OLD DRUGS, NEW TRICKS
The US National Institutes of Health has awarded nine grants to find uses for eight drugs abandoned by pharmaceutical firms.

Drug name	Original target(s)	New target(s)
PF-03463275	Schizophrenia	Schizophrenia (new mechanism)
AZD0530 (saracatinib)	Cancer	Alzheimer's disease; lymphangioleiomyomatosis
JNJ-39393406	Schizophrenia	Smoking cessation
ZD4054 (zibotentan)	Cancer; peripheral artery hypertension	Peripheral artery disease
PF-05190457	Type II diabetes	Alcoholism
LY500307	Prostate enlargement; urinary tract symptoms	Schizophrenia
Undisclosed (made by Sanofi)	Undisclosed	Calcific aortic valve stenosis
Undisclosed (made by Sanofi)	Undisclosed	Duchenne muscular dystrophy

Source: National Institutes of Health

Saracatinib inhibits the Src family kinases (SFKs), enzymes that are commonly activated in cancer cells, and was first developed by London-based pharmaceutical company AstraZeneca. But the drug proved only marginally effective against cancer, and the company abandoned it — after spending millions of dollars to develop it through early human trials that proved that it was safe. With that work already done, Strittmatter's group will be able to move the drug quickly into testing in people with early-stage Alzheimer's disease.

The team plans to begin a 24-person safety and dosing trial in August. If the results are good, NCATS will fund the effort for two more years, during which the scientists will launch a double-blind, randomized, placebo-controlled trial with 159 participants. Over a year, the team will measure declines in glucose metabolism — a marker for progression of Alzheimer's disease — in key brain regions, hoping to find that they have slowed.

"For this to happen in years instead of decades is only possible because of this programme," says Strittmatter. The NIH worked with eight pharmaceutical companies to develop a model agreement for the firms and academic investigators; it specifies how intellectual property will be apportioned and gives the companies first right of refusal to license any discoveries.

Now NCATS must wait for results. Using saracatinib to treat Alzheimer's is "a reasonable idea", says Tony Hunter, director of the Salk Institute Cancer Center in La Jolla, California. The Yale researchers hope that the drug will slow or halt progression of the disease by blocking the activity of Fyn kinase, an SFK that has been shown to induce damage to brain synapses in mouse models of Alzheimer's (J. Chin *et al. J. Neurosci.* **24,** 4692–4697; 2004). But Hunter warns that there may be side effects. SFKs have many functions, so if high doses of saracatinib are needed to inhibit Fyn kinase action in the brain, they could do damage elsewhere.

Strittmatter says that the main side effect of concern to him is reduced white-blood-cell counts, which could increase risk of infection. However, in saracatinib cancer trials, that side effect occurred at higher doses than he intends to use.

NCATS is barred by law from funding trials beyond early phase II, so further money will have to come from another backer, such as AstraZeneca. For that, observers say, Strittmatter will need startlingly good results.

"This is going to be hard for them to do," says John LaMattina, a senior partner at PureTech Ventures, a life-sciences venture-capital company in Boston, Massachusetts, and former president of research and development at the drug-maker Pfizer in New York.

But fans of the NIH programme say that it is not reasonable to expect quick success, given the time-consuming nature of drug development. "The commitment to creative repurposing is wise and timely," says Ann Bonham, chief scientific officer at the Association of American Medical Colleges in Washington DC. "Over time, even with a relatively modest success rate, the potential benefit is worth the investments." ■

ANIMAL DISEASE

Rinderpest research restarts

As moratorium lifts, oversight is put in place to assess studies on eradicated cattle virus.

BY DECLAN BUTLER

Research is set to resume on the rinderpest virus, the cause of a deadly cattle disease that was declared eradicated in 2011 and has been off limits for study ever since. The moratorium — part of efforts to guard against accidental or intentional release of virus that could reintroduce the disease — was lifted on 10 July and replaced by a new international oversight system for such research.

In its heyday, the disease — the only one other than smallpox to be eradicated from nature — killed hundreds of millions of cattle, mainly in Europe, Asia and Africa, often leaving famine in its wake. Under the new oversight system, run by the Food and Agriculture Organization of the United Nations (FAO) in Rome and the Paris-based World Organisation for Animal Health (OIE), the risks and benefits of research proposals will be assessed by a joint advisory committee, and then the FAO and the OIE will decide on approvals. Eligible research must show potential for substantial practical or scientific benefits and be conducted under stringent biosafety and biosecurity conditions.

The first project that has garnered approval will test whether vaccines developed against a closely related virus — *peste des petits ruminants* (PPR), which causes disease in sheep and goats — might also protect cattle against rinderpest. Led by Michael Baron, a rinderpest researcher at the Pirbright Institute in Pirbright, UK, the project, if successful, would eliminate the need to retain stocks of live-attenuated rinderpest vaccine. That would contribute to the goal of reducing the number of labs worldwide holding rinderpest material, thus decreasing the risk of reintroduction.

Some 55 labs in 35 countries still hold some kind of rinderpest virus, according to a 2011 survey published in January 2013 in the journal *Emerging Infectious Diseases*: 37% of them in Asia, 29% in Africa and 26% in Europe (G. Fournié *et al. Emerging Infect. Dis.* http://doi.org/m7w; 2013). The identities of the labs remain confidential. The most dangerous stocks are of live field strains of virus, estimated to be kept in at least 16 labs in 14 countries, and samples of blood and tissues from infected herds,

NATURE.COM
For more on rinderpest, see:
go.nature.com/nait5m

kept in at least 10 labs in 10 countries. Stocks of live-attenuated vaccine, currently held in at least 53 labs in 34 countries, are deemed less problematic, although some could, in theory, revert to disease-causing forms.

The FAO and the OIE hope to eventually reduce the number of sites holding live wild viruses to a handful of officially designated labs, ideally located outside regions where accidental releases could have devastating consequences, says David Ulaeto, a virologist and member of the joint advisory committee. Conversely, the agencies plan to centralize stocks of vaccines in a few high-containment repositories in regions at highest risk of disease, so that they can be deployed within hours of any confirmed recurrence of rinderpest. No siting decisions have been made, but one might imagine a repository in Africa, one or two in Asia and one in Europe, says Juan Lubroth, the FAO's chief veterinary officer.

The process of destroying virus or shipping it to centres with high biosafety levels must be done in a way that does not risk its release, says Ulaeto. The FAO and the OIE are working on high-security protocols for shipping the virus and ways to ensure that autoclaves in labs holding it are certified to function at levels guaranteed to provide a 100% kill.

Many countries are reluctant to give up their vaccine stocks in case the disease should reappear and threaten their food supply. They worry about becoming dependent on the willingness of the international community to swiftly provide them with needed vaccines. "The challenge is political," says Bernard Vallat, director general of the OIE. He says that the FAO and the OIE are drafting agreements and international contingency plans that should help reassure countries that swift help would be forthcoming and that they would have guaranteed access to vaccine from FAO–OIE repositories.

Many countries are reluctant to give up their vaccine stocks.

Vallat notes that if Baron proves that PPR vaccines can protect cattle against rinderpest, it would provide an elegant way around such political issues: there would no longer be any need to hold onto rinderpest vaccines. Baron says that he hopes to start the vaccine-challenge trials next spring and complete them by the end of 2014.

Additional potentially promising research areas include other improved vaccines, diagnostics and perhaps disease pathology, says Lubroth. He stresses, however, that the advisory committee will not be prescriptive but open to considering any research ideas put forward by scientists. ■

RADIATION BIOLOGY

Fukushima offers real-time ecolab

But ecologists say they need more funding.

BY EWEN CALLAWAY

***Zizeeria maha* with abnormal wings.**

CHIYO NOHARA & JOJI M. OTAKI

Hours after a magnitude-9 earthquake struck off Japan's eastern coast in March 2011 and triggered the Fukushima nuclear disaster, Marta Wayne e-mailed colleagues in Japan — first to check on their safety, and later to make plans.

The 1986 meltdown of a nuclear reactor at Chernobyl in Ukraine had been a missed opportunity for researchers to gather data on the ecological effects of low-level radiation, she says. Independent scientists didn't gain access to the area for a decade. This time, "I thought immediately that it was important to seize the moment, and study and get data on what the actual outcomes of such a disaster could be", says Wayne, a population geneticist at the University of Florida, Gainesville.

Last week, Wayne and other biologists studying Fukushima and Chernobyl came together at the annual meeting of the Society for Molecular Biology and Evolution in Chicago, Illinois, to report on what they'd learned so far — and what studies they feel are needed for the future. They believe their work on the effects of low-level radiation on animals such as butterflies and sparrows is relevant to understanding the impact of low-level radiation on humans, with implications for appropriate government responses to radiation releases.

The effects of such exposure in humans are poorly understood, says David Brenner, director of the Center for Radiological Research at Columbia University in New York. In an 18 March letter to John Holdren, the US president's chief science adviser, he and his colleagues called for a comprehensive research strategy on the problem. "We're stuck in a dilemma about having to make policy decisions based on nothing more than guesses," he says.

Brenner adds that the risks — mainly of cancer — are small. A March 2013 report by the World Health Organization in Geneva, Switzerland, identified hotspots in Fukushima prefecture where it is predicted that children may experience a slightly increased overall risk of some rare cancers, such as those affecting the thyroid. But most human epidemiological studies are not big enough to pick up small increases in the prevalence of rare conditions.

➲ NATURE.COM
For more on the Fukushima disaster see:
go.nature.com/ulsz2n

Scientists such as Wayne think they can fill in some of the knowledge gaps by studying other species, if they can secure the necessary funding. That has proved enormously difficult in a world where data on the effects of radiation are the subject of heated debate in arguments over the use of nuclear energy.

What Fukushima data do exist are sporadic — and contested. One research flurry concerns butterflies. Joji Otaki, an ecologist at the University of the Ryukyus in Nishihara, Japan, has for more than a decade studied the wing-spot patterns and other traits in a Japanese species, *Zizeeria maha*. "I never dreamed of using it for a nuclear accident," says Otaki, who presented his work at the Chicago meeting. But after the Fukushima meltdown, two of his graduate students convinced him to screen for abnormalities in the butterfly as an environmental indicator of radiation's effects.

The team went to Fukushima in May 2011, two months after the earthquake, when the butterflies emerge from their chrysalises, and again in September 2011. They collected butterflies from sites ranging from 20 to 225 km from the reactor. Insects collected in May showed few problems, but their lab-reared offspring had many abnormalities, such as misshapen wings and aberrant eyespots, and many died as pupae (A. Hiyama *et al. Sci. Rep.* **2,** 570; 2012). Among the September-collected butterflies, more than half of the progeny showed such defects.

Otaki's team also exposed butterflies to radiation doses in the lab akin to those that butterflies near Fukushima might have received. The offspring developed the same problems. "You can come up with alternative explanations, but I think the hypothesis that radiation caused death and abnormalities is the most reasonable," Otaki says. ▶