and therefore the simpler the model is. The path to scalability will probably involve the use of more-hierarchical and modular machine-learning architectures. Further research needs to be done to learn whether end-to-end control can be scaled up to guide complex machines that have dozens of actuators, including humanoid robots[7], or large systems such as manufacturing plants or smart cities — urban areas that use digital technology to improve the lives of citizens.

Another challenge is less technical and more personal. For some researchers, the transition from using relatively simple mathematical models to applying 'black box' machine-learning systems — in which the internal workings are unknown — signals the unfortunate end of insight, and brings with it the feeling of loss of control. I am not one of those researchers. For me, there is something satisfying about seeing a robot, like a child, learn to walk on its own.

The insights offered by Hwangbo *et al.* could also be considered in the context of the mysteries of the mind. Consciousness has been one of the longest-standing puzzles of human nature[8]. In my experience, human-devised definitions of self-awareness are so vague that they are of little practical value for building robotic software. Perhaps the converse is true, however, and the study of robotic software can offer insights into age-old questions about the human mind.

One could conjecture that self-awareness and, by extension, consciousness are, at their core, an indication of our ability to think about ourselves in the abstract — to self-simulate. I would argue that the further ahead in time a person can look, and the more detailed the mental picture of their future activities is, the greater that person's capacity for self-awareness will be. Now, robots are capable of learning to self-simulate. This breakthrough is not merely a practical advance that will save some engineering effort, but also the beginning of an era of robot autonomy. ■

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VIROLOGY

HIV remission achieved in the clinic again

A person infected with HIV who was treated for blood cancer with a stem-cell transplant has gone into viral remission, with no trace of the virus in their blood. A similar outcome in 2009 hadn't been replicated until now. SEE LETTER P.244

TIMOTHY J. HENRICH

HIV infects immune cells, and the current standard treatment is long-term use of antiretroviral drugs. This keeps virus levels low in the bloodstream but doesn't eradicate HIV from cells in the body. In 2009, it was reported[1] that a person with HIV (commonly referred to as the Berlin patient) who was treated for cancer using a stem-cell transplant subsequently went into viral remission — the virus became undetectable in their body, even in the absence of antiretroviral therapy. No other cases of long-term HIV remission occurring in this way had been recorded since then. But now, on page 244, Gupta *et al.*[2] report a person who has achieved HIV remission for at least 18 months.

The case reported by Gupta and colleagues is similar in many ways to the one described a decade ago[1]. Both individuals had developed immune-cell cancer and received stem-cell transplants from donors (who were not infected with HIV) to re-establish their immune-cell populations (Fig. 1). Both donors had a mutation (termed Δ32) in both of their copies of a gene called *CCR5*. This gene encodes a receptor protein on immune cells that HIV can bind to during the process of infection. Having a Δ32 mutation in both cellular copies of the *CCR5* gene results in the absence of functional CCR5 protein on the cell surface, and immune cells lacking this protein can resist infection by HIV strains that depend on CCR5. Both patients were infected with HIV strains that exclusively use CCR5, along with the protein CD4, to aid cellular entry[3], which was probably a key factor in explaining why stem-cell treatment resulted in HIV remission.

In some HIV strains, the virus gains entry to cells by using a different protein in addition to CD4, typically CXCR4, rather than CCR5. These HIV strains are often associated with drug resistance, or might arise if antiretroviral treatment starts later than normal in the course of infection. It has been reported[4,5] that a person infected with HIV who received a transplant of donor stem cells that had the Δ32 mutation in both copies of *CCR5* experienced a rapid rise in HIV levels in their bloodstream when they stopped antiretroviral treatment, owing to a pool of pre-existing virus that could use CXCR4 for viral entry.

In the case reported by Gupta and colleagues, and in the 2009 report, the success of the

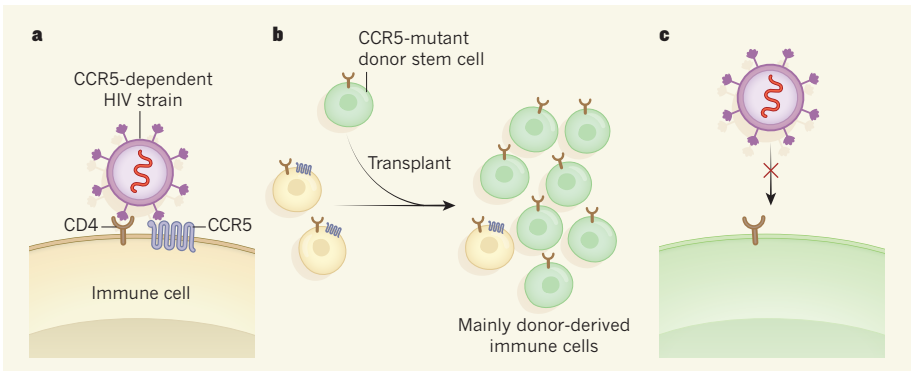

Figure 1 | HIV remission after cancer treatment. Gupta *et al.*[2] report the case of an HIV-infected person who underwent cancer treatment and then went into long-term HIV remission — the virus was undetectable in their bloodstream even in the absence of antiretroviral drug treatment — for at least18 months. This confirms an outcome[1] reported in 2009, which hadn't been repeated until now. **a**, The patient studied by Gupta and colleagues had a strain of HIV that depends on the CCR5 protein (along with the protein CD4) to attach to immune cells during infection. **b**, This person had treatment for blood cancer in which they received stem cells from a donor who had mutations that lead to the absence of functional CCR5 on the cell surface. The transplant resulted in the patient's immune cells being derived mainly from donor cells. **c**, The person's HIV went into remission, probably because the immune cells lacking CCR5 were resistant to infection by the HIV strain.

donor stem-cell transplant meant that the vast majority of cells (such as immune cells called $CD4^+$ T cells) that could harbour HIV were of donor origin and resistant to the HIV strains in the patients. Interestingly, when individuals with HIV have received stem-cell transplants to repopulate their immune cells from donors with wild-type copies of the *CCR5* gene, HIV is initially undetectable in the patients' bodies, but eventually rebounds if antiretroviral therapy is stopped[6–9]. In such cases, the viral rebound takes many months, rather than the usual two to four weeks, after antiretroviral therapy is withdrawn[10,11]. This suggests that if a person's HIV-infected immune cells become mainly replaced by uninfected immune donor cells that are protected from infection by antiretroviral treatment, the total burden of HIV in the body can be substantially reduced. However, to tip the balance of such a reduction into a situation of permanent HIV remission, what seems to be needed is the establishment of immune cells that are resistant to the HIV strains present in the body.

In the 2009 study, the patient required an intensive set of therapies, including a second stem-cell transplant when their cancer recurred, and they also underwent irradiation treatment. By contrast, the patient studied by Gupta and colleagues underwent a less-intensive treatment regime for their cancer and did not require irradiation. This is of interest, because it had been unclear whether the intense cancer treatment in the earlier study might have contributed to the successful HIV remission. Another difference is that, in the 2009 study, the patient already had the Δ32 mutation in one of their two copies of *CCR5*, which might have affected their total HIV burden before transplantation. Although these factors might have had a role in achieving the long-term HIV remission in the case reported in 2009, what seems to be the most important aspect linking the cases is a donor transplant of cells lacking functional CCR5 on the cell surface.

What has been learnt from these two reports that might guide future efforts towards HIV eradication or remission? A simple answer might be 'not too much'. In some ways, the case presented by Gupta and colleagues is mainly a repeat of a procedure that confirms the previously reported outcome. Substantial efforts are already under way to modify *CCR5* or other genes that facilitate HIV infection or replication in approaches to modify patients' own immune or stem cells. The knowledge gained from this second case of HIV remission is unlikely to cause a change in direction of strategies being developed for tackling HIV. Donor stem-cell transplantation is expensive, fraught with risks and requires intensive effort to tailor the treatment to specific individuals — as such, it cannot be scaled up easily. By contrast, the standard HIV treatment regimen of one or two pills per day is accompanied by relatively minimal adverse effects; therefore, it is not practical to consider replacing it with a procedure that might risk disease or death, and that creates the need for long-term immunosuppression.

Extremely low levels of residual HIV DNA or RNA have been intermittently detected using sensitive assays on blood cells taken from the patient in remission in Gupta and colleagues' study, and in the earlier study of the patient who underwent HIV remission[12]. Although these fleeting hints of persistent HIV are probably clinically insignificant, there is a remote possibility that the person studied by Gupta *et al.* will eventually relapse. Modelling suggests that the possibility of rebound becomes less likely the longer that HIV remains undetectable in the absence of antiretroviral treatment, so, in another six months' time, the long-term remission status of this patient should be clearer. For these and other reasons, such cases are usually called long-term HIV remission, rather than a cure, an analogy borrowed from the cancer field.

The impact of the news of a second case of HIV remission might be overlooked by some in the scientific community because the report simply confirms previous results and shows a lack of obvious scalability for treatment. However, the effect this news has had on the wider public, especially for people living with HIV, should not be forgotten. This case has certainly generated interest, and might have instilled a sense of hope in some individuals. Such cases also provide motivation to continue working on and refining research endeavours, even if scalable approaches to achieve long-term HIV remission might be many years away. Optimism does not need to be in conflict with rationalism. ■

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PALAEOANTHROPOLOGY

Unknown human species found in Asia

Excavations in southeast Asia have unearthed a previously unreported hominin species named *Homo luzonensis*. The discovery has implications for ideas about early hominin evolution and dispersal from Africa. SEE ARTICLE P.181

MATTHEW W. TOCHERI

Homo sapiens is the only living species of a diverse group called hominins (members of the human family tree who are more closely related to each other than they are to chimpanzees and bonobos). Most extinct hominin species are not our direct ancestors, but instead are close relatives with evolutionary histories that took a slightly different path from ours. On page 181, Détroit *et al.*[1] report the remarkable discovery of one such human relative that will no doubt ignite plenty of scientific debate over the coming weeks, months and years. This newly identified species was found in the Philippines and named *Homo luzonensis* after Luzon, the island where bones and teeth from individuals of this species were excavated from Callao Cave. Specimens of *H. luzonensis* were dated to minimum ages of 50,000 and 67,000 years old, which suggests that the species was alive at the same time as several other hominins belonging to the genus *Homo*, including *Homo sapiens*, Neanderthals, Denisovans and *Homo floresiensis*.

Rapidly changing knowledge about hominin evolution in Asia is forcing the re-examination of ideas about early hominin dispersals from Africa to Eurasia. Hominins appear in the fossil record about 6 million to 7 million years ago in Africa, and the earliest hominin fossils in Eurasia are about 1.8 million years old[2]. Explanations for the earliest hominin dispersals from Africa fall under what is known as the Out of Africa I paradigm[3]. Modern humans only come into focus in the Out of Africa II