal opportunities for biomimetic strategies for wetting synthetic nanofibres and for producing strong adhesives, and new ways of moving nanoscale objects. Their findings also imply that reducing or disabling the 1D wetting of *N. meningitidis* T4P would limit the bacterium's ability to colonize and infect host cells, opening up a potential avenue for drug discovery. More generally, 1D wetting might enable cell function and health to be manipulated through interactions of cells with nanofibres to which biologically active molecules have been attached. ■

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GENETICS

A genomic approach to mosquito control

A high-quality genome sequence for the mosquito *Aedes aegypti* has now been assembled. The sequence will enable researchers to identify genes that could be targeted to keep mosquito populations at bay. SEE ARTICLE P.501

SUSAN E. CELNIKER

Every year, millions of people are bitten by the mosquito *Aedes aegypti*. Thousands die as a result of infection by the viruses the mosquito carries[1], which can cause diseases such as yellow fever, dengue fever and Zika. Current mosquito-suppression methods typically involve pesticides. However, mosquitoes quickly develop resistance to these chemicals[2], and pesticides can accumulate in the food chain, with adverse effects on beneficial insects, other wildlife and humans. New control methods are therefore needed. On page 501, Matthews *et al.*[3] describe a high-quality genome sequence for *A. aegypti* (Fig. 1). This exemplary work could be a major step towards addressing our current inability to manage expanding mosquito populations.

Arguably the most promising alternatives to pesticide-based mosquito control are targeted molecular strategies based on genetics. The first requirement for the success of such strategies is high-quality sequencing of the mosquito genome. This would enable researchers to identify gene targets that could be manipulated to achieve a range of effects: to disrupt the mosquito's host-targeting systems; to make sterile males; to convert females into harmless males; or to render the insect incapable of harbouring viruses.

The repetitive nature of the 1.3-gigabase-long

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JOAO PAULO BURINI/GETTY

Figure 1 | The mosquito *Aedes aegypti*. Matthews *et al.*[3] describe a high-quality genome sequence for this mosquito species.

A. aegypti genome has severely hampered efforts to generate a high-quality sequence. Previous attempts[4,5] resulted in patchy genomes that were assembled using short sequence reads. To overcome these challenges, Matthews *et al.* used next-generation sequencing to generate 166 Gb of long sequence reads with an average length of 17 kilobases. The authors used sophisticated mapping and gap-filling techniques to determine the positions of 94% of their sequence reads on the mosquito's three chromosomes, successfully assembling 1.28 Gb of the genome. The assembly has many fewer gaps than previous assemblies, and is a 100-fold improvement in terms of its N50 — a statistical measure based on the median assembled DNA-sequence length.

With this assembly in hand, Matthews and colleagues were able to improve our knowledge of the sequences of thousands of genes, and to discover new members of existing gene families. For example, the researchers identified more than 300 genes that encode ligand-gated ion channels, which allow ions to pass through membranes. These genes fall into three classes of receptor: odorant, gustatory and ionotropic. Together, they sense a wide range of chemicals, including carbon dioxide and chemicals that emanate from humans. Matthews *et al.* identified 54 previously unknown genes encoding ionotropic receptors — almost doubling the number known before. These genes are ideal candidates to target for disruption, because they confer the mosquito's ability to detect odours that indicate the presence of a host.

Of note, the authors identified 14 members of the best-studied subgroup of ionotropic receptors, nicotinic acetylcholine receptors, which act in the insect nervous system[6]. These receptors are the targets of insecticides called neonicotinoids, which have gained much attention owing to their adverse effects on beneficial insects such as bees. Knowing the sequences of the genes that encode these receptors should enable researchers to design insecticides that specifically target mosquitoes, sparing beneficial species.

Gene duplication is one mechanism by which insects can develop resistance to pesticides. Matthews *et al.* used their assembly to resolve a complicated gene-repeat region involved in one such resistance event. The region contains a cluster of three *Glutathione S-transferase (GST)* genes, which the authors found had been duplicated four times. These genes are important for metabolizing toxins, with one gene, *GSTe2*, capable of metabolizing the insecticide DDT. Increased expression of *GSTe2* has been associated with DDT resistance in a laboratory-colonized *A. aegypti* strain[7], supporting the idea that the gene duplication identified by the authors is involved in pesticide resistance. These data provide a proof of principle that the new genome will be an invaluable resource for researchers looking to analyse any gene family implicated in pesticide resistance.

Sex determination in *A. aegypti* is controlled by a sex-specific region called the M locus that is located on chromosome 1 in males only. It was known that the region contained the male-specific genes *myo-sex* and *Nix*, but they were absent from previous genome assemblies. This gap has been filled in the new genome. The authors estimate the M locus to be 1.5 megabases long (0.1% of chromosome 1), and show that it contains a much more repetitive sequence than does the rest of the genome — 73.7% compared with 11.7% genome-wide. The high repeat density is similar to that found in the Y chromosome of other animals[8].

Apart from the M locus, the sequence of chromosome 1 is very similar in males and females. This type of chromosome structure is known as homomorphic. Matthews and colleagues' genome will provide researchers with the opportunity to examine how the homomorphic sex chromosomes of *A. aegypti* are maintained, rather than evolving into heteromorphic chromosomes that are broadly different between the sexes — a better-understood phenomenon that is exemplified by the human X and Y chromosomes.

Finally, the authors used genetic-mapping techniques to identify regions of the genome that are associated both with the ability of mosquitoes to act as vectors for dengue virus and with resistance to the pesticide deltamethrin. The latter analysis highlighted candidate genes not previously known to be involved in pesticide resistance.

Even though Matthews and co-workers' genome is a radical improvement on previous assemblies, important genes might still be missing, because there are a few thousand gaps in the main chromosomes, and large gaps spanning specialized structures called centromeres, to which proteins bind during cell division. Nonetheless, the authors' sophisticated genome-sequencing strategy should act as a template for future efforts to assemble complex genomes. The genome and the gene sets themselves are publicly available for others to use (see go.nature.com/2dc6kxp), and, thanks to genome-editing technologies such as CRISPR–Cas9, researchers will easily be able to explore the effects of disrupting each gene identified as a candidate for targeting.

The use of tools rooted in genomic analysis and manipulation is a key step towards a pesticide-free world. Matthews and colleagues' work makes a major contribution to this goal. ■

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CORRECTION

The News and Views article 'Beating the quantum limits (cont'd)' (*Nature* **331**, 559; 1988) gave the wrong citation for Masanao Ozawa's paper. It should have referred to M. Ozawa *Phys. Rev. Lett.* **60**, 385 (1988).

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