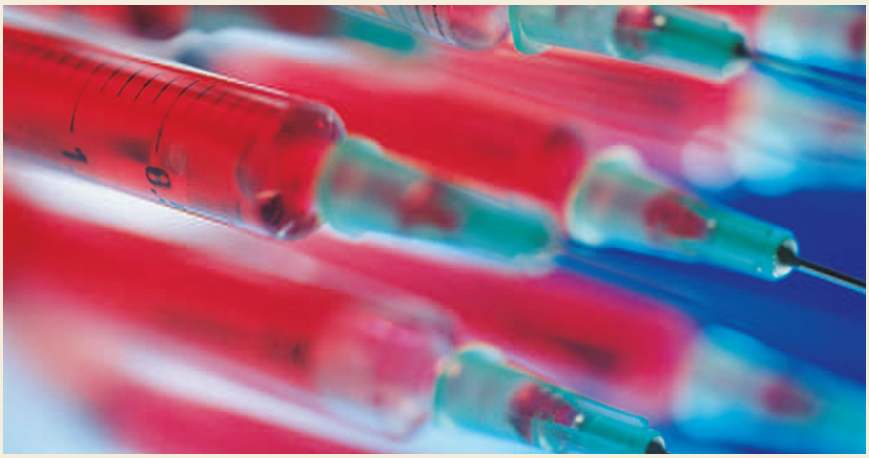
NEWS IN BRIEF



Success uncertain for HIV vaccines

Scientists unsure whether an HIV vaccine can ever be created.

The lowdown: An HIV vaccine remains the best hope for combating the AIDS epidemic. But it is unlikely that any of the dozens of vaccines currently being tested will completely protect people from HIV, admitted members of the International AIDS Vaccine Initiative (IAVI) during the launch of their report, *AIDS Vaccine Blueprint 2006: Actions to Strengthen Global Research and Development*, at the XVI International AIDS Conference in Toronto. Creating a vaccine for HIV could be the most difficult vaccine challenge in history, because of the elusive and evasive behaviour of the virus, and because no one knows what parts of the immune system to stimulate and how. There are also logistical obstacles to testing vaccines, such as a lack of volunteers and facilities to carry out the clinical trials. But the IAVI researchers called for a new vaccine development model to move novel candidates targeting different immune responses into the pipeline, and maintained there is reason to remain optimistic for the future. One cause for hope is the creation of the Global HIV/AIDS Vaccine Enterprise, a big-science approach funded by US$300 million from the Gates Foundation. Another is that valuable information could be gleaned from candidates, even if they fail. The next major milestone for the field is likely to be results from Merck's vaccine trial in 2008 or 2009. The vaccine is designed to improve the effectiveness of the killer T cells that seek and destroy infected human cells. But even if the study is a success, Merck researchers have admitted that it will not be the end of the search for a vaccine. Designing an HIV vaccine is a huge and complicated problem, and there well be many failures along the way. But researchers insist that it is far too early to admit defeat.

Double Vioxx setback for Merck

Recent run of victories for company halted.

The lowdown: Just when Merck might have thought it was making headway in Vioxx cases after three victories in a row, the company received a double blow. A victory for a plaintiff in a New Orleans court was quickly followed by the announcement that a judge reversed the ruling in the first case Merck won in November 2005. A New Jersey jury had found that Merck wasn't liable for the heart attack of Frederick Humeston. But the judge, Carol Higbee, has asked for a retrial because of new evidence published in an 'Expression of Concern' in the *New England Journal of Medicine* a month after the trial verdict. The journal claimed that Merck failed to include data on three additional heart attacks that occurred among patients taking Vioxx in the VIGOR study (Curfman G. D. *et al. NEJM* 353, 2813–2814; 2005). Merck argued that the additional heart attacks occurred after the study's cut-off point and did not affect the overall message of risk. The fallout from the retrial request is not clear at the time of going to press, but together the two recent decisions are bound to re-energize plaintiffs and attorneys.

Study confirms theory for unexpected effects of TG1412

Drug shown to induce cytokine storm.

The lowdown: Doctors who treated the six healthy volunteers left in intensive care after taking the T-cell-stimulating antibody from TeGenero have described their observations in the *New England Journal of Medicine*. Within 90 minutes of receiving a single dose of the anti-CD28 antibody, all six volunteers had an inflammatory response indicative of a cytokine storm, accompanied by headache, myalgias, nausea, diarrhoea, erythema, vasodilatation and hypotension (Suntharalingam, G. *et al. NEJM*, published online 14 August 2006; doi: 10.1056/NEJMoa063842). Within 12–16 hours the volunteers became critically ill, with lung injury, renal failure and coagulation in blood vessels. Within 24 hours, patients experienced severe and unexpected loss of lymphocytes and monocytes. The 'elephant man' swelling that so captured the media's attention was not a direct result of TG1412, but was in fact caused by the large amount of fluid that doctors injected into the volunteers

to replenish fluids lost through leaking blood vessels. Why TGN1412 caused the unexpected effects in humans is still unclear. The authors suggest that the affinity of the anti-CD28 antibodies might be different in humans than in preclinical models, or that laboratory models have more naive T cells than humans. The findings are derived from tests carried out up to 30 days after the trial, and do not reflect the recent claims from one volunteer that he has developed the early signs of lymphatic cancer and is at risk of autoimmune diseases.

Club drug for depression?

Study shows ketamine could treat depression quicker than existing antidepressants.

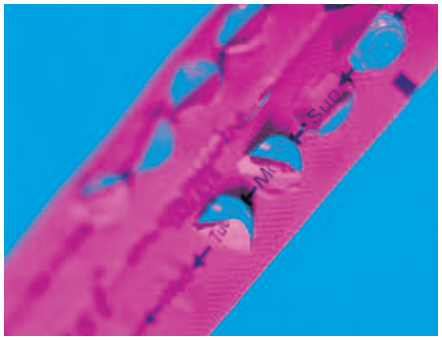
The lowdown: Veterinary anaesthetic turned club drug, could the latest incarnation of ketamine be as a next-generation antidepressant? A preliminary study on seventeen subjects with treatment-resistant major depression showed that a single dose of ketamine improved symptoms in patients within 2 hours (Zarate Jr, C. *et al. Arch. Gen. Psychiatry* 63, 856-864; 2006). Five patients reported improvements meeting the criteria of remission one day after receiving the NMDA antagonist, and the response lasted for more than a week. The study researchers have been quick to point out that the study was small, and ketamine was administered under tightly controlled conditions, because the drug is known to cause hallucinations and dangerous reactions. But the findings do suggest that ketamine's mechanism of action, NMDA receptor inhibition, could be the starting point for developing faster-acting antidepressants. Current antidepressants such as selective serotonin-reuptake inhibitors act slowly and the time lag can prove fatal in some patients, with a risk of suicidal behaviour thought to be heightened during the first 9 days of treatment.

Avian flu vaccine success

Preliminary analysis suggests crucial milestone in immune response to deadly flu strain.

The lowdown: Several companies are competing to develop a successful vaccine that targets the H5N1 strain of the flu virus. In a press release, GlaxoSmithKline threw its hat into the ring by announcing results that suggest that its vaccine could produce a higher and more sustained response, at lower doses than its rivals. GSK said a trial involving 400 adults in Belgium aged 18–60 detected a strong immune response in 80% of people, as measured by antibodies raised against the vaccine. GSK's vaccine is an inactivated form of the H5N1 virus isolated in Indonesia last year with a proprietary adjuvant that GSK says is responsible for the strong effect. Being able to immunize people with a small dose means there is a greater chance of producing the amount of vaccine needed to cope with a pandemic. By contrast, Sanofi-Aventis' vaccine, the most advanced in development, protected around 50% of people at a much higher dose than GSK's candidate. Although many experts in the field say they are impressed with the results from GSK's vaccine, they caution whether these results will translate to a real-world setting. The big unknown is whether any vaccine effective against H5N1 in humans would work well against new pandemic strains.

FDA moves to approve plan B



Wait for over-the-counter contraceptive could be nearing end.

The lowdown: The US FDA has at long last taken steps towards ending the controversy surrounding the emergency contraceptive Plan B (Barr Laboratories), by proposing that access to the combination pill should be restricted to women aged 18 and over. The move is controversial because in 2003 an FDA Advisory Committee overwhelmingly voted for approval of a switch to over-the-counter status for the contraceptive for women of all age groups. Since then the agency has delayed its decision to approve Plan B while it seeks data on whether young adolescent women can safely use the contraceptive for emergency purposes — a decision critics say is motivated more by political interference than by scientific knowledge. The latest announcement by the FDA coincided with the appearance of acting FDA Commissioner Andrew von Eschenbach at a Senate committee to confirm his nomination as full-time Commissioner. Senators Hillary Clinton and Patty Murray, feeling that they had been duped by false promises made in the run up to the appointment of the previous FDA head Lester Crawford in 2005, have refused to back von Eschenbach until the decision on Plan B is finally made. Barr Laboratories said it will resubmit its Plan B application, tailored to the 18-and-older guidelines. Whether this will result in the successful approval of Plan B, and consequently von Eschenbach, remains to be seen.

Women less likely to patent

Study shows gender differences in academic entrepreneurship.

The lowdown: At a time in which gender differences in academia has become a hotly debated topic, an analysis of 4,227 life-science researchers who earned their Ph.D. between 1967–1995 makes for interesting reading. According to the study, female faculty members patent at about 40% of the rate of men (Ding, W. W. *et al. Science* 313, 665-667; 2006). A big reason for the difference was that women scientists had less industrial contacts than men. Without these contacts women found it more time-consuming to find out whether an idea was worth patenting. Another reason is that women are more concerned that pursuing commercial opportunities might hinder their academic careers. Female faculty members frequently depended on male collaborators to initiate the patenting process, and many women stressed the importance of formal institutional sponsorship, such as provided by technology transfer offices. The study showed that the gender gap is shrinking: the gap was largest in older faculty members, and smallest in younger scientists.