

causing enzyme. Ever since the problem of Gleevec resistance became apparent, pharmaceutical companies have been pulling previously created Src inhibitors off the shelf to test how well they also inhibit ABL, says Brian Druker of Oregon Health & Science University in Portland, one of the original developers of Gleevec.

In test tube studies, the Src inhibitor BMS-354825 stopped the kinase activity of 14 of 15 Gleevec-resistant versions of BCR-ABL. Sawyers and his colleagues then tested the drug on a mouse model of leukemia; instead of dying in weeks, treated animals remained healthy. The drug also exhibited activity against cancerous bone marrow cells from Gleevec-resistant patients.

BMS-354825 or a similar drug—many of which are in development, including ones at Novartis, the maker of Gleevec—could

help patients even before resistance becomes a problem, notes Sawyers. Treating with multiple drugs, a strategy now used against HIV and other infectious diseases, may slow the development of resistance that occurs in single-drug therapy. Given BMS-354825's apparent potency, combination therapy might also eliminate the residual cancer cells that persist even in a person whose CML Gleevec controls, says Druker.

There's still at least one widespread Gleevec-resistant form of BCR-ABL that BMS-354825 does not inhibit. George Daley of Children's Hospital in Boston calls it the "mutant from hell." And because BMS-354825 inhibits Src as well as the rogue BCR-ABL, concerns remain about the new drug's long-term side effects. Clinical testing has already begun, and Sawyers says the results so far are "promising." —JOHN TRAVIS

INFECTIOUS DISEASES

Avian Influenza Makes a Comeback, Reviving Pandemic Worries

Most virologists believed the question wasn't whether the bird virus H5N1 would return, but when. They were right. In the past 2 weeks, China, Vietnam, and Thailand have all reported new outbreaks of the strain that scientists fear could evolve into a global catastrophe if unchecked. Meanwhile, the World Health Organization (WHO), frustrated by a lack of cooperation, stepped up pressure last week on countries to provide samples that could be used to monitor the gathering threat.

A massive epidemic of avian influenza swept through eight Asian countries early this year, killing at least 23 people and leading authorities to cull more than 100 million fowl. In May, the virus appeared to have been conquered, but given its vast geographical range and its ability to infect wild birds, "you could not expect that one [round of] stamping out and control measures would eradicate the virus completely," says Hans Wagner of the United Nations' Food and Agricultural Organization in Bangkok.

Experts worry that the H5N1 virus may evolve or recombine to produce a virus that humans can transmit easily, setting the stage

for a potential flu pandemic. Two recent papers reinforce concerns about H5N1, WHO warned last week. A study published online by the *Proceedings of the National Academy of Sciences* showed that H5N1 is widespread

in ducks in southern China and has become more lethal to mice between 1999 and 2002. And a paper in last week's issue of *Nature* showed that the virus has evolved since 1997 to spread more easily among poultry, and that wild birds may help spread it. "We are facing a very tough virus," says Yi Guan of the University of Hong Kong, a co-author of the *Nature* paper.

But studies like these have been hampered by the fact that, despite months of subtle prodding by WHO, several countries have

failed to provide all virus isolates and patient samples to the agency's reference laboratories, says WHO spokesperson Dick Thompson. Yet maintaining a close watch on the most recent isolates is "extremely important" in keeping tabs on the virus's behavior, says virologist Albert Osterhaus of Erasmus University in Rotterdam, the Netherlands.

—DENNIS NORMILE AND MARTIN ENSERINK



Contained? Thailand declared victory over H5N1 in May, but chicken deaths continued.

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Paltry Raise for NIH

A House of Representatives spending subcommittee last week approved a bill that would give the National Institutes of Health (NIH) a \$727 million increase, to \$28.5 billion, in 2005. Advocates for biomedical research were dismayed by the amount, a 2.6% hike that is comparable to the president's request but trails the annual rate of inflation for biomedical research activities.

The increase, for the fiscal year that begins 1 October, would be the smallest in 2 decades, says Oklahoma Medical Research Foundation immunologist Paul Kincade, president of the Federation of American Societies for Experimental Biology (FASEB). Kincade says he is "terrified" about the consequences for researchers, who had benefited from a doubling of NIH's budget between 1998 and 2003. "This is going to take an immediate toll on investigators," who may have to cut back on buying equipment and lab animals or giving technicians and postdocs raises, Kincade says.

FASEB and other advocacy groups are pinning their hopes on the Senate, which may not take up a comparable spending bill until September. FASEB's Howard Garrison says that Senator Arlen Specter (R-PA), who chairs the panel, is pushing for a larger increase. —JOCELYN KAISER

Clouds Darken for Rainfall Satellite

NASA's Tropical Rainfall Measuring Mission (TRMM) will be sent plummeting into the ocean next spring, if NASA Administrator Sean O'Keefe signs off on a plan soon to reach his desk. The \$600-million-plus satellite has been gathering environmental data on the tropics since it was launched in 1997 on a Japanese rocket, originally for an 18-month mission. But space agency managers say they can't afford the annual \$7 million to \$8 million needed to operate it. They also worry that it could crash into a populated area if there is insufficient fuel to guide it into a safe reentry.

NASA has held off killing TRMM because of opposition from earth scientists and its partner, Japan's space agency. But last week, Japanese officials agreed with NASA's proposal, paving the way for O'Keefe to order TRMM's execution in the near future. Meanwhile, NASA hopes this week to launch the last large component of its multibillion-dollar Earth Observing System, the Aura satellite to monitor the atmosphere. —ANDREW LAWLER