Nobel hopes are clarified. The existing smallpox vaccine is defended. And the significance of a study of behaviors measured across three laboratories using the same mouse strains is discussed: "We should...use these results to highlight that scientific progress is a changing mosaic of overlapping studies that correct, build, and expand on earlier findings," say one set of letter writers.

Brazilian Nobel Hopes

The article "Brazil lobbies for first Nobel" by Cassio Leite Vieira (News Focus, 27 Aug., p. 1346) is most timely. Yet small clarifications are in order: (i) It is implied that the candidacy has attracted extensive media attention because of my efforts, when many other people are working hard to promote chemist Otto Gottlieb's research. Some very fine science journalists deserve credit for drawing the media's attention to highly complex topics and stressing their implications for sustainable development of Brazilian biodiversity. (ii) There is no lobby, only a sincere attempt to overcome two enormous handicaps: the interdisciplinary nature of the work and the language in which some important aspects were reported (had the underlying principles been closer to biochemistry than to botany or a larger part of the results communicated in English instead of Portuguese, these efforts would probably not be necessary).

Peter Rudolf Seidl
Federal University of Rio de Janeiro, Rio de Janeiro, Brazil

Smallpox Vaccine

I find Donna E. Shalala's justification for retaining, and experimenting with, viable variola (smallpox) virus (Editorial, *Science*'s Compass, 13 Aug., p. 1011) misleading. The existing vaccine is entirely satisfactory and was the basis of the successful World Health Organization eradication campaign. Its present short supply could easily be remedied by manufacturing more. The small number of immunocompromised individuals, and, more important, pregnant women, for whom it is contraindicated could be protected by vaccination of contacts and herd immunity.

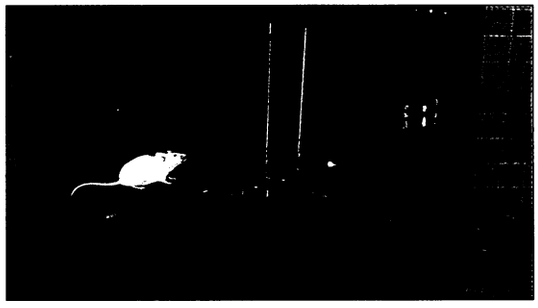
New vaccines cannot be licensed because their efficacy cannot be proved in the absence of humans exposed to smallpox. If smallpox reappeared, it would be unethical to offer an experimental vaccine in place of the traditional vaccine, known to be effective.

Manipulation of viable variola will always involve a risk of escape; containment systems can fail, most likely by human error. If such experiments are done, it is essential that all involved be currently vaccinated, as has been standard practice.

Jonathan Katz
Washington University, St. Louis, MO 63130, USA. E-mail: katz@wuphys.wustl.edu

Testing the Genetics of Behavior in Mice

The important study by J. C. Crabbe *et al.* of behaviors measured across three laboratories using the same mouse strains (Reports, 4 June, p. 1670) demonstrates clearly what is widely known in the neuroscience field: behavior is a complex phenomenon that is strongly affected by both genetics and environment. News reports about this study have glossed over the rather striking finding that the majority of behavioral measures were consistent between laboratories. Indeed, the data largely confirm many strain-dependent differences reported in the literature. Although the study demonstrates that differences in investigators and unforeseen environmental factors from laboratory to laboratory can alter behavioral results, these phenomena are not limited to studies in behavioral neuroscience, or even to the biological sciences for that matter. Far from precluding scientific advances, interlab variability generates controversies that stimulate further investigation, resulting in methodological improvement over time. No single, exciting finding, whether at the behavioral, physiological, or molecular level, can stand on its own.



Results in this elevated plus maze varied from lab to lab.

CREDIT: BRUCE DUDEK/SUNY

The interlab differences reported by Crabbe *et al.* illustrate that techniques for behavioral analysis are still evolving. It is imperative that strong communication exist between researchers in many disciplines so that advances in unraveling the complexities of behavior can be rapidly incorporated into experiments using newly engineered mice. An important message conveyed by this study is that several different approaches should be used, either within or between laboratories, before a definitive interpretation of a behavioral change is made. We should not conclude from this study that behavioral analysis is beyond rigorous scientific investigation or that genetic engineering will not help elucidate the molecular basis of complex behaviors. We should instead use these results to highlight that scientific progress is a changing mosaic of overlapping studies that correct, build, and expand on earlier findings.

Marina R. Picciotto
Departments of Psychiatry and Pharmacology, Yale University School of Medicine, New Haven, CT 06508, USA. E-mail: marina.picclotto@yale.edu
David W. Self
Department of Psychiatry, Yale University School of Medicine. E-mail: david.self@yale.edu

The laudable attempt of Crabbe *et al.* to standardize behavioral testing conditions for studies of genetic determinants of behavior has significant ramifications. One issue not completely addressed in their discussion is the use of group housing. There can be significant individual differences in behaviors of group-housed rodents, depending on their social rank within the colony. Rank-related differences in behaviors are expressed in such paradigms as the open field, and these behaviors also differ when one compares rats from aggressive and nonaggressive groups. Second, it is likely that there were differences in the handling of mice by the experimenters and also in maintenance-related conditions in the vivariums. Although acclimatization of rodents to repeated human handling is important, it is difficult to control for idiosyncratic differences in picking up and in handling rodents during behavioral testing. Moreover, the care and behavior of personnel involved in the maintenance of the animal room is also important. We have noted significant behavioral differences in the behavior of rats associated with certain cleaning activities carried out by the caretakers. Also, for health or other personal reasons, caretakers are substituted from time to time, which can introduce further unexpected, and most likely unknown, variability in the behavioral response of experimental ani-