fields for HIV-1 infection and replication. Yet another signal — CD80, induced by sICAM-1 — has to be expressed on the surface of B cells to allow productive replication of HIV-1 in the target T cells, rather than just allowing infection. Otherwise, the T cell becomes infected but has a provirus that may act as a 'Trojan Horse of non-production'[12], allowing viral expression and release to take place only after a second signal, such as CD80, is applied from a further activated subset of B cells. In previous work, the Swingler group[13] had demonstrated that HIV-1 Nef produced from macrophages may, through chemotaxis, also actually attract T cells into physical proximity with the infected macrophage.

If this sounds complex, it is — even for experts in the study of retroviruses. But no one said that understanding HIV-1's reservoirs would be simple. The data presented by Swingler *et al.* are unique in that they demonstrate that viral reservoirs during highly active antiretroviral therapy in HIV-1-infected patients may be far more intricate than consisting simply of low-level replication in activated T cells and latency in fully resting T cells[12]. These new data indicate ways in which productive replication from certain viral reservoirs can be upregulated, and also may explain how some non-cell-cycling T cells can become a latent but inducible viral reservoir *in vivo*. Overall, they show that there is an entire spectrum of interactions between the virus and host cells, which together produce the general pattern of HIV-1 reservoirs and residual disease.

Cell-to-cell cross-talk, such as that described here, may represent a series of mechanisms by which viruses alter a particular microenvironment, and change the cellular milieu to one that is conducive to viral replication and maintenance. We need to understand these mechanisms, so as to manipulate that milieu to favour antiviral therapies. The aim will be not only to decrease the production of HIV-1 but also to destroy the cellular reservoirs that have so far kept us from being able to eradicate HIV-1 infection[14]. ■

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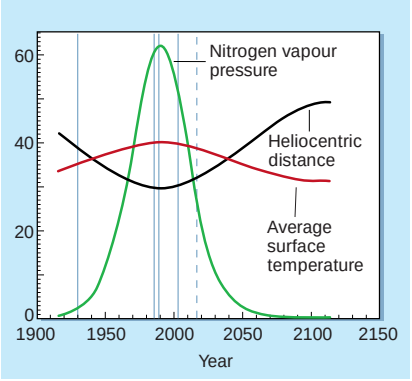

Figure 1 **Pluto variations. As Pluto's distance from the Sun changes (black curve, in astronomical units), its average surface temperature should vary roughly inversely as the square root of the distance (red curve, in kelvin). The vapour pressure of surface nitrogen ice changes even more markedly (green curve, in microbar), and should have been decreasing between 1988 and 2002. In fact, Elliot *et al.*[1] and Sicardy *et al.*[2] show that Pluto's atmosphere increased in size over this interval, but this could possibly be attributed to a time-lag in surface-layer cooling as the planet moves away from the Sun. The vertical blue lines indicate, left to right, the 1930 discovery of Pluto; the occultation observations in 1985, 1988 and 2002, the last of these by Elliot *et al.*[1] and Sicardy *et al.*[2]; and (dashed) the earliest possible arrival of a spacecraft at Pluto.**

Planetary science

Pluto's atmospheric surprise

William Hubbard

Last year, for the first time in 14 years, an alignment of stars with Pluto created an opportunity to observe the atmosphere of this most remote of planets. Though tenuous, the atmosphere has, remarkably, expanded.

Pluto is the only planet in the Solar System still unvisited by spacecraft. But an appropriate conjunction of stars with the planet can make some Earth-bound observations possible. In particular, Pluto's thin atmosphere (exerting a surface pressure roughly a million times lower than that at the Earth's surface) comes into view as the planet passes in front of, or 'occults', a bright star. On pages 165 and 168 of this issue, Elliot *et al.*[1] and Sicardy *et al.*[2] report the first new data on Pluto's atmosphere from stellar occultation in more than a decade. The observations are timely: Pluto's orbit over the next few years offers an opportunity to learn more about this planet, at a time when technological developments make it feasible to consider a mission to it. But both time and money are in short supply.

As Pluto is the most distant of the nine planets, its 248-year orbit around the Sun is lengthy compared with human timescales. It is also the most eccentric: Pluto's heliocentric distance varies between 30 and 50 astronomical units (one astronomical unit, or AU, is equivalent to the mean distance between the Earth and the Sun). In accordance with Kepler's second law of planetary motion, Pluto spends most time in each orbit at almost its maximum distance from the Sun and the Earth. But, in 1989, Pluto coincidentally made its closest approach to the Sun (called its perihelion) during a period of heavy spacecraft exploration and in precisely the year that the spacecraft Voyager 2 had its final encounter with Neptune and Neptune's icy satellite Triton. Triton seems to be a very similar body to Pluto and is perhaps a close relative[3]. The Voyager 2 encounter revealed, through a slight distortion of the spacecraft's radio link to Earth, that Triton too has a tenuous atmosphere, with a surface pressure of perhaps 10 to 20 microbar (atmospheric pressure on Earth is one bar).

At the time of the Triton encounter, Pluto was actually slightly closer to the Sun than Neptune was. But Pluto always maintains a healthy distance from Neptune, because their orbits are synchronized. So a spacecraft visit to Pluto would require a specially planned trajectory and a lengthy trip, rather than any straightforward extension of an existing mission. And as Pluto's diameter is only some 2,400 km, substantially smaller than the Moon's, is it worth the trip?

In 1988, just one year before the Voyager 2 encounter with Triton, distortion of light from an occulted star revealed that Pluto had a tenuous atmosphere, to which Triton's is somewhat similar. In fact, the earliest evidence for Pluto's atmosphere seems to have been gathered in 1985 by the Israeli astronomer Noah Brosch: observing in the Negev desert, he saw a gradual dimming of starlight caused by refraction in Pluto's atmosphere, rather than the knife-edge drop expected when an atmosphere-less planet (such as the Moon) occults a star. Brosch's data were so unexpected that he was widely disbelieved until the case was clinched by observations of the 1988 occultation by

several telescopes, including NASA's Kuiper Airborne Observatory[4].

What process could produce microbar atmospheres on tiny objects such as Triton and Pluto? Triton and Pluto are thought to belong to the Kuiper belt — a ring of icy bodies beyond the orbit of Neptune — and so bear a generic relation to short-period comets whose orbits pass through the belt. Like comets, they seem to be able to generate fluctuating atmospheres in response to variable solar heating of their icy surface layers. The difference, though, is that Triton and Pluto are just massive enough to retain the gas as a bound atmosphere, whereas comets produce an escaping envelope of gas, known as a coma. And because the solid surface layers of Triton and Pluto never get warmer than about 40 kelvin, any gas that erupts must be much more volatile than the water vapour thought to power the spectacular tails of those comets whose orbits bring them within a few AU of the Sun.

By a process of elimination, a likely candidate for the main gas in Pluto's atmosphere is the volatile molecule nitrogen. As Fig. 1 shows, its vapour pressure could build to a maximum at perihelion well in excess of the pressures measured in Pluto's atmosphere. But because the vapour pressure of nitrogen decreases strongly as the surface temperature falls, the atmosphere ought to collapse as Pluto's surface cools during its retreat from the Sun over the next few decades.

Following the initial detections of Pluto's atmosphere in 1985 and 1988, there was an unproductive 14-year period during which astronomers sought, to no avail, either to place portable telescopes in an occasional narrow path of Pluto's starlight shadow on the Earth, or to predict feasible occultation opportunities at fixed observatories. There were, typically, one or more aborted campaigns every few years or so. The forecast shadow paths invariably turned out to be off Earth or otherwise inaccessible. The shutdown of the Kuiper Airborne Observatory did not help. Planetary scientists have now become strong advocates for a spacecraft mission to Pluto while the planet is still warm enough to exhibit the volatile molecules embedded in its surface layers.

As discussed by Elliot *et al.*[1] and Sicardy *et al.*[2], Pluto's atmosphere has, unexpectedly, expanded rather than contracted over the past 14 years, but temperature variations in planetary surface layers do typically lag somewhat behind solar heating variations. In the long run, cooling and atmospheric contraction are inevitable. To understand what is going on, we need a spacecraft mission to Pluto: an occultation measurement of the atmosphere at radio wavelengths, together with ultraviolet measurements of a solar occultation, could tell us much more — and both of these require an antenna or telescope to aim past Pluto back towards the Earth or the Sun. Meanwhile, possible light extinction caused by particles in Pluto's atmosphere (reported by Elliot *et al.*) may be bad news for detailed stellar-occultation studies of the atmosphere, as standard analysis methods assume that there is no loss of photons.

The first of NASA's New Frontiers line of space missions will be a Pluto–Kuiper-belt mission called New Horizons[5]. The mission has a planned launch in 2006 and a Pluto flyby about ten years later (Fig. 1). But New Horizons is in trouble because of unexpected extra costs. Similarly, NASA's Planetary Astronomy programme, which has supported much of the Pluto occultation work in the United States, had to cancel some of the ground stations that could have provided more data. Like mountaineers preparing an assault on Mount Everest, scientists are closely watching the calendar and their budgets, hoping to reach their objective before the snows come. ■

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Cell biology

The molecules that make muscle

Donald Gullberg

The role of integrin proteins in the formation of skeletal muscle has been hotly debated, as studies of whole animals and of cultured cells have yielded conflicting results. The controversy may now be resolved.

Every conscious action we perform requires skeletal muscle. Without it, we wouldn't be able to run for the bus, lift a pipette or turn the pages of this journal. So called because it attaches to the skeleton, this type of muscle has been studied for centuries; incredibly, the idea that it works by contracting can be traced back more than two millennia. As a consequence, a great deal is known about the structure of skeletal muscle and about how it functions. The step-by-step process by which it forms has also been well studied, at least at the cellular level. Nowadays, however, the goal of much research effort is to identify the molecules that are involved in specific biological processes — and the molecular mechanisms underlying muscle formation have long eluded researchers. That now looks set to change: writing in *Developmental Cell*, Schwander and colleagues[1] report evidence supporting a key role for members of the integrin family of cell-adhesion proteins.

Integrins are proteins, found in multicellular organisms, that are embedded in the plasma membrane. They enable cells to adhere to the matrix of molecules in which they find themselves, and they also bind to various intracellular proteins, thereby connecting the cell exterior and interior. Each integrin is made up of two proteins, one from the α subfamily and one from the β subfamily, and they are involved in a variety of biological functions, such as cell proliferation, differentiation and migration, and the prevention of cell death.

Many of these functions have been inferred from animal studies, in which individual integrin proteins were mutated and the effects studied. But studies of integrins *in vitro* have yielded conflicting data — as have studies involving different species. One example concerns skeletal muscle formation (myogenesis; Fig. 1)[2]. During this process, individual muscle precursor cells first become 'destined' to form muscle; at this stage they are called myoblasts. The myoblasts then migrate to the site of future muscle formation, where they fuse to produce skeletal muscle cells — myotubes — that have multiple nuclei. The smallest contractile unit in a mature myotube is the sarcomere, a regular assembly of filaments made up of the myosin and actin proteins. The sarcomere is assembled as the myotubes mature into muscle fibres.

So what is the confusion over integrin's role in this process? Early studies in the 1980s showed that blocking integrins containing a β1 subunit on chick myoblasts *in vitro* inhibited fusion[3]. Later work with fruitfly myoblasts lacking the invertebrate variant of the vertebrate integrin β1 chain pointed to a role for the protein in sarcomere assembly as well[4]. But attempts to show convincingly that β1 integrins are involved in these events in mice have failed. One of the problems is that mouse embryos engineered to lack functional integrins throughout the body die long before the effects of the deficiency on muscle function can be studied[5–7].

To overcome these problems, cells lacking both functional gene copies for specific integrins have been injected into wild-type early embryos, thereby generating chimaeric mice (in which only some of the cells lack