Life and times

THE recovery of no fewer than eleven kinds of filamentous microfossil from 3,465-million-year-old rocks in Western Australia (J. W. Schopf *Science* **260**, 640–646; 1993), shows that life was not only in existence a few hundred million years after the planet formed, but was thriving: rarely does one find single fossils of this antiquity, let alone entire communities. The fossils represent bacteria and presumably photosynthetic (and therefore oxygen-producing) cyanobacteria little different from those a billion years younger. But, as Schopf asks, if such diverse communities were present at this early date, why did their members remain essentially unchanged for so long?

Waste disposal

THE growing end of a neuron receives the necessary materials by axonal transport from the cell body. The metabolic products of the activity at the growth cone come back down the axon by retrograde transport and home in on lysosomes in the cell body, or in some cases are processed by proteases in the cytosol. P. J. Hollenbeck now illuminates the mechanisms by which the unwanted proteins are despatched from the growth cone (*J. Cell Biol.* **121**, 305–315; 1993). The vehicles that carry them back, he finds, are membrane-encased vacuoles, which take up fluorescent dextran, introduced into the cell, and convey it to the lysosomes in the cell body. If the neuron is allowed to take up similarly labelled materials from the outside world by endocytosis at the growth cone, all the fluorescence again appears in the same kind of vacuole, travelling down the axon. This is a finely tuned mechanism for responding to the imperatives of the law of conservation of mass.

Slit decision

THE number of games that can be played to illustrate wave–particle duality is proliferating. Besides diffracting light through material slits (Young's slits), one can diffract atoms through gratings composed of immaterial light waves, atoms through slits composed of other atoms and, now, light off a pair of atoms suspended in a vacuum in a magnetic field (U. Eichmann *et al. Phys. Rev. Lett.* **70**, 2359–2362; 1993). The alert might recall that various groups have made unusual, tenuous 'crystals' out of small numbers of ions suspended in a magnetic field; the pair of mercury ions in the new experiment constitutes the simplest such crystal. So the diffraction of laser photons becomes a novel form of Bragg reflection, which effect showed originally that X-rays are electromagnetic waves and that atoms in solids line up in ordered arrays. Such is progress.

Planet X: a myth exposed

Gerald D. Quinlan

THERE is no reason for the planetary system to end at Pluto. Astronomers have long debated the possibility of a more-distant tenth planet, usually referred to as Planet X. But the scant dynamical evidence requiring the existence of this planet is largely refuted in a new analysis by Myles Standish of the Jet Propulsion Laboratory¹.

The history of the hypothetical tenth planet begins with the discovery of Neptune². By the late 1830s the existence of this unseen planet had become undeniable because of discrepancies approaching one arcminute between the observed and computed orbits of Uranus, attributable to gravitational perturbations. The discovery of Neptune in 1846 within one degree of its predicted position was without question the greatest triumph of celestial mechanics at the time. The discovery reduced the discrepancies in Uranus's orbit to the level of arcseconds, comparable with the noise in the observations, but that did not stop some astronomers from predicting a planet beyond Neptune, of a few Earth masses. A long series of searches beginning with Lowell in 1905 culminated with Tombaugh's discovery of Pluto in 1930.

Pluto appeared tiny right from the start; it is now known to have a mass only 0.2 per cent of that of the Earth, far too small to have caused the irregularities in the orbits of Uranus and Neptune attributed to Planet X. A dedicated group of astronomers have maintained that a tenth planet is required. Some have proposed other reasons for Planet X, blaming it for causing periodic comet showers and mass extinctions on Earth, or for stealing Pluto from Neptune and reversing the motion of Neptune's satellite Triton. Observational surveys by Tombaugh, Kowal and the Infrared Astronomical Satellite (IRAS) would almost certainly have revealed another Pluto or larger planet, but their failure to do so has not stopped many predictions from being made^{2,3}, including two more in just the past year^{4,5}.

Standish shows in his new work¹ that the dynamical evidence for Planet X is readily explained by uncertainties in planetary ephemerides. The construction of an ephemeris involves processing and evaluating the wide variety of data on planetary positions, choosing a dynamical model for the Solar System, and varying the adjustable parameters to give computed orbits that best fit the observations. Planet X's supporters point to three ephemeris difficulties suggesting a tenth planet: the Uranus

observations cannot all be made to fit, and the residuals show systematic trends; a few known sightings of Neptune before its identity was established are difficult or impossible to fit; and predictions of Neptune's orbit have tended to be inaccurate. Standish examines the first two difficulties; the third is not surprising given Neptune's long orbital period, 165 years (so that not even one orbit has been completed since it was discovered).

The Uranus difficulties result mainly from the use of an incorrect mass for Neptune. The masses of the jovian planets are now known accurately from the Voyager missions, but in the past they were not, and much of the speculation on Planet X has been based on residuals from the Jet Propulsion Laboratory's ephemeris DE200 and its predecessors, which used a Neptune mass in error by 0.5 per cent. Standish has constructed a new ephemeris with the correct mass and finds that this reduces the root-mean-square Uranus residuals by about 20 per cent and, more importantly, removes the systematic trends. There remains a strong positive bias in the right-ascension residuals from 1895–1905, but Standish has traced the majority of these to a single catalogue of the US Naval Office 9-inch transit telescope (data from two other sources do not show this bias); an observational error such as an incorrect equinox correction is a plausible explanation.

Regarding the predisccovery sightings of Neptune, Lalande's in 1795 is said to differ from ephemeris predictions by seven or more arcseconds, but Standish shows by extrapolating two ephemerides backwards that the predictions are uncertain by at least several arcseconds; combined with the scatter in Lalande's observations this makes the discrepancy rather dubious. The discrepancy for Galileo's observation in 1613 is larger if true, but Galileo's notes are ambiguous, and, moreover, Standish and Nobili have found another Neptune observation by Galileo, this one agreeing with ephemeris predictions (personal communication).

Accurate planetary observations being collected today will in time lead to more stringent tests for a tenth planet. These observations are valuable irrespective of Planet X, because planetary ephemerides are needed for other purposes such as spacecraft navigation and pulsar data reduction, and are instrumental in precise tests of theories of gravitation. But for now the search for Planet X is futile.

The search for smaller objects in the

outer Solar System has only just started, however. Dynamical limits⁶ allow a few tenths of an Earth mass in a belt of planetesimals beyond Neptune. This belt, named after Kuiper who suggested it would be left over from the formation of the planets, has been much-discussed as a possible source of short-period comets⁷. In 1987 David Jewitt instituted a systematic search of the outer Solar System for faint, slow-moving objects. The effort was rewarded with the discovery⁸ last August of the faint smudge (7,000 times fainter than Pluto) which he and Jane Luu tagged 1992QB₁ (they later named it Smiley, after le Carré's spy). Four months' observations of QB₁ reveal an orbit that would be expected for a Kuiper-belt object, although there is still considerable uncertainty in the eccentricity. QB₁'s estimated diameter of 200 km puts it at one tenth the size of Pluto: much larger, and the whole distinction between planets

and minor planets would be thrown into doubt. There is now news^{8,9} of a second possible Kuiper-belt object, 1993FW, also found by Jewitt and Luu. The discovery of even a few of these objects could tell us much about the early history of the Solar System, perhaps more than we would learn from the elusive (or illusory) Planet X. □

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SCHISTOSOMIASIS

Proselytizing with immunity

Edward J. Pearce

THE reality of schistosomiasis is that at least as many people are infected today as ten years ago — this despite the availability of the wonder drug praziquantel. It was against this gloomy backdrop, and in the knowledge that disease resistance, disease severity and drug efficacy are contingent upon the immune response to the parasites concerned, that immunologists got together earlier this year* to assess the state of play in understanding and tackling the disease.

The outlook, however, is not altogether depressing. The meeting provided a sparkling overview of the very real advances in getting to grips with the immunoregulatory and immunopathological mechanisms involved, and in vaccine development. Even the sceptics were left with no doubt that the production of an effective vaccine against schistosomiasis is not only necessary, but possible.

There is, it is clear, more than one way to make a vaccine against schistosomiasis. Recombinant schistosome glutathione-S-transferase, which confers only a partial resistance to infection, induces a potent anti-fecundity immune response that dramatically reduces the number and viability of eggs produced by female parasites, and so reduces the risk of transmission and the pathology associated with infection¹ (A. Capron, Pasteur-Lille). The anti-pathology

effects of this vaccine are most striking in calves and patas monkeys, both of which were essentially protected from disease when unvaccinated controls developed severe lesions. There was, too, an intriguing report of unprecedented levels of immunity induced in rodents, and partial protection in baboons, by a recombinant surface-antigen (rIrV5), which shares homology with myosin II (M. Strand, Johns Hopkins). The plan is to take these vaccines into phase I human trials in the near future.

There is also progress to report in identifying immune effector mechanisms, an area in which research on schistosomiasis has been central. Amongst those working with human populations in endemic areas there is accord that the intensity of reinfection following treatment, as assessed by faecal egg counts, is negatively correlated with levels of immunoglobulin E (A. Dessein, INSERM; D. Dunne, University of Cambridge), lending support to the view that IgE protects against schistosomes. (Incidentally, the time-honoured use of faecal/urine egg counts to assess infection intensities may be on the way out; many groups are now planning to use circulating adult antigen to provide specific information on worm burdens.) On the subject of responses mediated by the Th2 subset of CD4⁺ cells, the story of the eosinophil grows more intriguing with news that these cells are a major source of interleukin-5 and possess IgA receptors (M. Capron, Pasteur-Lille).

Another approach to vaccine development is the elicitation of Th1-like responses, as illustrated by the report that immunity in mice immunized with attenuated parasites is entirely dependent on the Th1 cytokine, interferon- γ (ref. 2; A. Wilson, University of York). The demonstration that endothelial cells can be activated by IFN- γ to kill schistosomes (S. James, NIAID) raises the prospect that these cells, which line the pulmonary capillaries (a dangerous bottleneck in schistosome migration), have a part in the IFN- γ -mediated effect. The take-home message here is that both Th1- and Th2-stimulating vaccines have the potential to be protective.

During the egg-laying stage of infection, Th responses in mice are highly Th2-like, suggesting that pathology, which is Th dependent, is mediated by Th2 cytokines. This concept was discussed in light of observations that IL-2 (D. Boros, Wayne State; A. Sher, NIAID), the α form of tumour necrosis factor (ref. 3; Boros; J. McKerrrow, UCSF) and IL-4 (Boros; Sher) are all involved in granuloma formation; further, in mice, high TNF- α levels seem to be predictive of severe disease (D. Colley, Centers for Disease Control). Studies of the antigens involved in anti-egg Th responses show egg proteases to be particularly immunogenic (B. Doughty, Texas A&M).

The involvement of IL-10 in the inhibition of macrophage anti-schistosome effector functions (James), and the Th1 down-regulation which accompanies egg-associated Th2 responses, came in for some debate. This is a critical area — experimentally, the suppression of Th1 and CD8⁺ cell activity makes mice with schistosomiasis more susceptible to experimental vaccinia infection⁴ (in these mice, virus persists specifically in granuloma fibroblasts; Sher). These data bear on the correlation between hepatitis and schistosomiasis, and (possibly) on how the human immunodeficiency virus is dealt with by helminth-infected individuals. The extent to which Th1 responses are down-regulated in infected patients, who clearly are mounting anti-parasite Th2-like responses, remains unclear, although some studies have indicated less of a suppression than that seen in infected mice (Dunne; C. King, Case Western Reserve).

The belief that pathology in schistosomiasis is wholly egg-centred requires reassessment in light of the report of 'capillarization' of hepatic sinusoids in infected mice before the onset of egg production (J.-A. Grimaud, Pasteur-Lyon). Other news on pathogenesis is that fibroblast stimulating factor 1, a cytokine first described in schistosomiasis, stimulates deposition of extracellular matrix (D. Wyler, Tufts). The relationship between a failure to down-

* *Fundamental Immunology and its Application to the Study of Schistosomiasis*, Sharm El Sheikh, Sinai, Egypt, 31 January–11 February 1993.