anatomically intact but functionally dormant neuronal pathways from contributing to movement after an SCI.

What are the clinical implications of the findings? Chen *et al.* used a small molecule that is well tolerated in mice, even at a high concentration[6]. However, the relevance of this treatment for humans with severe SCI remains unclear. The authors' experimental model poorly mimics severe spinal-cord contusions commonly found in humans, in which nearly all the connections from putative relay neurons above the injured site are interrupted[9]. It therefore remains unclear whether Chen and colleagues' results could be reproduced after a clinically relevant SCI. Indeed, because CLP290 does not promote the growth of new neural connections, this treatment would be expected to be effective only after an SCI that spares a substantial proportion of nerve fibres. In addition, SCI causes a cascade of detrimental changes, so effective treatments must target multiple facets of spinal-cord repair and recovery[4], but CLP290 targets a single mechanism.

However, this type of orally administered pharmacological treatment is particularly attractive in combination with complementary strategies — notably, with interventions that promote the formation of relays in the spinal cord. For example, Chen and colleagues predict that CLP290 treatment will act synergistically with rehabilitative training, especially electrical spinal-cord stimulation, which promotes relay formation[6]. Alternatively, neural stem cells grafted into the injured spinal cord can enable reconstitution of relays across an SCI in monkeys[10]. Reducing neuron-mediated inhibition in the vicinity of the grafted relays could aid the functional integration of the relays into the host's neuronal networks.

We are reaching an exciting time in SCI medicine, when multiple interventions that have strong synergistic potential are approaching clinical applications. There are now realistic opportunities to develop treatments that improve recovery after SCI in humans. ■

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The author declares competing financial interests: see go.nature.com/2pdfupt for details.

HIGH-ENERGY PHYSICS

Proton bunches rapidly accelerate electrons

Experiments show that short bunches of protons can produce electric fields that are strong enough to accelerate energetic electrons compactly. This discovery could lead to miniaturized high-energy particle accelerators. SEE LETTER P.363

TOSHIKI TAJIMA

For almost a century, particle accelerators have revealed the microscopic structure of the Universe in ever-increasing detail. This continual improvement has required progressively higher particle energies and, in turn, larger accelerators (the latest accelerator for such exploration[1] has a circumference of 27 kilometres). In conventional accelerators, particles are propelled by electromagnetic waves that are produced by external circuits. To drastically reduce the size of accelerators, scientists are exploring ways to use waves that are instead generated internally, in an ionized gas known as a plasma[2]. On page 363, Adli *et al.*[3] report such a method, which makes use of an experiment in which the plasma waves are driven by bunches of protons — much like a motorboat on a lake drives waves in its wake.

The authors demonstrated their method using the Advanced Wakefield (AWAKE) experiment[4], which is located at CERN, Europe's particle-physics laboratory near Geneva, Switzerland. In this experiment, a proton bunch is injected into a plasma and sets electrons bobbing in its wake (Fig. 1). This electron motion generates a spatial modulation in the electric-charge density of the plasma, which in turn produces an electric field known as a wakefield. If another electron is injected into the plasma a short distance behind the proton bunch, it is captured by the wakefield and is accelerated to high energies.

Because the proton bunch moves at close to the speed of light, the wakefield can be extremely strong. It can even be at the level of the Tajima–Dawson field[2], the amplitude of which is several orders of magnitude larger than that of the fields used in conventional accelerators. This is the reason that scientists see wakefield acceleration as a means of substantially miniaturizing particle accelerators.

The amplitude of a proton-driven wakefield can be so large only when the proton bunch and the plasma's internal clock (in this case, the oscillation period of the plasma waves) are in resonance — a condition that enhances the amplitude of the waves, akin to pushing a child on a swing synchronously with the swing's oscillation period. This condition is met when the length of the proton bunch matches the wavelength of the plasma waves. The plasma's ability to sustain strong fields increases when the plasma density is increased, which decreases the wavelength

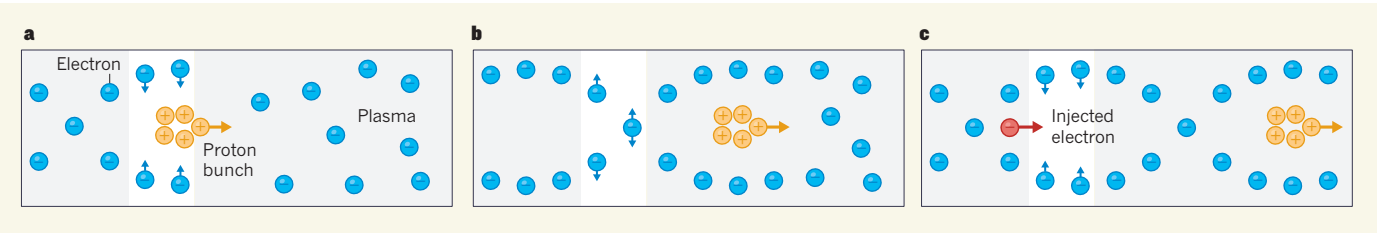

Figure 1 | The AWAKE experiment. **a**, In the Advanced Wakefield (AWAKE) experiment[4], a bunch of protons is injected into an ionized gas known as a plasma. As the proton bunch travels through the plasma, it attracts electrons contained in the plasma, pulling them towards the centre. **b**, By the time these electrons have reached the centre, the proton bunch has moved on. The electrons overshoot and begin to move outwards. **c**, The region that the electrons vacated is now positively charged. The electrons start to move inwards again, and the cycle repeats. Adli *et al.*[3] show that if an electron is injected into the plasma a short distance behind the proton bunch, this cycling of positive and negative charge can rapidly accelerate the injected electron.

of the waves. Consequently, a stronger wakefield requires a shorter proton bunch.

The main innovation in Adli and colleagues' work was, therefore, to make the length of the proton bunch as short as possible so that the bunch resonates with the plasma's internal clock, maximizing the amplitude of the wakefield. The authors achieved this feat using a feature of the plasma known as collective force. Although the electric force produced by each particle in the plasma is small, the collective force generated from all of the particles can be large, and becomes larger as the plasma density is increased[2]. The authors used this force to chop a long proton bunch into a series of shorter bunches. Because proton bunches are stiff (difficult to deform) at the extremely high particle energies present in the AWAKE experiment, this chopping was possible and effective only by using the plasma's collective force.

Adli *et al.* found that the wakefield produced by the short proton bunches could accelerate electrons to energies of up to 2 gigaelectronvolts in a plasma that is only about 10 metres in length. For comparison, at the European X-ray free-electron laser facility (European XFEL) in Germany, electrons are accelerated to energies of up to 17.5 gigaelectronvolts in an accelerator that is about 2 km long (see go.nature.com/2n6857t). In addition to providing compact acceleration, the authors' approach has a key advantage over standard accelerators and other wakefield accelerators. Because the proton bunches are stiff, they maintain their structure and speed. As a result, high-energy electrons can be produced in a single acceleration stage, as opposed to the complex multi-stage process that is needed in other accelerators.

Usually, the higher the energy of a particle beam, the longer it takes to stop (dump) the beam after use. The dumping of high-energy beams has become a serious issue because of the requirement of longer dumping lengths, which in turn increases the production of unwanted radioactive isotopes in the dense materials used for the dumping. The authors show that their accelerated electrons can form a beam of short electron bunches, which would encounter a large collective force if injected into an appropriately prepared plasma. Such a beam could therefore be stopped over a much shorter distance than conventional beams, inducing little radioactivity[5]. Overall, the authors' work represents a major step towards the development of future high-energy particle accelerators that use collective force. ■

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CANCER

RETRACTED

T cells home in on brain tumours

Immunotherapies activate T cells to destroy tumours, but the approach has failed in some brain cancers. A strategy to improve migration of T cells across the blood–brain barrier could overcome this limitation. SEE ARTICLE P.331

MICHAEL PLATTEN

Therapies that activate immune cells called T cells to target tumours are an efficient way to combat many types of cancer[1]. But an aggressive brain cancer called glioblastoma has proved a particular challenge for immunotherapies[2]. The blood–brain barrier protects the brain against immune-cell infiltration to prevent the potentially life-threatening effects of brain inflammation. This phenomenon is beneficial in normal circumstances, but it prevents T cells from reaching glioblastomas, making the tumours immunologically 'cold'[3]. On page 331, Samaha and colleagues[4] report a way to trigger infiltration of T cells into the brains of mice, thus making glioblastomas vulnerable to immunotherapy.

In the disease encephalitis, brain inflammation occurs because T cells that are typically excluded from the brain migrate across the blood–brain barrier. This migration is a coordinated process that requires activated T cells circulating in the bloodstream to adhere to endothelial cells, which line blood vessels. Adhesion is mediated by the binding of ligand molecules on T cells to cell-adhesion molecules such as ALCAM, ICAM-1 and VCAM-1 on endothelial cells[5]. These cell-adhesion molecules are expressed at higher than normal levels in encephalitis[6]. Binding between ALCAM and the T-cell ligand CD6 halts the progress of activated T cells through blood vessels, allowing subsequent binding by ICAM-1 and VCAM-1.

50 Years Ago

A campaign was opened last week for funds to refloat the Great Britain, one of the three major ships designed by Brunel. The object is to tow her back from the Falkland Islands to the Bristol shipyard … The Great Britain was the first ocean-going iron ship and the first to be driven by propeller … Brunel intended the ship to carry passengers of the Great Western Railway … to New York, but the Great Britain made only a few transatlantic voyages before running aground … Brunel managed to refloat the ship, which for the next 20 years carried emigrants to Australia … In 1875, the Great Britain's engines were removed and she was converted to sail, plying between Liverpool and San Francisco until put out of service by a fire near the Falkland Islands … Despite the ship's age, her structure is still sound enough to survive the journey back to Britain.
From *Nature* 21 September 1968

100 Years Ago

On the afternoon of Saturday, August 24 last, the allotment-holders of a small area in Hendon … were sheltering in their sheds during a heavy thundershower, when they observed that small fish were being rained to the ground. The fish were precipitated on three adjoining roads and on the allotment-gardens enclosed by the roads; the rain swept them from the roads into the gutters and from the roofs of the sheds … It is not easy to say how many fish fell, but … they were numerous … All the examples which came into my hands … prove to be the lesser sand-eel (*Ammodytes tobianus*) … The place where the sand-eels in question were deposited lies about one-quarter of a mile from the seashore … The only explanation … is that a shoal of sand-eels was drawn up by a waterspout.
From *Nature* 19 September 1918