of the family. By extending the sequence range of the SH2 domains, the Cbl structure should now allow structural analysts to explore the rapidly growing genomic databases for other remote offspring of the SH2 domains. The *Dictyostelium* SH2 domain will then not be the only indicator of how the intimate relationship between phosphotyrosine and SH2 domains first got going. ☐

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Cosmology

Evolution of the cosmological constant

P. J. E. Peebles

Contrary to expectation, the evidence is that the Universe is expanding at about twice escape velocity — the speed required to overcome the gravitational pull of all the matter in the Universe[1]. This would mean we live at a special time: in the past, the greater density of mass in the Universe was gravitationally slowing the expansion; in the future, the expansion rate will be close to constant or maybe speeding up under the influence of a new type of matter that some call quintessence. In *Physical Review Letters*, Steinhardt and colleagues[2] argue that the gravitational effect of a particular form of quintessence takes a long time to grow comparable to the effect of ordinary matter and radiation. If so, it is not so surprising that we have come on the scene just as quintessence has become a factor in the evolution of the Universe.

Quintessence began as Einstein's cosmological constant, Λ. It has negative gravitational mass: its gravity pushes things apart. Einstein hoped the repulsion would balance the gravitational attraction produced by ordinary matter, so the Universe could be static. The discovery of the expansion of the Universe led him to abandon Λ as an unnecessary hypothesis. Particle physicists later adopted Einstein's Λ as a good model for the gravitational effect of the active vacuum of quantum physics, although they are at odds with the small value of Λ indicated by cosmology. Theoretical cosmologists noted that as the Universe expands and cools Λ tends to decrease. When water freezes, it releases latent heat; ice has a lower energy density than water. As the Universe cools, symmetries among forces are broken, particles acquire masses, and these processes tend to release the analogue of latent heat. The vacuum energy density accordingly decreases, and with it the value of Λ. Perhaps an enormous Λ drove an early, rapid expansion that smoothed the primeval chaos to make the near uniform Universe we see today, requiring Λ to decrease over time to its current level. This is the cosmological inflation concept.

A decade ago we began debating the idea that Λ is still present and that it is not, in fact, constant, but still decreasing. Perhaps Λ has a small value now simply because the Universe is old[3]. Steinhardt and colleagues[2] add the idea that in simple theoretical models of Λ-like matter, or quintessence, a broad range of initial conditions in the early Universe evolve to a similar situation, in which the gravitational effect of quintessence is less than that of ordinary matter, and remains that way for a long time. This means Λ would be expected to become important again only late in the career of the Universe, maybe about now. A more convincing story will require a better understanding of how Λ-like matter might fit in the fundamental basis for physics, perhaps in the dynamics of the quantum-mechanical vacuum or ultra-low energy excitations of fields we have yet to discover.

Observational cosmologists can measure the present value of Λ[4,5]. Distant galaxies are seen as they were in the past, because of the time it takes light to travel. Their recession velocities, inferred from the Doppler shifts of their light, are a measure of how fast the Universe was expanding then. The observations suggest that Λ does have an effect: the expan-

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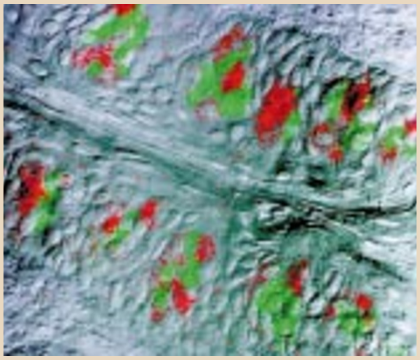
Signal transduction

A taste of things to come

It used to be the case that, if you wanted to know anything about taste, the best person to ask was probably a chef. We still know relatively little about the molecular basis of taste perception compared with, say, vision or touch. But a report by Charles Zuker, Nick Ryba and colleagues (*Cell* 96, 541–551; 1999) now adds to the picture. Using standard molecular biological recipes, these authors have discovered two potential mammalian taste receptors.

Mammals are thought to have five basic taste modalities — sweet, bitter, salty, sour and umami (the taste of monosodium glutamate). Different regions of the tongue prefer these various modalities. So, for example, the circumvallate papillae at the back of the tongue are particularly sensitive to bitter substances, whereas the fungiform papillae at the front of the tongue prefer sweet compounds.



Zuker, Ryba and co-workers identified the new proteins — known as TR1 and TR2 — starting from complementary DNA libraries of sequences expressed only in taste cells. Both proteins are guanine-nucleotide-binding (G) protein-coupled receptors with sequence homologies to other candidate chemosensory receptors.

When they studied the topographic expression of TR1 and TR2, the authors found that TR1 is expressed in all fungiform taste buds, and that TR2 localizes to the circumvallate taste buds. What's more, as the image on the left shows, these proteins (green) do not colocalize with gustducin (red).

Studies using knockout mice indicate that gustducin is involved in bitter and sweet transduction. But this image shows that it is probably not responsible for signalling from TR1 and TR2. Finding the agents that are could well be the next chapter in the taste story. Alison Mitchell sion rate started increasing when the Universe was 60% of its present size. That can be compared to 75% of the present size when our Solar System formed.

The measurements that provide evidence for this Λ-like matter have been beautifully done, but there is no guarantee that all systematic errors are under control. You would do well to bet no more than two dollars to get one that Λ has really been detected. I am offering ten dollars to get one on the proposition, which has been more thoroughly cross-checked, that our Universe is expanding faster than escape velocity. In either case, the origin of life on Earth coincided with another cosmological event, the end of the gravitational brake on the expansion of the Universe.

There are checks on the measurement. For example, the oldest observed stars have to be younger than the time it took the Universe to expand from densities too high for stars to have existed. If the expansion were now accelerating (that is, the expansion rate was slower in the past), then the time elapsed since the Big Bang would have been longer and the Universe would be considerably older, than if the expansion were still slowing down. People are making impressive progress in the difficult art of measuring star ages. If this condition on the age of the Universe and other cosmological tests consistently indicate that the expansion is accelerating, it will compel acceptance of Λ.

If Λ has been detected, it became a serious factor in the expansion rate just as life appeared on Earth: this is known as one of the cosmic coincidences. Deciding whether a coincidence is of some significance or only an accident is not easy. If observers existed when the Universe was half its present size, they would have lived through an abrupt reduction in star formation — from a rate that had held nearly constant well into the past, to the decline that persists to the present day. Similar beings to us could have existed when the Universe was only 3% of its present size, if their Cambrian explosion had happened a lot faster than ours. Such observers may have noticed the remarkable coincidence that the Universe was too hot for water-based life just a factor of three earlier in its expansion history. Life as we know it is still possible when the Universe reaches ten times its present size, near stars formed from the dregs of interstellar gas. These observers would find the Universe a lonely place; other host stars would be exceedingly rare. And they may well find it was too late to search for life on planets in other galaxies; they could see distant galaxies, but Λ would be pushing them away so fast that light could no longer reach distant stars even in principle.

The great advances in detectors, telescopes and observatories on the ground and in space have given us a rough picture of what happened as our Universe evolved from a dense, hot and maybe quite simple early state to its present complexity, and observations in progress are filling in the details. That in turn is driving intense debate on how the behaviour of our Universe can be understood within fundamental physics. Those who work on the fundamentals are well aware of the issue of Λ-like matter; they're certainly trying to solve this theoretical detail. It will help when we know for sure whether Λ has really been detected, and it would help even more if the measurements showed Λ to be decreasing. Maybe we will discover that there is some cosmic significance to when we appeared — apart from our need for a comfortable planet in stable orbit around a long-lived star. □

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Immunology

Accessory to murder

Ton N. M. Schumacher

Cytotoxic T cells rid the body of cells that have been invaded by viruses or bacteria. They do this by recognizing foreign peptide fragments associated with class I molecules of the major histocompatibility complex (MHC) in the membrane of the affected cells. The biggest challenge for the T cells lies not so much in killing the infected cells, as in tracking them down. The body contains 10^{13} nucleated cells whereas, for a given viral antigen, there are perhaps a few hundred naive T cells — clearly, these few T cells could not scan all nucleated cells for signs of infection. In fact, naive T cells don't even try to enter peripheral tissues, and they are activated within the lymph nodes and spleen (immunologists consider all cells that are not derived from the bone marrow or lymphoid tissue to be peripheral). How, then, can a rare, virus-specific T cell in the lymphoid compartment detect viral antigens produced in distant locations such as the skin? Sigal *et al.*[1] provide evidence (on page 77 of this issue) that bone-marrow-derived antigen-presenting cells (APCs) are the messengers that convey the news.

Over 40 years ago it was observed[2] that, during a local allergic reaction, initiation of the immune response requires the lymphatic vessels that drain the skin. Subsequent experiments pointed to migratory cells (that is, APCs) as the cells that transfer the antigen from the skin to the lymph node. So, for viruses that infect such migratory cells, the picture seems clear. But many viruses do not infect these migratory APCs. How does the T cell see these viruses?

As a rule, MHC-bound peptide fragments are derived from virus-encoded proteins produced inside the infected cell

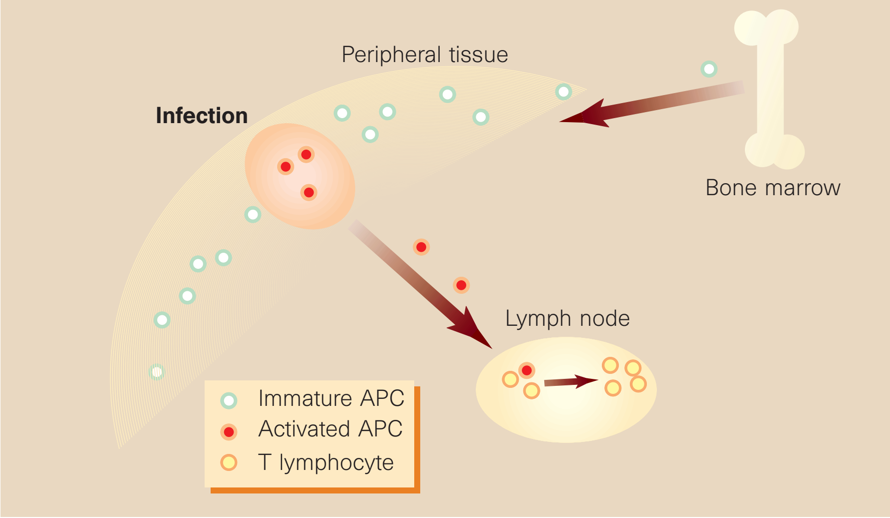

Figure 1 **Detection of viral infection in peripheral tissues, based on the results of Sigal *et al.*[1]. Bone-marrow-derived antigen-presenting cells (APCs) are produced from stem cells in the bone marrow and, subsequently, migrate to peripheral tissues. Following infection, APCs in the infected tissues take up viral proteins or infected cells. After processing, viral antigens are displayed on the cell surface in association with major histocompatibility complex class I and class II molecules[4,5]. When virus-specific helper and killer T cells encounter these activated APCs in the draining lymph node, the result will be a virus-specific cellular immune response.**