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# How Much at Risk Are Cone Snails?

Thomas F. Duda, Jr., *et al.*

*Science* **303**, 955 (2004);
DOI: 10.1126/science.303.5660.955

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# LETTERS

## French Scientists Take a Stand

**OVER 35,000 FRENCH SCIENTISTS HAVE** signed an open letter to the French government to express strongly their concerns about current French research policies and their consequences for the future (*1*). Deep cuts in the research budget made in 2002 and 2003, followed by a major reduction in the number of staff scientists to be recruited in 2004 by national research agencies (e.g., CNRS and INSERM), offer a gloomy perspective for French science.

> **"Deep cuts in the research budget... offer a gloomy perspective for French science."**
>
> –FISCHER

French scientists are angered by the contrast between the actual facts and claims emanating from the highest ranked governmental members and President Jacques Chirac that research is a national priority. There is a general feeling that this government sees academic research, including basic science, as a costly activity of secondary importance. Although the research minister Claudie Haigneré was correct in pointing out that private industry research is weak and needs to be reinforced, she seems to hold the very naïve view that it can grow on its own without permanent nurturing from academic research. At a time when the EU research commissioner Philippe Busquin is making a plea for massive support of basic research (*2*), the French government is moving in the opposite direction!

French scientists want the government to pay the millions of euros it has owed since 2002 to national research agencies and to reestablish the recruitment of young scientists to agencies and universities. However, this movement is not just another simplistic request for more money. Rather, the signatories of the letter strongly advocate a thorough appraisal of research politics in France. They are asking for an in-depth review process, through a national debate. A model for this was the "colloque de Caen," organized in 1956 by the former prime minister Pierre Mendes France, which led to a revival of French research under De Gaulle. This historical comparison is pertinent given the growing gap between France's research effort (with the exception of nuclear physics and aerospace) and those of many other countries where R&D is strong.

The French scientific community wants to see a reform of the complex and rigid organization of the research system. Among the important topics to be addressed are how to make science careers attractive, the role of universities vis à vis research agencies, the formation of post-doctoral training organizations, and how academic research can influence private research. They want an action plan demonstrating that science is indeed a national priority, because strong science is a sign of a strong country and is vital to long-term economic interests. Many French scientists are committed to working hard for these goals, and they are pressing for urgent action by the government.

If these demands are not met by 9 March, the members of the "Save Research Movement" are determined to resign their administrative responsibilities to make clear that they will not comply with a program that dismantles research.

**ALAIN FISCHER**

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1. An English translation of the letter is available at www.sciencemag.org/cgi/content/full/303/5660/954b/DC1.
2. See http://europa.eu.int/comm/research/press.cfm.

## Thailand's Prime-Boost HIV Vaccine Phase III

**THE THAILAND MINISTRY OF PUBLIC HEALTH** will pursue the Prime-Boost HIV Vaccine Phase III Trial in Chon Buri and Rayong provinces, as planned. The Ministry and collaborating institutions remain confident in the scientific merit of the prime-boost vaccination concept and the combined immune response induced by ALVAC-HIV vCP1521 and AIDSVAX B/E, as demonstrated in Phase I and II safety and immunogenicity studies conducted in Thailand.

The Ministry is aware of the comments made by 22 scientists in a recent Policy Forum in *Science* (D. R. Burton *et al.*, 16 Jan., p. 316; see also the related Policy Forum on p. 961). Although we welcome constructive input, we find the underlying premise of the Policy Forum flawed in that it uses data from efficacy trials of a single vaccine concept to predict the results of a prime-boost combination vaccine study. Only by conducting the trial will we be able to determine if the combination of two candidate vaccines will induce both cellular and humoral immunity and protect against HIV infection.

Both the Screening Protocol and Vaccine Protocol of the Prime-Boost Study were reviewed and endorsed by Institutional Review Boards and Expert Committees in Thailand and the United States, and by the World Health Organization (WHO)/UN AIDS Programme (UNAIDS). Thailand's leading researchers, all of whom have international standing and extensive experience in AIDS vaccine studies, from the Faculty of Tropical Medicine, Mahidol University; the Armed Forces Research Institute of Medical Sciences, Medical Corps, Royal Thai Army; and the Thai AIDS Vaccine Evaluation Group, are involved in the conduct of this trial under the Ministry of Public Health.

The Prime-Boost Study was carefully considered within multiple venues, including a special WHO/UNAIDS/Centers for Disease Control consultation on the impact of the lack of efficacy of the AIDSVAX trials in North America and Thailand, which concluded that "because of its independent scientific rationale," it was appropriate to go forward with efficacy evaluation of the prime-boost combination.

There is no such thing as wasting time or money in researching an AIDS vaccine. Regardless of the efficacy results, Thailand is benefiting from conducting this trial in several areas: Experience will be gained by its scientists and health workers, and its laboratory infrastructure and specimen archiving will be strengthened. Close collaboration has also been established with NGOs and community groups to plan and implement community engagement activities. Another important gain is the intensified HIV/AIDS awareness campaign around the trial, which directly benefits the local communities in Chon Buri and Rayong.

Thailand intends to share knowledge and experience gained and lessons learned in conducting this large-scale community-based efficacy trial. Needless to say, if the vaccine is proven efficacious, other countries will benefit as well.

### Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted by e-mail (science_letters@aaas.org), the Web (www.letter2science.org), or regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

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The Ministry of Public Health will continue to strive to find the best preventive measure to stop the spread of HIV. It is the Ministry's responsibility to further reduce the yearly HIV infection rate in Thailand, which is currently 25,000.

CHARAL TRINVUTHIPONG
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## How Much at Risk Are Cone Snails?

IN THEIR LETTER, "THE THREAT TO CONE snails" (17 Oct., p. 391), E. Chivian *et al.* estimate that "hundreds of thousands" of cone snails are sacrificed annually for research purposes. We recognize that habitat loss and possible overexploitation of cone snails may indeed threaten the survival of *Conus* taxa, but we question Chivian *et al.*'s estimate. This number is huge and shocking in light of the low numbers of individual snails that we as members of the *Conus* and conotoxin research community typically utilize yearly. The techniques we apply require only small amounts of venom, tissue, or mRNA to identify and characterize conotoxin peptides and their gene sequences, and conotoxins are commonly synthesized for analyses of function. For example, Duda and Palumbi (*1*, *2*) sacrificed six specimens to identify 13 unique conotoxins from three *Conus* species, Sandall *et al.* (*3*) used less than 20 specimens to describe a conotoxin from *Conus victoriae* that shows tremendous promise in alleviating pain, and Raybaudi Massilia and colleagues (*4*, *5*) used less than 15 specimens to identify and characterize an unique bioactive conopeptide from *Conus ventricosus*. Moreover, we commonly milk venom from cone snails without sacrificing them (*6*).

Examination of the past 5 years of publications on *Conus* and conotoxins reveals that, at most, 20 research groups or individual researchers actively acquire cone snails from the field for conotoxin or other analyses. Each group would have to process 10,000 animals every year to be responsible for 200,000 *Conus* sacrificed yearly for research purposes, as estimated by Chivian *et al.* (under the assumption that "hundreds of thousands" represents at least 200,000). Based on experience in collecting *Conus* and studies of their maximum densities (*7*, *8*), sample sizes this large would require intensive search effort over large areas and considerable time in the field or teams of collectors. From actual numbers of animals we use and estimates for other research groups, we calculate that on average no more than 5000 animals per year, a number nearly two orders of magnitude less than that of Chivian *et al.*, are likely sacrificed collectively by *Conus* researchers.

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IN THEIR LETTER, "THE THREAT TO CONE snails" (17 Oct., p. 391), one of E. Chivian *et al.*'s recommendations for conserving cone snails is that companies "finance development of culturing techniques…", although they do not state if they are advocating culturing of *Conus* snails or of venom ducts. If the former, they would be well advised to read the pioneering studies of Frank Perron (*1*, *2*), who to date has been the only individual brave enough to try to culture Conidae under laboratory conditions. The multiyear life-span and the complex development of these organisms render this a major challenge for any marine mollusc, and the costs involved have been economically justified only for bivalve species cultured on mass scale for mariculture. Tissue or cell culture from *Conus* venom ducts is likely to be an equally difficult challenge, given the fact that to date, there is only one single molluscan cell line listed in the ATCC catalog, and that is from a freshwater



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species. The most effective method of conserving the 50,000 or so naturally occurring *Conus* toxins for future generations would be to set up a cDNA and protein extracts bank from 20 or so specimens per species. This is sufficient biological material to identify all toxins in a given venom by EST sequencing (*3*), and this could be followed up by identifying the posttranslational modifications on these toxins by high-resolution mass spectrometry (*4*). The principal threat to wild *Conus* populations, as well as other marine fauna, is most likely habitat loss and destruction. Unfortunately, a CITES listing is woefully inadequate to counteract such a threat.

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## Response

**WE ARE RELIEVED TO HEAR FROM DUDA *ET AL.*** that they believe the extent of cone snail harvesting for research to be far less than we estimated, and we welcome Fainzilber's suggestions for reducing demand for wild-caught animals. Our figure was based on communication with a prominent cone snail researcher at a major university in the United States who had direct knowledge of at least one lab having acquired 1 kg of snail venom ducts, which we calculated would require the sacrifice of some 10,000 snails. We extrapolated from this figure to arrive at our estimated annual harvesting rate for research purposes. Although we acknowledge the anecdotal nature of this estimate, the availability of such a large number of ducts suggests that a well-organized harvesting apparatus is in place, given the difficulties of collecting so many snails, as Duda *et al.* rightly point out. Furthermore, this makes us suspect that this lab is not alone in making use of such services.

It seems clear that no one accurately knows the extent of cone snail harvesting, either for biomedical research or the ornamental shell trade. The latter undoubtedly is many times greater than the research take. There are thousands of known outlets for cone snail shells worldwide, and we estimate, conservatively, that millions of shells are traded annually. Increases in human population and in people's disposable income, combined with a greater globalization of trade, suggest that such exploitation may intensify over time, unless controls, like a CITES listing for cone snails, are enacted. We recognize the present limitations of CITES, which is why we recommend expanding its purview to all wild-caught species, thus moving it from a reactive to a more proactive management mechanism. Listing cone snails would require countries involved in their trade to develop management plans for their sustainable exploitation.

Finally, we agree that protecting the coral reef habitats of these remarkable creatures, in decline partly due to global warming (*1*), is an urgent priority.

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## TECHNICAL COMMENT ABSTRACTS

### COMMENT ON "Parasite Selection for Immunogenetic Optimality"

Philip W. Hedrick

Wegner *et al.* (Brevia, 5 Sep. 2003, p. 1343) reported that for an MHC gene, three-spined sticklebacks with an intermediate number of alleles appear to have the lowest parasite load. Using a population genetics model, I show that intermediate optimum selection does not generate the observed variation in gene numbers unless an unrealistically high mutation rate is assumed.

Full text at www.sciencemag.org/cgi/content/full/303/5660/957a

### RESPONSE TO COMMENT ON "Parasite Selection for Immunogenetic Optimality"

K. Mathias Wegner, Martin Kalbe, Joachim Kurtz, Thorsten B.H. Reusch, Manfred Milinski

Hedrick's model contains some unrealistic implicit assumptions. We argue that variance around the optimal number of MHC alleles is a consequence of the allelic polymorphism of MHC genes. When balancing selection exerted by co-evolving parasites maintains this polymorphism, processes other than mutation—such as linkage and recombination—will inevitably generate the observed variance in allele numbers.

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