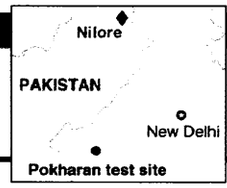
PAGE 1936
Deep-sea factory for protein precursors



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India disputes bomb analyses

BIOMEDICAL POLICY

Raising the Stakes in the Race For New Malaria Drugs

A group of scientists and funders last week gave an initial thumbs-up to a new strategy for bankrolling what could amount to a $30-million-a-year program to develop drugs against malaria, one of the world's biggest scourges. Although details are still being worked out, drug company representatives and potential donors—who gathered at a closed-door meeting on 17 September at the Rockefeller Foundation in New York City—believe they have overcome key hurdles that undermined a similar effort last November. "Real offers of genuine cash are now on the table," says initiative proponent Trevor Jones, director-general of the Association of the British Pharmaceutical Industry.

In the cross hairs. Initiative would aim to produce a new malaria drug every 5 years.

If the plan stays on track, it would amount to a welcome reversal of fortune for public health officials. They have been clamoring for years for new drugs against malaria, a disease that kills up to 2.7 million people a year, mostly in developing countries. Because the disease strikes relatively few people in rich countries, it has failed to attract much interest from Western drug companies. To tackle this problem, the World Health Organization (WHO) and other groups last fall proposed that drug companies pool resources and invest the lion's share of funds needed to launch a nonprofit that would develop new treatments. But the effort began to unravel last November, when industry leaders balked, saying the $180 million project was too costly and that some companies were already developing malaria drugs (*Science*, 5 December 1997, p. 1704).

Taking a new tack, officials at the WHO and other organizations are soliciting support from foundations and other public sources. The idea is to create "the public-sector equivalent of a venture capital fund for one product," says Tim Evans, head of the health sciences division at the Rockefeller Foundation. Acknowledging that industry isn't likely to offer substantial cash, organizers of the project—dubbed Medicines for Malaria Venture (MMV)—plan to hit up companies and government agencies for in-kind support. Such contributions could include access to chemical libraries and other "technologies that don't exist in the public sector," says Robert Ridley, a malaria researcher at Hoffmann-La Roche in Basel, Switzerland, on leave to help WHO develop the project.

Like other venture capital funds, the MMV would look to bet heavily on labs that are poised to move a tested idea closer to the marketplace. It would disburse research funds competitively, most likely to academic groups teamed up with drug companies. Evans says the grantees would develop potential drugs to the point where they are ready for phase I clinical trials or an investigational new drug application. "That's the pump that we're trying to prime," he says. After that, the drug companies would run the show. The goal will be to develop on average one new drug every 5 years. Intellectual property rights would "be worked out on a case-by-case basis," Evans says, although he anticipates that some royalties would get plowed back into the fund to help sustain it.

The organizers hope to raise $15 million a year for starters and eventually ramp up to $30 million a year within 3 to 5 years. "That's probably the kind of commitment that would be required in the private sector to develop a drug," says John La Montagne, deputy director of the National Institute of Allergy and Infectious Diseases. Last week's meeting, held to drum up support from foundations, drew an enthusiastic response, participants say. "It was a pretty positive meeting," La Montagne says. Among the possible donors are the World Bank, the Rockefeller Foundation, and the United Kingdom's Department for International Development. Although organizers decline to comment on how much money has been committed so far, Ridley says enough funding is available "to get the show on the road in the coming year."

Lending impetus to the MMV is "Roll Back Malaria," a global campaign to cut malaria deaths by 75% by the year 2015 launched in May by new WHO director Gro Harlem Brundtland (*Science*, 26 June, p. 2067). The MMV is also expected to build on the Multilateral Initiative on Malaria, an international effort to coordinate malaria research funding. The stepped-up commitments from public health agencies will only help in building a groundswell of support for MMV among foundations and other potential players in the fight against malaria, says Evans: "There's a strong sense of optimism that there is really a window of opportunity" to make headway against this disease.

–JOCELYN KAISER

MICROSCOPY

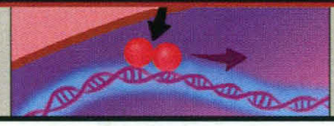
Semiconductor Beacons Light Up Cell Structures

Quantum dots are all the rage among physicists and chemists. Now these multitalented flecks of semiconductor, which can serve as components in tiny transistors and emit light in rainbow hues, look set to catch biologists' eyes as well. In this issue of *Science*, two separate teams of researchers report using quantum dots as fluorescent tags capable of tracing specific proteins within cells.

Because dots that glow in different colors should be easier to use in tandem than combinations of conventional fluorescent dyes, "there's a real application here," says Louis Brus, a chemist and quantum-dot expert at Columbia University in New York City. "It's quite likely these particles will replace conventional organic dyes" for many applications. D. Lansing Taylor, a biologist who specializes in fluorescence imaging at Carnegie Mellon University in Pittsburgh, agrees. The new particles, he says, appear to have "important advantages."

The current generation of fluorescent tags, made from small organic dye molecules, can be toxic, they burn out quickly, and

ARTHUR M SIEGELMAN/VISUALS UNLIMITED

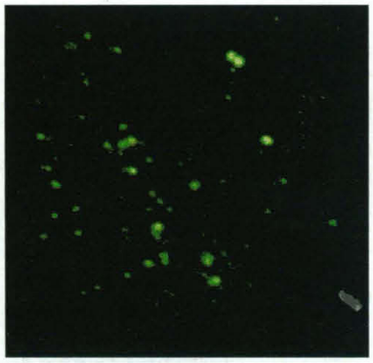


they are difficult to use in tandem, for each dye must typically be excited with photons at a different wavelength. Quantum dots are a tempting alternative. They can match dyes color for color because their electrons, like those of all semiconductors, exist at discrete energy levels, known as bands. Adding energy—say, from a photon of light—kicks an electron up from a lower "valence" band to a higher "conduction" band. When the excited electron drops back into the valence band, it can give up its excess energy as a photon with an energy equaling the gap between the bands. In quantum dots, this bandgap increases as the dots get smaller, confining the electrons into tighter spaces. Thus, smaller dots with larger bandgaps give off more energetic, or bluer, photons.

These 1- to 5-nanometer-sized particles, chemically synthesized at high temperatures, also lack many of the drawbacks of organic dyes. They are nontoxic and fluoresce up to 100 times longer. "That means that you can get better signal to noise and thus better detection," notes Taylor. And laser photons energetic enough to excite small dots can also excite fluorescence from larger dots at the same time. "They can all be excited with one laser," says A. Paul Alivisatos, a chemist at the University of California, Berkeley, who led one of the two teams. "That's important in biology," he adds, "because it allows you to do multiplexing"—watch many different colors, and therefore different biomolecules, at once.

To test this promise, Alivisatos, together with Lawrence Berkeley National Laboratory's Shimon Weiss and their colleagues, and another team led by Shuming Nie at Indiana University, Bloomington, started with what are known as core-shell quantum dots, which have an inner core made from one semiconductor surrounded by an ultrathin shell of a semiconductor with a higher bandgap. The shell, Alivisatos explains, helps confine all of the excitation energy in the dots to the core, resulting in a purer color.

After selecting their dots, both teams chemically altered their surfaces so the dots would dissolve in water, enabling them to diffuse throughout cells. The researchers then linked the light emitters to molecules that would guide them to specific cellular targets. Alivisatos and his colleagues, for example, turned to a molecule called avidin, which binds to another molecule, biotin, like a key in a lock. They linked avidin to red-light–emitting dots and, in mice fibroblast cells, used biotin to label a filament-forming protein called actin. When they added the dots to the cells, the avidin keys found their biotin locks and lit up the filaments in red. In the same experiment, described on page 2013, the group decorated green-emitting dots with negatively charged urea and acetate groups, which helped direct the dots into the cells' nuclei, turning them green.



S. NIE/INDIANA UNIVERSITY

M. BRUCHEZ JR. *ET AL.*

Technicolor. Semiconductor light emitters linked to targeting molecules highlight a cell's actin filaments (red) and nucleus (green). High magnification shows individual emitters within a cell *(top)*.

To get the quantum dots into the cells, the Berkeley group had to pretreat the cells with acetone, which eats holes in the cell membrane, killing the cells in the process. But on page 2016, Nie and his graduate student Warren Chan describe a different approach that works on live cells. They linked their dots to transferrin proteins, which help ferry compounds through a living cell's membrane.

Neither group is ready to stop there. Alivisatos says his group is developing quantum-dot probes that can light up DNA and might replace organic fluorophores in gene-sequencing machines. Nie plans to take advantage of the dots' bright fluorescence to improve the sensitivity of diagnostic tests, such as those that detect minute quantities of the AIDS virus. If either effort succeeds, biologists can expect a bright future from quantum dots. **–ROBERT F. SERVICE**

W. STONE/GAMMA LIAISON

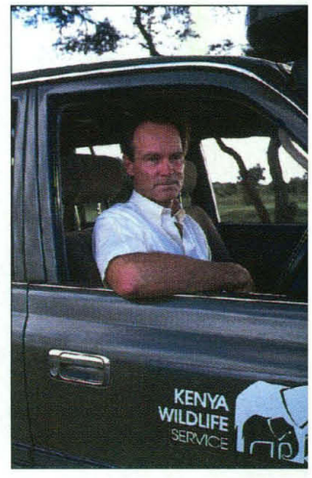
CONSERVATION

Kenya Parks Chief Ousted—Again

Kenya's fickle political winds have again blown conservation leader David Western out of office—this time permanently. Just 4 months after losing and then regaining his post as head of the Kenya Wildlife Service (KWS), which manages some of the world's best known natural areas, Western was abruptly sacked again last week by Kenyan President Daniel arap Moi.

The unexpected ouster, which came just weeks after Western had secured a $5 million grant from the Kenyan government that will allow the embattled KWS to survive a financial crisis, prompted dismay among observers in Kenya and international conservation circles. "What an end to a sad, sordid story," says David Woodruff, a University of California, San Diego, biologist who supported Western's sometimes controversial efforts to reorient the KWS (*Science*, 5 June, p. 1518). Western, however, is taking his dismissal philosophically. "Conservation is an extremely tough business—one has to accept reversals and go on," he told *Science*.

Western was appointed head of Kenya's premier conservation agency in 1994, after the resignation of Richard Leakey, a noted anthropologist who is now a leading opposition politician. Almost immediately, Western faced financial problems brought on by a decline in tourism and the end of several large grants provided by foreign donors. He also faced withering criticism from Leakey and others over his management style, his moves to cut staff, and his efforts to enlist people living on wildlife-rich lands outside the parks in conservation. The simmering controversy boiled over in May, when Moi fired Western, only to rehire him 6 days later following an international outcry from conservationists—and threats from



At ease again. Conservationist David Western.