DISEASE WATCH | IN THE NEWS

Silent mutations cause a stir

STOCKBYTE

Silent mutations can be used to create non-virulent strains of viruses, which could provide a new strategy for vaccine development, say scientists at Stony Brook University, New York, USA. Although different codons can encode for the same amino acid during protein synthesis, many organisms tend to have biases towards particular codons. In humans, for example, the alanine codon GCG is fourfold more common than the synonymous GCC codon. Previous findings have indicated that the introduction of silent mutations, which change a codon without changing the amino acid it encodes, have detrimental effects on the viability of viruses, possibly because some codons are easier to translate than others. To examine whether such mutations are useful for vaccine development, Steffen Mueller and colleagues introduced 631 silent mutations into the poliovirus genome, thereby creating a mutant that was under-represented in the normal codon bias. Inoculation of mice with this mutant variant did not cause polio symptoms, but did provide mice with immunity to exposure to wild-type poliovirus. Because this approach involves the introduction of hundreds of silent mutations, rather than only a handful of mutations, the virus is less likely to revert to its former virulence. ***Science***

Not so tropical diseases

At least 300,000 Americans suffer from diseases that are typically associated with tropical developing countries, reports Peter Hotez of the George Washington University, Washington DC, USA. Hotez identified 24 viral, bacterial and parasitic 'neglected infections of poverty' that are surprisingly common in America. These included brucellosis, dengue fever, cytomegalovirus, Chagas disease and schistosomiasis. According to the report, many of these diseases have been present in the United States for a considerable amount of time, and people of colour in poverty-stricken regions, such as Appalachia, the Mississippi Delta and inner cities, are most affected. Hotez suggests that more active surveillance, epidemiological studies, mass or targeted treatments and vector control, together with new diagnosis and treatment tools, are needed. ***PLoS Negl. Trop. Dis./Los Angeles Times***

Unsafe sex

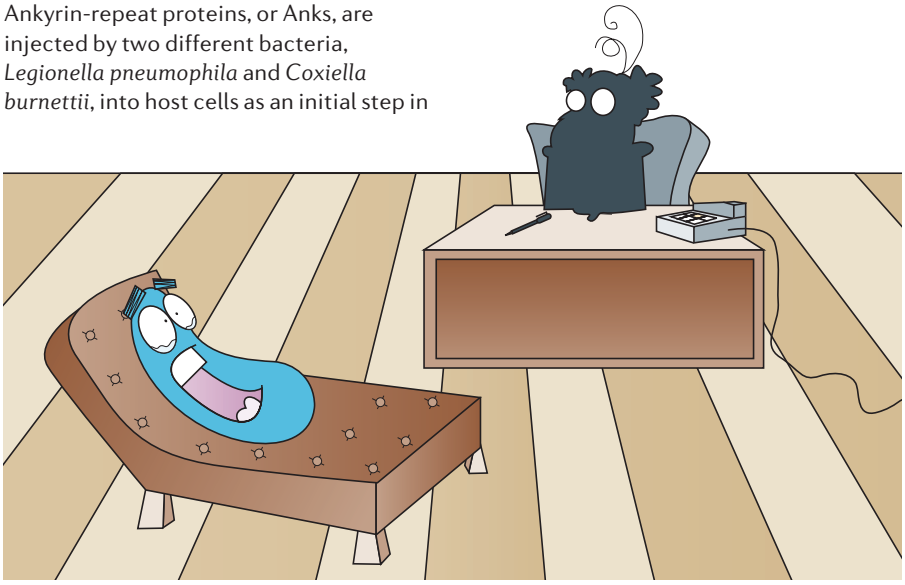
A third of men who have sex with men are having unprotected sex, both in the United Kingdom and in New York. In the United Kingdom, Anne Johnson, of University College London, and colleagues surveyed 3,501 men who have sex with men, tested all volunteers for HIV and reported their findings in *AIDS*. According to their survey, sexual risk and sexually transmitted infections were highest among those who knew they were HIV positive. Testing revealed that 9.1% of the volunteers were HIV positive, and of these, 41.2% were unaware of their HIV-positive status. In a separate study, the New York Department of Health and Mental Hygiene surveyed 10,000 New York residents and found that 36% of men who have sex with men and who had 5 or more partners in the past year do not use condoms. ***AIDS/New York Times***

Anks angst

Ankyrin-repeat proteins, or Anks, are injected by two different bacteria, *Legionella pneumophila* and *Coxiella burnettii*, into host cells as an initial step in infection, researchers show. Craig Roy and colleagues at Yale University, Connecticut, USA, set out to examine whether Anks are injected into host cells by the type IV secretion system (T4SS). Indeed, they found that *L. pneumophila* injects four Anks by the T4SS, whereas *C. burnettii* injects eight Anks. Furthermore, *L. pneumophila* AnkX enabled infection by ensuring that the host cell could not interfere in the fusion of *L. pneumophila*-containing vesicles with late endosomes. These findings indicate that Anks have effector functions that enable bacteria to infect mammalian cells. ***Science***

Faster TB tests on their way

Faster diagnostic tools for multidrug-resistant tuberculosis (MDR-TB) that take only 2 days, as opposed to 2–3 months, and access to appropriate treatment will be available to people in developing countries, following the launch of 2 new initiatives. It is currently estimated that only 2% of MDR-TB cases are diagnosed worldwide, mainly owing to inadequate laboratory services. In developing countries, patients with TB are only tested for MDR-TB after typical TB treatments fail. As current tests take at least 2 months, MDR-TB spreads unnecessarily, and patients often die before the infection is diagnosed. Both initiatives are funded by the international drug-purchasing facility UNITAID. In the first initiative, laboratory facilities and supplies will be provided and staff will be trained in 16 countries over the next 4 years so that MDR-TB can be



Neil Smith

diagnosed in 2 days. In the second initiative, the Global Drug Facility will increase its supply of MRD-TB drugs to 54 countries. UNITAID has pledged a total of US$60 million for these two initiatives, which will be rolled out in partnership with WHO, the Stop TB Partnership and the Foundation for Innovative New Diagnostics. **WHO**

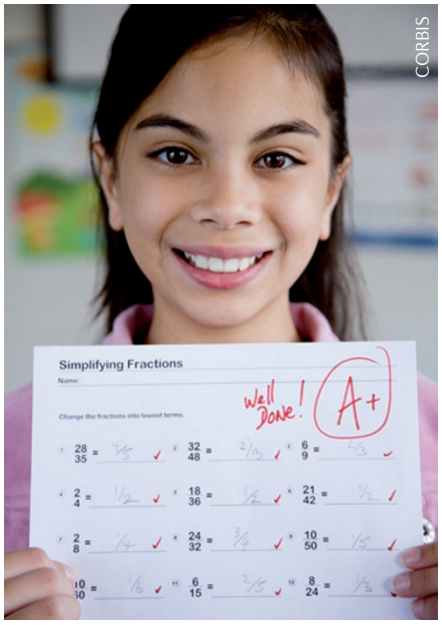
Herpes drug does not stop HIV

Contrary to expectations, the herpes drug aciclovir does not reduce the chances that high-risk individuals will contract HIV-1. Previous studies had shown that patients infected with herpes simplex virus 2 are twofold to threefold more likely to develop HIV-1 infections. Consequently, many AIDS prevention programmes distribute anti-herpes drugs to control the spread of HIV-1. In a trial of over 3,000 people, Connie Celum from the University of Washington in Seattle, USA, and colleagues tested whether the antiviral drug aciclovir reduces the risk of HIV-1 infection. The difference in infection rates between those individuals who were given aciclovir or a placebo was insignificant — approximately 0.047% of those given aciclovir contracted HIV-1, compared with approximately 0.040% of those given a placebo. "It's a significant, disappointing finding," said Francis Ndowa, coordinator of the sexually transmitted infections control team at WHO. These findings suggest that AIDS prevention programmes may need to revise the current approach of trying to control AIDS by treating other sexually transmitted infections, such as herpes. ***Lancet***

Access denied

AIDS prevention programmes have another big problem — 69% of HIV-positive patients in low- and middle-income countries did not have access to antiretroviral therapy (ART) in 2007. Fewer than 3 million patients in low- and middle-income countries received ARTs in 2007, up from only ~2 million in 2006. Although this represents an almost sevenfold increase in the availability of ART in just 4 years, it still comes 2 years later than WHO's '3 in 5' target. The authors partly credit the increase in ART availability to reduced prices, improved delivery systems and increased demand from patients who have been diagnosed as HIV-positive, but warn that access to ART will probably slow in the future because of weak health-care systems in the worst-affected countries. **WHO**

Cheap cholera vaccine passes test



A cheap form of cholera vaccination has passed its first pilot trial, a study reports. Only one internationally licensed cholera vaccine is currently available, and it is too expensive for use in the developing world, where it is most needed. Officials in Vietnam have been distributing their own two-dose oral vaccine since the 1990s, at a cost of around $0.40 per dose, but this vaccine has not been internationally licensed. Sujit Bhattacharya of the National Institute of Cholera and Enteric Diseases in Kolkata, India, and colleagues reformulated the Vietnamese vaccine to comply with WHO standards, and tested the vaccine in 100 children and 101 adults. Vaccination provided at least a fourfold increase in *Vibrio cholerae* O1 antibody levels in 80% of children and in 53% of adults, and caused no adverse side effects. A larger trial of 70,000 people in Kolkata is now underway. "If the vaccine is found to be safe and protective, this could pave the way for the use of this vaccine worldwide", the researchers write. ***PLoS ONE*/SciDev.net**

Toxo protection

Toxoplasma gondii is an obligate intracellular parasite that replicates within a specialized parasitophorous vacuole. Proinflammatory cytokines, such as tumour necrosis factor, together with $CD8^+$ T cells, are known to be crucial for the control of *T. gondii* infection, but little has been known about the *T. gondii* antigens that stimulate protective immunity. $CD8^+$ T cells recognize antigenic peptides that are derived from endogenous proteins and are presented by major histocompatibility complex (MHC) class I molecules. Nicolas Blanchard and colleagues used unbiased expression cloning to identify *T. gondii* proteins that are presented to $CD8^+$ T cells as peptide–MHC class I complexes, and then went on to discover that the $CD8^+$ T-cell response to *T. gondii* infection is dominated by a single immunodominant antigen that is derived from the dense granule protein GRA6. Moreover, mice that are deficient in the endoplasmic reticulum aminopeptidase ERAAP are susceptible to *T. gondii* infection, and the authors confirmed that this is because GRA6, as for other endogenous proteins, is subject to processing by ERAAP. ***Nature Immunol.***

Outbreak news

Salmonella. More than 800 cases of *Salmonella enterica* serovar Saintpaul (*S. enterica* Saintpaul) have been reported in America since April. The outbreak, which is suspected to be caused by tomatoes, has spread across 36 states. Officials are still trying to identify the source of the outbreak. Consumers are urged to avoid raw red plum, red Roma and red round tomatoes unless they are from states and countries that are not under suspicion. Typically, 400 cases of *S. enterica* Saintpaul infections are reported to the CDC each year. **CDC/FDA/Reuters**

Poliovirus. Wild poliovirus type 1 is currently spreading through northern Nigeria and beyond. Ninefold more cases of polio have been reported in northern Nigeria this year than over the same period in 2007 (224 compared with 24). Polio has also spread west into Benin, north into Niger and east into Chad. More than 20% of the children in high-risk areas have not been immunized, but there are plans to have large-scale immunization drives in Nigeria in July and August. **WHO/Global Polio Eradication Initiative**

In the News was compiled with the assistance of David Ojcius, University of California, Merced, USA. David's links to infectious disease news stories can be accessed on Connotea (http://www.connotea.org), under the username NatureRevMicrobiol.