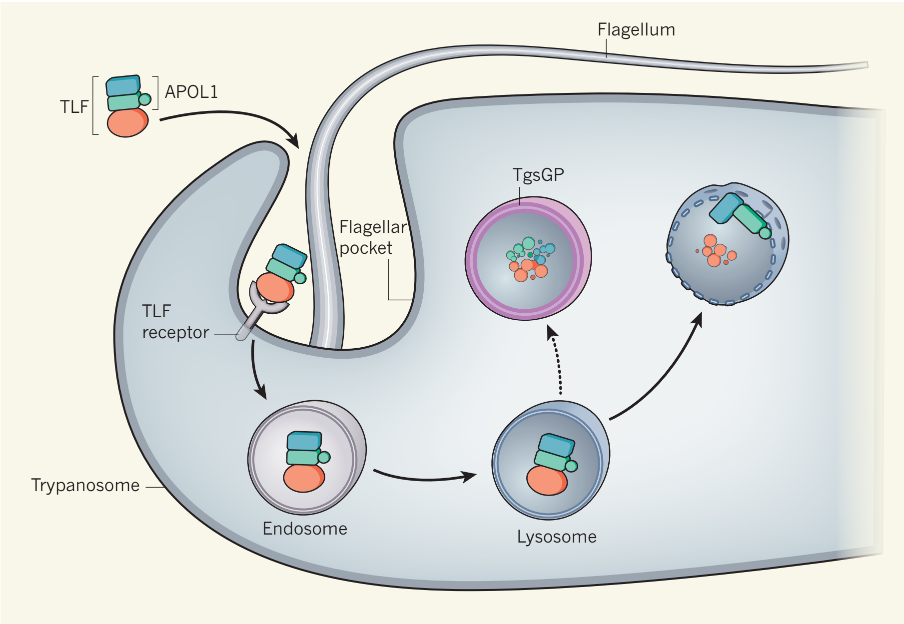

Figure 1 | Trypanosome resistance to host immunity. The trypanolytic factors (TLFs) found in human serum are high-density lipoprotein molecules that include the protein APOL1. TLFs bind to receptors on the trypanosome surface within the flagellar pocket. The TLFs are then internalized and transported through intracellular organelles for degradation — first to endosomes and then to the lysosome. The acidic pH of the lysosome induces a change in the conformation of APOL1 such that it is released from the TLF and incorporated into the lysosome membrane. This leads to the formation of membrane pores that upset the intracellular ionic balance and cause the trypanosome to burst and die. Uzureau *et al.*[2] propose that *Trypanosoma brucei gambiense* type 1 combines three processes to resist this immune defence: the expression of the protein TgsGP, which stiffens the lysosomal membrane and prevents APOL1 incorporation, modification of the TLF receptor and changes in lysosomal physiology.

human-infective trypanosome *T. b. rhodesiense* has evolved a different way to escape killing by TLF. This species has not acquired mutations in the TLF receptor, even though malaria (and therefore hypohaptoglobinaemia) is endemic throughout sub-Saharan Africa. Instead, the parasite has evolved a protein called the serum-resistance-associated protein (SRA)[8], which alone is sufficient to confer complete resistance to the TLFs present in most humans. SRA binds to APOL1 with high affinity and prevents either the insertion and/or oligomerization of APOL1 in membranes[9]. However, some people produce APOL1 variants (called G1 and G2) that arose in Africans after the migration of ancestral humans out of Africa; sera from individuals with these variant proteins kill *T. b. rhodesiense in vitro*[10], but their ability to protect against infection has yet to be confirmed. There are multiple African-restricted APOL1 variants in addition to G1 and G2, and one of these may prove to confer resistance to *T. b. gambiense*[11].

One surprising consequence of these evolutionary events is that African-Americans who express only the G1 or G2 APOL1 variants have 7–30-fold higher rates of several types of kidney disease[10,12]. This scenario resembles the human mutations in haemoglobin that provide protection against malaria but lead to the blood disorder sickle-cell anaemia. It is possible that kidney disease or other deleterious effects of these trypanosome-protective APOL1 variants may have prevented them from becoming fixed throughout the population.

Uzureau *et al.* have contributed a significant advance to our understanding of natural selection involving African trypanosomes and humans, but their work points towards ever more complex and interrelated events involving different trypanosome species, and perhaps malaria parasites, in this long-running battle with humans. So who is winning this epic arms race? Perhaps it is the non-human primates — baboons, for example, express APOL1 variants that seem capable of killing human-infective trypanosomes[13,14] but that do not cause kidney disease. Figuring out the secrets of baboon APOL1 may answer crucial questions that will help to solve the riddles of both African sleeping sickness and kidney disease. ■

Jayne Raper *is at Hunter College, City University of New York, New York, New York 10065, USA.* **David J. Friedman** *is in the Renal Division, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts 02215, USA.*
e-mails: raper@genectr.hunter.cuny.edu; dfriedma@bidmc.harvard.edu

1. Smith, E. E. & Malik, H. S. *Genome Res.* **19,** 850–858 (2009).
2. Uzureau, P. *et al. Nature* **501,** 430–434 (2013).
3. Vanhollebeke, B. & Pays, E. *Mol. Microbiol.* **76,** 806–814 (2010).
4. Gibson, W., Nemetschke, L. & Ndung'u, J. *Infect. Genet. Evol.* **10,** 453–458 (2010).
5. Symula, R. E. *et al. PLoS Negl. Trop. Dis.* **6,** e1728 (2012).
6. Higgins, M. K. *et al. Proc. Natl Acad. Sci. USA* **110,** 1905–1910 (2013).
7. Kieft, R. *et al. Proc. Natl Acad. Sci. USA* **107,** 16137–16141 (2010).
8. De Greef, C., Chimfwembe, E., Kihang'a Wabacha, J., Bajyana Songa, E. & Hamers, R. *Ann. Soc. Belg. Med. Trop.* **72,** Suppl. 1, 13–21 (1992).
9. Stephens, N. A., Kieft, R., MacLeod, A. & Hajduk, S. L. *Trends Parasitol.* **28,** 539–545 (2012).
10. Genovese, G. *et al. Science* **329,** 841–845 (2010).
11. Ko, W.-Y. *et al. Am. J. Hum. Genet.* **93,** 54–66 (2013).
12. Kopp, J. B. *et al. J. Am. Soc. Nephrol.* **22,** 2129–2137 (2011).
13. Thomson, R., Molina-Portela, P., Mott, H., Carrington, M. & Raper, J. *Proc. Natl Acad. Sci. USA* **106,** 19509–19514 (2009).
14. Kageruka, P. *et al. Ann. Soc. Belg. Med. Trop.* **71,** 39–46 (1991).

MATERIALS SCIENCE

Fast-track solar cells

The ultimate goal of the solar-cell industry is to make inexpensive devices that are highly efficient at converting sunlight into electricity. The advent of perovskite semiconductors could be the key to reaching this goal. **SEE LETTER P.395**

MICHAEL D. MCGEHEE

After the discovery of a new semiconductor that has potential for solar-cell applications, it has always taken numerous teams of researchers more than ten years to figure out how to use it to make devices that convert sunlight into power with greater than 15% efficiency. Liu and colleagues' report[1] on page 395 of this issue is therefore truly remarkable*. They describe cells that have slightly greater than 15% conversion efficiency, and which are based on perovskites, a class of semiconductor material that was first used for this application just four years ago. This follows hot on the heels of another *Nature* paper by Burschka *et al.*[2], who in July reported a perovskite-containing solar cell that reached the 15%

*This article and the paper under discussion[1] were published online on 11 September 2013.

TOMOHIRO OHSUMI/BLOOMBERG VIA GETTY IMAGES

Figure 1 | Solar-power generator in Tokyo. Electricity generated from sunlight is already economically viable in many regions. Solar cells containing perovskite materials, such as those reported in two recent papers[1,2], might one day convert sunlight into power more efficiently than currently available devices.

conversion milestone. The fact that multiple teams are making such rapid progress suggests that the perovskites have extraordinary potential, and might elevate the solar-cell industry to new heights.

Researchers started using organometal trihalide perovskite semiconductors (which have the formula $(CH_3NH_3)PbX_3$, where Pb is lead and X can be iodine, bromine or chlorine) in solar cells in 2009 (ref. 3). Since then, the performance of perovskite-containing solar cells has skyrocketed.

Initially, perovskites were used as dye replacements in dye-sensitized solar cells. In these devices, dyes act as light absorbers coating the surface of a film of titanium dioxide (TiO_2) nanoparticles. When light is absorbed by a dye, electrons and positive-charge carriers known as holes are generated and transferred to different transport materials: to TiO_2 for electrons, and to another material for holes. The transport materials then carry the charges to separate electrodes and so generate a voltage. Burschka and co-workers raised the world record for conversion efficiency in this kind of solar cell from 12% by packing lots of light-absorbing perovskite into the TiO_2 film, so that most of the light striking the cell was absorbed in a very thin film.

Liu *et al.* have now shown that the perovskite semiconductor not only strongly absorbs light, but also transports both positive and negative charges. This allowed them to do away with the TiO_2 nanoparticles, and so to implement a more conventional solar-cell architecture than that of Burschka and co-workers: in Liu and colleagues' device, the light-absorbing semiconductor is sandwiched between electron- and hole-selective electrodes. Remarkably, it maintains high conversion efficiency.

The rapid emergence of perovskites comes at an interesting time in the solar-cell industry's history. In locations where sunlight is abundant and electricity is fairly expensive, the production of electricity using solar cells is now cost-competitive with that of conventional electricity sources (Fig. 1). However, there is still a need to reduce the costs of making and installing solar cells, and to improve conversion efficiency so that fewer panels need to be installed.

Almost all solar cells manufactured today are made with approximately 150-micrometre-thick wafers of crystalline silicon, and have conversion efficiencies in the range of 17–23%. For decades, many researchers have attempted to develop high-efficiency and lower-cost alternatives to crystalline silicon by depositing semiconductor films that are less than a few micrometres thick on inexpensive substrates such as glass, metal or plastic. Of the thousands of semiconductor materials that have been tried, only a few (such as cadmium telluride and copper indium gallium selenide) have enabled conversion efficiencies in the range of 15–20% (ref. 4).

Moreover, the efficiencies of such cells are limited by the many defects formed during the rapid deposition of the semiconductor films. These defects promote the recombination of electrons and holes, which drains power and reduces voltage. Because thin-film solar cells are not as efficient as crystalline silicon cells, they are less desirable to customers, who want to minimize installation costs, and so most of the companies making them are going out of business.

It is therefore scientifically interesting and technologically important that the voltage produced by the perovskite solar cells[1,2] is more than 1 volt; silicon and most thin-film solar cells typically produce only 0.7 V under 'open circuit' conditions. Apparently, there is something special about perovskites that slows down recombination. What this special something is remains unknown, making it hard to estimate how efficient the perovskite solar cells could be, but it seems likely that their efficiency will continue to climb. It is even possible that perovskites will emerge as the champion material for solar cells.

Perovskites and crystalline silicon need not compete with each other as solar-cell materials. Because silicon has a smaller bandgap (the energy required to generate conducting electrons) than the perovskites, it absorbs a chunk of the solar spectrum that perovskites do not. One could therefore place a silicon cell underneath a perovskite cell to form a tandem cell[5]. Perovskites could be printed on top of silicon in a way that would add little to the manufacturing cost, and because perovskites generate a higher voltage than silicon, the tandem cell would be more efficient than a silicon cell. A rough calculation suggests that the performance of currently available, commercial solar cells could be boosted by 25%, and would require only minor modifications to existing factories.

The news that perovskites perform extraordinarily well in solar cells has spread fast, and many academic and industrial researchers are already discussing their potential for commercialization. Most are optimistic that the efficiencies of perovskite cells will continue to improve until they are competitive with, or better than, existing commercially available solar cells. However, there are concerns that lead toxicity will be a problem, because the perovskites are soluble in water and could be washed out of a leaky module. The race is on to discover perovskites containing non-toxic elements that have the same desirable properties as the lead compounds.

Another possible issue is the long-term stability of perovskites. The results of preliminary tests performed on short timescales are promising, but some researchers remain concerned that a water-soluble material that can be sublimed at a low temperature (as perovskites can) will lack the rock-like stability that enables silicon solar cells to last for more than 25 years.

Further breakthroughs in perovskite solar cells can certainly be expected in the months and years to come. The history of these materials may be brief, but their performance so far suggests that their role in the solar-cell field will be anything but. ■

Michael D. McGehee *is in the Department of Materials Science and Engineering, Stanford University, Stanford, California 94305-4045, USA.*

e-mail: mmcgehee@stanford.edu

1. Liu, M., Johnston, M. B. & Snaith, H. J. *Nature* **501,** 395–398 (2013).
2. Burschka, J. *et al. Nature* **499,** 316–319 (2013).
3. Kojima, A., Teshima, K., Shirai, Y. & Miyasaka, T. *J. Am. Chem. Soc.* **131,** 6050–6051 (2009).
4. www.nrel.gov/ncpv
5. Beiley, Z. M. & McGehee, M. D. *Energ. Environ. Sci.* **5,** 9173–9179 (2012).

STEM CELLS

Down's syndrome link to ageing

Triplication of the enzyme USP16 in models of Down's syndrome creates defects in the stem cells resident in adult tissues. This finding provides insight into stem-cell homeostasis during ageing. SEE ARTICLE P.380

GEORGE P. SOUROULLAS & NORMAN E. SHARPLESS

Down's syndrome is a complex developmental disorder involving congenital malformation and mental retardation. It affects 1 in about 700 individuals, and is caused by an extra copy of chromosome 21. Individuals with Down's syndrome therefore have three copies (trisomy) of some 300 protein-encoding genes, and of an even larger number of non-coding RNA sequences. Although a few candidate genes have been linked to the spectrum of disorders associated with Down's syndrome, generally it is unclear how trisomy of specific genes contributes to the condition. In a paper published in this issue, Adorno *et al.*[1] (page 380) implicate the deubiquitinating enzyme Usp16 in an impaired ability of adult-tissue stem cells to self-renew*.

As childhood death among individuals with Down's syndrome has declined sharply, it has become clear that the condition is associated with an early onset of age-related disorders, such as Alzheimer's disease, immune dysfunction, premature menopause and disorders of the endocrine system[2]. Consequently, gerontologists have long wondered whether Down's syndrome is a form of segmental progeria[3] — that is, whether its diverse aspects result from a shared mechanism with accelerated ageing (progeria).

But Down's syndrome is distinct from progerias that result from alterations in DNA metabolism (such as Werner's and Bloom syndromes and dyskeratosis congenita), because cells from individuals with Down's syndrome do not show significant defects in DNA metabolism or repair. Moreover, affected individuals exhibit a peculiar pattern of cancer incidence — an increased risk of childhood disorders associated with the proliferation of haematopoietic (blood-lineage) cells, but a much reduced risk of more common solid tumours[4,5]. By contrast, DNA-metabolism disorders associated with progeria are accompanied by a general increase in cancer incidence.

Against this confusing backdrop, Adorno *et al.* suggest an explanation for accelerated ageing in Down's syndrome in terms of impaired function of somatic stem cells — tissue-resident cells that self-renew throughout life to repair damaged cells; the functional decline of these stem cells is thought to underlie aspects of mammalian ageing. Using two mouse models of Down's syndrome, as well as cultured human cells, the authors show that certain aspects of Down's syndrome, including phenotypes (traits) of premature ageing, are associated with misregulation of the machinery involved in cellular senescence — a state of permanent growth arrest associated with tumour suppression and ageing.

Of the two mouse models, one (Ts65Dn) carries three copies of around two-thirds of the 132 genes that are the equivalent of those triplicated on human chromosome 21, whereas the other is trisomic for 79 of these 132 genes. The authors examined the self-renewal capacity of stem cells and progenitor cells obtained from the bone marrow and brain and breast tissue of these animals. They observed disrupted homeostasis of somatic stem cells in Ts65Dn mice, and found that cultured cells isolated from these mice showed signs of increased senescence. A comparison of the triplicated chromosomal regions in the two models led the researchers to suspect trisomy of the *Usp16*

*This article and the paper under discussion[1] were published online on 11 September 2013.

50 Years Ago

Sir Nevill Mott spoke about research in the universities and repudiated the view that university research is just an expensive luxury to stimulate the dons and keep them up to date … The third and last discussion ranged widest of all. There were those who took for granted, so it seemed, that the modern undergraduate at entry was fundamentally perverse and irresponsible, overdeveloped intellectually and socially as well as emotionally immature; those who defended him warmly against the criticisms of his elders; those who felt that he … was too much 'of the world' already and needed to be withdrawn during his university years from the pressure and hurly-burly of ordinary existence; for them the hall of residence on the university campus was the right answer; those, on the contrary, who felt that segregation — whether from family or other social ties — and an artificially high standard of living were wholly bad; these approved of the civic university whose students live with their own families … But all united in one aim — to prevent, if possible, the university from turning out a lop-sided individual, intellectually precocious but humanly underdeveloped.
From *Nature* 21 September 1963

100 Years Ago

A curious story comes from Ireland that Mr. E. S. Dodgson, of Jesus College, Oxford, has discovered at Killult, Falcurragh, Donegal, a stone said to contain an Ogham inscription giving a clue to a great treasure concealed in the neighbourhood by an ancient Irish chieftain … We wish the discoverer success in unearthing the treasure, but until he succeeds, or some other interpretation of the supposed inscription is suggested, it may be well to reserve opinion on the matter.
From *Nature* 18 September 1913