between these gatekeepers of double-strand break repair is especially pertinent to attempts at gene replacement in mammalian cells — in this case, most of the injected DNA ends up stuck together end to end and inserted in nonhomologous locations. So an understanding of how DNA damage is channelled towards one repair process or another is a key step in future attempts to manipulate the genome. □

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Astronomy

Fine-structure variable?

Antoinette Songaila and Lennox L. Cowie

How constant are the 'constants' of nature? Ever since Dirac[1] speculated that temporal changes in the values of various dimensionless physical constants might have occurred over the lifetime of the Universe, vigorous but fruitless attempts have been made to detect such variability. The fine-structure constant, $\alpha = 2\pi e^2/hc$, which characterizes the strength of the electromagnetic attraction between photons and electrons, has attracted particularly aggressive attention. Now an Australian–British group is claiming in *Physical Review Letters*[2] that it might have detected evidence for a varying α, at a level of about one part in 10^5, over roughly half the lifetime of the Universe. The authors investigated possible time variation in α using cosmological observations of the absorption spectra of distant (high-redshift) quasars. The result must still be considered extremely preliminary, because of the very real possibility of systematic errors in this type of measurement. But given its importance if correct, it can be expected to provoke considerable scrutiny.

The modern expectation of variation in the fine-structure constant arises from theories such as those unifying gravity with the other forces of nature. The best terrestrial limit on the time variation of α outside the laboratory is based on examination of the decay products of the Oklo phenomenon — an ancient natural fission reactor discovered in 1972 in the Oklo uranium mine in Gabon, West Africa. Analysis[3] of the 1.8-billion-year-old decay products gives a range for a fractional change in the fine-structure constant ($\Delta\alpha/\alpha$) of between 0.9×10^{-7} and 1.2×10^{-7} over this period, which would scale linearly to a limit of about one part in 10^6 over the lifetime of the Universe. But there is no reason to expect the time dependence to be linear (an oscillating α is even allowed in some schemes) and longer time baselines afforded by our ability to measure α by observing the atomic and molecular wavelengths of cosmologically distant objects offer a powerful alternative route.

Wavelength spectra of cosmologically distant quasars provide a natural laboratory for investigating changes in α. Dark, narrow lines in quasar spectra are produced by absorption of radiation in intervening clouds of gas, many of which are enriched with heavy elements. The wavelength separation between two lines produced by absorption from alkaline atoms and ions (an alkaline doublet) is proportional to α^2, so any small variation in this separation will be roughly proportional to α, to a first approximation. Because quasar spectra contain doublet absorption lines at a number of redshifts — and so at different times in the history of the Universe — it is possible to check for time variation in α simply by looking for changes in the doublet separation of alkaline-type ions with one outer electron (such as C^{3+} or Si^{3+}), as a function of redshift. Although this sounds straightforward, any change in α will be very small, and so the accuracy of measurement needs to be high.

Not surprisingly, this method has a long history of null measurements stretching back to its first application by Savedoff[4] in 1956. We obtained the most accurate estimate[5] on the fractional change $\Delta\alpha/\alpha$, prior to the present paper, of $3.5(\pm 5.5) \times 10^{-6}$. This limit was reached by comparing the absorption lines of neutral hydrogen and carbon in a cloud of intergalactic gas at a redshift (z) of 1.8 lying nearly two-thirds of the way across the Universe. The relative wavelengths of the lines would have been shifted by any change

Earth science

A big slip

Examples of past landslides that are known to have been triggered by earthquakes are rarities. But Hervé Philip and Jean-François Ritz believe they have identified one, and it was huge.

From satellite and aerial images of the Gobi-Altay mountain range in Mongolia, and data from ground surveys, Philip and Ritz conclude that the structure shown here, running from the ridge at the bottom of the picture downslope into a valley to the north, is a 'palaeolandslide'— one of uncertain age, which was triggered by ground-shaking and involved the slippage of 50 km³ of earth. The authors calculate that some 100 billion tons of material moved which, put another way, is enough to cover The Netherlands waist deep in mud and rock.

The account appears in *Geology* (27, 211–214; 1999), and the authors surmise that there is an earthquake connection for various reasons, most notably the landslide's occurrence close to the currently active Bogd fault system. The fault ruptured most recently in 1957, in an earthquake of magnitude 8.3. But the most curious aspect of the story is that the average slope from ridge to valley in the landslide area is a very gentle 3°. That

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means that, once the ground shaking had stopped, there must have been some unusual conditions for such a mass of material to continue in motion for several kilometres; this picture shows an extent of ground about 34 km from bottom to top, 18 km of which was affected by the slump.

Philip and Ritz suggest that part of the explanation is that there was little or no frictional or cohesive strength at the landslide's shear plane, a condition that might have pertained when the water table was much higher than it is now. Tim Lincoln

in the fine-structure constant, but no such change was seen. This is not that surprising: theories allow enormous latitude in the actual variation of α, and a detection at the current level of measurement sensitivity will always be unexpected.

Webb *et al.*[2] introduce a new variant of this technique that compares the absorption wavelengths of magnesium and iron atoms in the same absorbing cloud, which they demonstrate in a companion paper[6] to be an order of magnitude more sensitive than the alkaline-doublet method. They observe a number of intergalactic clouds at redshifts from 0.5 to 1.6, seen in absorption against a background of quasars. For the entire sample they find $\Delta\alpha/\alpha = -1.1(\pm 0.4) \times 10^{-5}$, consistent with a null result (to within three standard deviations), but crucially most of the signal comes from a small subset of quasars near a redshift of 1. Restricting the sample to $z > 1$ systems gives a significant change of $\Delta\alpha/\alpha = -1.9(\pm 0.5) \times 10^{-5}$. Such a result would be consistent with little time variation in the past 1.8 billion years since the Oklo event, but larger variation at earlier times when $z > 1$, although it then becomes hard to understand the previous null result[5] at a redshift of 1.8. Webb *et al.*[2] also seem unimpressed by the redshift dependence they have apparently uncovered, and interpret their results as "stringent upper limits on any possible time variation rather than a positive detection of change", in part because "a genuine physical effect confined to one specific epoch ... does not seem at present to be well motivated by theoretical expectations".

Of course, the real problem (as Webb *et al.* discuss at length) is the subtle and not-so-subtle systematic errors that, alas, in this type of measurement are potentially legion. The authors mention most of the likely culprits: the wavelength calibration, uncertainties in the laboratory wavelengths of iron and magnesium, and the effect of unresolved velocity substructure in the absorption lines. The redshift dependence of the effect makes the last by far the most likely: it is not hard to imagine that some of their many lines of sight could have hit an absorbing cloud or two in which their assumptions about the relative distribution and kinematics of light and heavy ions were not correct.

Another potential source of systematic error is the use of both very strong and very weak absorption lines of singly ionized iron: any small perturbation would affect the latter much more than the former and could skew the results. Still, for now, and until we can really probe the details of this investigation, subtle effects in the structure of the absorption lines of the two atoms or slight systematic problems in the wavelength calibration remain the most likely reasons. Because of these problems, it is indeed probably best to regard this measurement as an upper limit, albeit a provocative one.

This new technique ultimately could and should be pushed to higher redshift by using shorter-wavelength lines. And the only thing currently limiting the alkaline-doublet method[5] is the laboratory measurement of the doublet separation of triply ionized silicon lines. The final irony is that both techniques are limited in sensitivity or scope by poorly defined laboratory wavelengths. Webb *et al.* conclude their paper with a plea for more laboratory work to be done, with which we can only concur. □

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Immunogenetics

Defence by diversity

Adrian V. S. Hill

Twenty five years ago Zinkernagel and Doherty[1] discovered that, for virally infected cells to be destroyed, viral antigens must be presented to killer T cells by class I molecules of the major histocompatibility complex (MHC). This finding suggested how the remarkable diversity of the MHC class I might be selected and maintained in a population. First, certain MHC class I variants — in man, called the human leukocyte antigen (HLA)-A, -B and -C types — might present antigens from a virus more effectively than other variants, generating a stronger, more protective, T-cell response[2]. And second, a variety of HLA types could be selectively maintained by heterozygote advantage[3]. What this means is that heterozygotes (people who have two, rather than one, types of antigen-presenting molecule per HLA class I locus) could present a wider range of pathogen antigens, and again generate stronger immune responses (Fig. 1). Large-scale studies of HLA class I antigens, reported in *Proceedings of the National Academy of Sciences*[4] and *Science*[5], now support the operation of these mechanisms in human viral diseases.

Jeffery *et al.*[4] report that the common MHC class I type, HLA-A*02, is associated with a greater than two-fold reduction in the risk of disease induced by human T-lymphotropic virus-1 (HTLV-1). In a two-stage study, the frequency of HLA-A*02 was consistently lower in Japanese patients with disease than in infected people without disease. Each of the main HLA-A*02 subtypes present appeared protective, and the authors detected high levels of virus-specific T cells. Among the healthy carriers of HTLV-1, viral load was much less in those with HLA-A*02 — consistent with a protective role for these T cells. The HLA-A2 lineage is unusual in that it is unique to humans, and this study identifies one pathogen that may have contributed to its selection[6]. Carrington *et al.*[5] report that Americans who are heterozygous for HLA-A, -B or -C antigens are protected against rapid progression to AIDS after

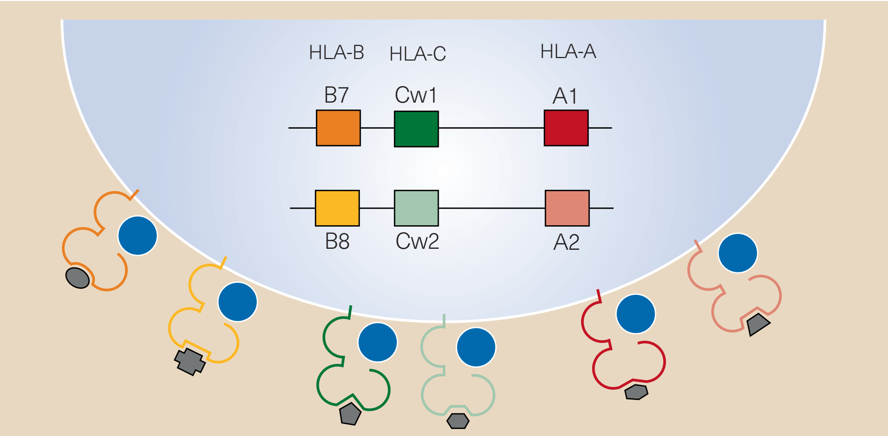

Figure 1 **A greater diversity of human leukocyte antigens (HLAs) may protect against some infectious diseases. Jeffery *et al.*[4] and Carrington *et al.*[5] have shown that people with certain HLAs are less likely to develop disease after infection with HTLV-1 and HIV-1, respectively, than people without. People with two (rather than one) types of antigen-presenting molecule at each HLA class I gene locus, HLA-A, HLA-B and HLA-C, express six different peptide-presenting molecules on the cell surface. So, these people may generate a stronger immune response against intracellular viral pathogens than those with only one type of antigen-presenting molecule per locus. Virally derived peptides are shown (grey) in the antigen-presenting groove of the HLA class I molecules.**