RÉSUMÉ

Whipple's bacterium

It was over 80 years ago that George Whipple described a rare and then invariably fatal intestinal disease that now bears his name, and some 30 since the probable causative agent was confirmed as a bacterium. But which bacterium? In a striking example of how molecular techniques are superseding traditional methods of bacterial taxonomy, D. A. Relman *et al.* have identified the organism responsible by amplifying its 16S ribosomal RNA gene and sequencing it (*New Engl. J. Med.* **327**, 293–301; 1992). Curiously, the bacterium, dubbed *Tropheryma whippelii* seems to be akin to the actinomycetes, a group most commonly found in soil. So as well as paving the way for a new diagnostic test, the study may suggest approaches by which the hitherto intractable *T. whippelii* might be cultured for study.

Sticking point

J. H. Hoh *et al.* believe they may have observed individual hydrogen bonds using an atomic force microscope (*J. Am. chem. Soc.* **114**, 4917–4918; 1992). The microscope consists of a silicon nitride tip, mounted on a cantilever, which scans over a glass surface. Sensitive to forces as weak as 10^{-11} newtons, the tip appeared to snag on individual features on the glass surface, producing a kind of microfriction. The adhesion force was 1.2×10^{-11} newtons, although multiples of this value were also seen. The authors suggest that microscope tip stuck to the glass through hydrogen bonds — each surface carries a profusion of silanol groups — although they allow that ordered layers of water (in which the experiments were performed) will have modified the force.

Staying alive

The mass extinction at the close of the Cretaceous 65 million years ago had a far more drastic effect on land animals than those living in freshwater habitats. Aquatic creatures could have survived a temporary loss of primary productivity by relying on a food chain based on detritus feeding, according to P. M. Sheehan and D. E. Fastovsky (*Geology* **20**, 556–560; 1992). Their data come from the inventory of Uppermost Cretaceous and Lowermost Palaeocene vertebrates from eastern Montana compiled by J. D. Archibald and L. J. Bryant which, when analysed, shows that about 88% of species of land animals did not survive the end of the Cretaceous, but that some 90% of freshwater animals did. The authors emphasize that the data apply only to eastern Montana; nevertheless, the results are consistent with a variety of circumstances inferred as consequences of bolide impact.

well. The mirrors' thickness and separation were selected (and exquisitely grown) to reflect the carriers and make them interfere to form a bound state at the wide well. The energy E_c of the bound state was set by the mirror spacing to be within the continuum of extended states from the wide well.

This trapped state was observed by optically exciting electrons from a lower, bound state (E_b) of the wide well. Instead of the broad response indicative of a continuous band of above-well states, the authors observed a narrow resonance at $E_c - E_b$, just where it was expected for the particular arrangement of mirrors. The energy and the width of the resonance could be adjusted by changing the separations and the number of mirrors. The resonance even seems to have the characteristic asymmetric shape expected for level crossings[7,8]. These results are an elegant confirmation of an old prediction[12,13] and a step toward more sophisticated optical-electronic circuits in which tailored energy states serve to mimic classical optics. □

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TUBERCULOSIS

Back to a frightening future

Barry R. Bloom

Lessons unlearned and opportunities lost have come back to haunt us[1]. Tuberculosis — the largest cause of death in the world from a single infectious disease[2] — has been virtually ignored for 20 years and more. While TB remains a major problem in developing countries, cases have increased by 33.3% in Switzerland, 30.7% in Denmark, 28% in Italy and 11.8% in the United States in recent years. Most ominous, the emergence of multidrug-resistant strains has reduced the efficacy of treatment almost to the level of the pre-antibiotic era[3]. The work described by Zhang *et al.*[4] on page 591 of this issue offers hope that molecular genetics may be one way to tackle the growing problem of drug-resistant tuberculosis. This paper reports the first characterization of a molecular target for any antituberculosis drug, even though the earliest antibiotic effective against tuberculosis, streptomycin, was introduced 40 years ago.

The drug, isoniazid (isonicotinic acid hydrazide, INH), was first synthesized in 1912 and has been the cornerstone of all effective regimens for treatment and prophylaxis of tuberculosis since the 1950s. Zhang *et al.* selected INH-resistant mutants in a rapidly growing surrogate mycobacterium, *Mycobacterium smegmatis*, because *M. tuberculosis* grows only slowly. By screening DNA libraries from virulent *M. tuberculosis*, they identified a gene that restored sensitivity to INH in the *M. smegmatis* mutants and in *Escherichia coli*, which is intrinsically resistant to the drug. This gene (*katG*) encodes a catalase–peroxidase enzyme. The authors were keenly aware that clinical INH-resistant isolates often lack catalase activity, so they used DNA probes for *katG* to show that a subset of INH-resistant isolates from TB patients had deletions in this catalase–peroxidase gene. They suggest that the enzyme encoded by *katG* may chemically convert INH to a biologically active form. One hope is that it will be possible to synthesize the active INH metabolite, which, if it is stable, might then be useful in treatment. But analogues of INH are unlikely to be effective if the catalase–peroxidase gene has been deleted, so it is now important to search for the target(s) of the activated form of INH, a strategy that could lead to the development of new drugs. Because with current technology it takes between two and eight weeks to isolate *M. tuberculosis* from clinical samples, and between one and thirteen weeks to establish their sensitivity to antibiotics[5], to have specific DNA probes for the critical mutant targets of the major drugs used against tuberculosis would be a great advantage for the molecular assessment of patterns of drug resistance. Early application of effective treatment is the key to curing and blocking transmission of this disease. ▶