50 Years Ago

In *Nature* of October 12, 1957 … we were glad and proud to congratulate the scientists and technologists of the U.S.S.R. on the successful launching of the first artificial Earth satellite (*Sputnik I*). Less than a month afterwards … we again had occasion to congratulate the U.S.S.R., when the second satellite (*Sputnik II*) was launched, this time containing a dog ... Now again, on April 12, a still further point in scientific advancement was reached, for on that day scientists and technologists in the U.S.S.R. reaped a rich reward for concentrated and ingenious research by successfully launching another space-vehicle (*Vostok*) into space. This satellite carried, among other things, a man (Major Yuri Alekseyevich Gagarin), travelled in orbit around the Earth in 89 min. 6 sec., and a little later was brought back safely to Earth, with Major Gagarin unharmed — all in about 108 min.
From *Nature* 22 April 1961

100 Years Ago

The first non-stop flight from London to Paris was made, on April 12, on a Blériot monoplane by M. Pierre Prier in 3h. 56m. M. Prier, who is the chief instructor of the Blériot School at Hendon, left that ground at 1.37 p.m., taking a course for Dover via Hampstead, Highgate, Greenwich, Chatham, and Canterbury … [H]e reached Dover, at 2.50 p.m. Thirty minutes later he was over Boulogne, and steering a straight course over Abbeville and Beauvais for Paris, where he arrived at 5.33 p.m., making a perfect landing in front of the Blériot sheds at the Issy-les-Moulineaux aviation ground … M. Prier … suffered no inconvenience throughout the journey except slight inflammation of the eyes, due to his neglecting to equip himself with goggles.
From *Nature* 20 April 1911

these tumour sites stimulates their chemoprotective functions. It will then be possible to investigate whether a similar TAM subset exists in human breast tumours — and in other types of tumour.

The authors also found that the combination of TAM depletion and chemotherapy reduced tumour-vessel density by 50% and led to greater tumour destruction. TAMs are known to stimulate excessive tumour vascularization[3,7,10,12], and their persistent expression of pro-angiogenic factors such as VEGF induces the formation of abnormal, hypo-perfused blood vessels, which limit the delivery of chemotherapy to tumours[10,11]. It is therefore conceivable that TAM depletion at sites away from blood vessels[4] may have skewed the perivascular TAMs from a pro-angiogenic[3,10] to an angiostatic function[12], thereby 'normalizing' the remaining vessels to acquire the structure and function of vessels in healthy tissues. This would temporarily increase blood flow to the tumour, enhancing the delivery and so the efficacy of the chemotherapeutic agent.

The findings of DeNardo and colleagues[4] add weight to an emerging compelling case for deciphering the complexity of leukocyte infiltrates in breast cancer. Their findings suggest that this may provide clinically relevant indications of the likely response to chemotherapy and thus patient survival. Future studies should show the relevance of the chemoprotective subset of TAMs that these authors identify for human cancer, and may even highlight molecular targets for therapies that restrain the activity of these cells or even reactivate their antitumour functions. Such reprogramming of the immune microenvironment in tumours is a promising strategy for improving the efficacy of standard anticancer treatments. ■

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ELECTRONICS

Power surfing on waves

Wavy strips of piezoelectric materials on stretchable substrates can both withstand larger applied mechanical strain without cracking and harvest energy more efficiently than their flat counterparts.

MIN HYUNG LEE & ALI JAVEY

Bendable and stretchable electronics such as roll-up keyboards and displays have garnered tremendous attention because of their portability and versatility. However, a major limitation of all portable devices available today is their short battery life, which often limits their functional use to just a few hours after a full charge. If an electronic device could be self-powered — for instance, by harvesting energy from the mechanical deformation it undergoes during typing, rolling and unrolling — then the power problem would be greatly reduced. Writing in *Nano Letters*, Qi *et al.*[1] describe a technique to produce thin ribbons of wavy piezoelectric materials on rubber substrates that paves the way to the realization of highly stretchable, energy-harvesting devices.

In piezoelectric materials, applied mechanical strain results in the accumulation of electric charge and the generation of electricity. This phenomenon, known technically as the piezoelectric effect, was first observed in 1880 by the French physicists and brothers Pierre and Jacques Curie. Since then, the effect has been used in a wide range of applications, including sensors and energy-harvesting devices. A few popular examples of inorganic piezoelectric materials include zinc oxide, aluminium nitride and lead zirconate titanate (PZT).

In their bulk form, these inorganic semiconductors are mechanically rigid. But once miniaturized to strips or wires of nanometre-scale thickness, they become mechanically flexible. Stretchability, however, is more challenging. In the past, researchers have demonstrated[2] that buckled silicon ribbons with periodic, wavy (sinusoidal) shapes can accommodate extreme increases in maximum

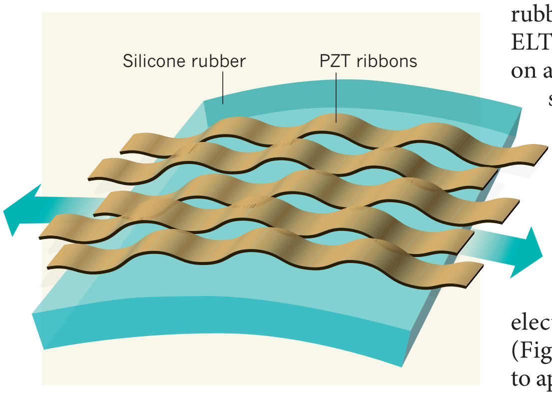

Figure 1 | The design of Qi and colleagues' energy-harvesting devices[1]. The stretchable devices consist of wavy ribbons made of piezoelectric material (lead zirconate titanate; PZT) on silicone rubber. They can withstand greater applied mechanical strain without cracking than can equivalent materials made into flat ribbons.

strain without fracturing. Qi *et al.*[1] have now extended this concept for the fabrication of stretchable, energy-harvesting devices using the technique of epitaxial layer transfer (ELT).

ELT involves the selective etch, lift-off and transfer of a single-crystalline thin film from a primary substrate, on which the film has been grown, to a secondary, receiver substrate. The technique allows the placement of a user-defined semiconductor 'X' on a substrate 'Y' (termed X-on-Y, or XoY) and has proved useful in a broad spectrum of electronic and photonic applications. ELT was used[3,4] as early as 1975, when micrometre-scale gallium arsenide/aluminium gallium arsenide (GaAs/AlGaAs) films were transferred from bulk GaAs wafers to glass substrates to enable the production of GaAs night-vision goggles and solar cells. In the late 1980s, a similar process was used[5] to fabricate thin-film GaAs diode lasers and other optoelectronic devices on glass substrates. And in the mid-to-late 2000s, researchers demonstrated[2,6] the ability to extend the ELT technique to substrates that are mechanically flexible and stretchable. This then led to the development of electronic devices that can conform to cover irregular and curvy surfaces.

Recently, the utility of ELT was further expanded[7] to allow the transfer of ultrathin films of type III–V semiconductors — down to a few nanometres in thickness — to silicon/silicon oxide (Si/SiO_2) substrates. This advance[7] offers the advantage of combining III–V semiconductors, which have high electron mobility, with well-established silicon technology for the exploration of energy-efficient electronics. Qi and colleagues' work[1] demonstrates yet another application of the ELT process: the production of buckled PZT strips on a rubber substrate for use as piezoelectric energy-harvesting devices.

More specifically, their approach is as follows. First, they pre-stretched a slab of silicone rubber. Second, they transferred, by means of ELT, PZT ribbons that had been patterned on a magnesium oxide substrate to the pre-stretched silicone substrate. After releasing the rubber substrate, the initially flat ribbons buckled, forming wavy geometries of amplitude and wavelength that depended on, among other factors, the thickness of the ribbons and their interaction with the rubber.

Next, the authors measured the piezoelectric response of the wavy PZT ribbons (Fig. 1), as well as that of flat PZT ribbons, to applied mechanical strain. In comparison to flat PZT ribbons, which exhibited failure under less than 1% strain, wavy ribbons withstood up to about 8% strain without cracking. Interestingly, wavy PZT ribbons also displayed an enhancement of up to 70% in piezoelectric response compared with flat ribbons, which the authors attribute to the large location-dependent strain gradient of the wavy structures.

Qi and colleagues' stretchable, piezoelectric energy-harvesting materials are an important advance in the rapidly growing field of conformal electronics and sensors. But as they themselves note[1], as far as the actual manufacturing of devices is concerned, a number of engineering challenges remain. Specifically, low-cost generation of wavy piezoelectric strips on large areas of substrate — ranging from cubic centimetres to metres of surface coverage — has yet to be demonstrated, and requires further research. In addition, more work is needed to determine the maximum density of electrical energy that can be generated by the devices, which will effectively establish their potential niche applications. ■

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IMMUNOLOGY

TRIM5 does double duty

TRIM5 proteins limit retroviral infection by targeting the viral coat. It now seems that these proteins can also serve as pattern-recognition receptors, which initiate cellular innate immune responses. **See Letter p.361**

CHRISTOPHER AIKEN & SEBASTIAN JOYCE

Mammalian proteins use various mechanisms to restrict retroviral infection[1]. One such protein, TRIM5, blocks HIV-1 infection in some primate species: when the virus enters a cell, TRIM5 engages with the viral coat, or capsid, inducing premature uncoating[2]. On page 361 of this issue, Pertel and co-workers[3] report that this protein has another function: TRIM5 is involved in activating cellular innate immune responses.

Cells sense infection with viruses and bacteria by detecting pathogen-specific molecules, including double-stranded RNA, lipids and carbohydrates. These molecules often form repeating structures — referred to as pathogen-associated molecular patterns — that bind to pattern-recognition receptors and activate signalling pathways that result in inflammation and cellular resistance to infection.

Pertel *et al.* show that increased expression of TRIM5 promotes the expression of specific genes by activating immune signalling pathways that are mediated by the transcription factors AP-1 and NF-κB. Accordingly, the removal of TRIM5 from cells not only reduces the expression of specific genes involved in innate cellular responses, but also allows HIV-1 to infect cells exposed to LPS. (LPS is a bacterial membrane component that binds the pattern-recognition receptor TLR4 and prevents HIV-1 infection by inducing a cellular antiviral state.) TRIM5's contribution to LPS-induced resistance to HIV-1 is probably independent of viral recognition: the cells Pertel and colleagues studied contain human TRIM5α, which does not bind the HIV-1 capsid efficiently. Nonetheless, their data indicate that TRIM5 contributes to innate immune responses triggered by a specific pattern-recognition receptor.

In addition to binding to and restricting retroviral capsids, TRIM5 is an E3 ligase enzyme that catalyses the attachment of the small modifier protein ubiquitin to itself and, potentially, to other proteins[4]. Whether the ubiquitin-ligase activity of TRIM5 plays a part in its retrovirus-restriction activity had remained unclear.

The attachment of multiple ubiquitin molecules to a target protein often leads to