

teacher training; interactive, hands-on tools to enhance the knowledge value of exhibit components; and family-oriented learning experiences. Thus these museums play a key role in promoting scientific literacy, including exposure to the scientific process, for the young.

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### Confidentiality

There is a pending proposal pertinent to the unresolved confidentiality of submissions to peer-reviewed journals ("Suit alleges misuse of peer review," E. Marshall, *News & Comment*, 22 Dec., p. 1912). The definition of "research misconduct" recently recommended by the Commission on Research Integrity includes the intentional or reckless "use of any information in breach of any duty of confidentiality associated with the review of any manuscript or grant application." The word "any" leaves open whether a duty obtains.

The situation presents the following anomalies.

1) Authors make submissions voluntarily, and usually without entering into agreements about confidentiality with editors. (They sometimes even assign copyright shortly after submission.) When X voluntarily provides a document to Y, we expect confidentiality from Y only to the extent that X and Y have so agreed before Y's receipt. To what confidentiality treatment are journals willing to agree?

2) The nub of confidentiality is that a recipient not divulge the information. But journals are allowed to disclose submissions to referees as they choose.

3) Whether a duty of confidentiality is undertaken by a referee is merely contingent. It often rests on no more than an editor's transmittal letter, to which a referee usually does not expressly assent. Nor are such letters uniform.

4) A referee does not, and in virtue of anonymity, cannot, become bound to the author, the person whose ideas any duty protects.

Bentley Glass once observed that, to avoid using information in breach of its confidentiality, a referee or study section member would have to attempt noble self-deception, purporting to forget all, which is

nearly impossible. Hence he proposed that study sections consist only of senior scientists no longer doing research in the pertinent field. All this confirms the truism that science depends on the trustworthiness of colleagues. Still it remains essential to clarify the duty of confidentiality if breach thereof is to be misconduct. One sensible convention would stipulate that (i) there is a duty not to effect or allow the appropriation of the contents of a submission; and (ii) a journal is answerable for the conduct of its anonymous referees unless it chooses, in the event of a dispute, to present to the author the explicit agreement of each referee to abide by (i). Such convention would induce journals to reach such agreements with referees.

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### Attenuated HIV Vaccine: Caveats

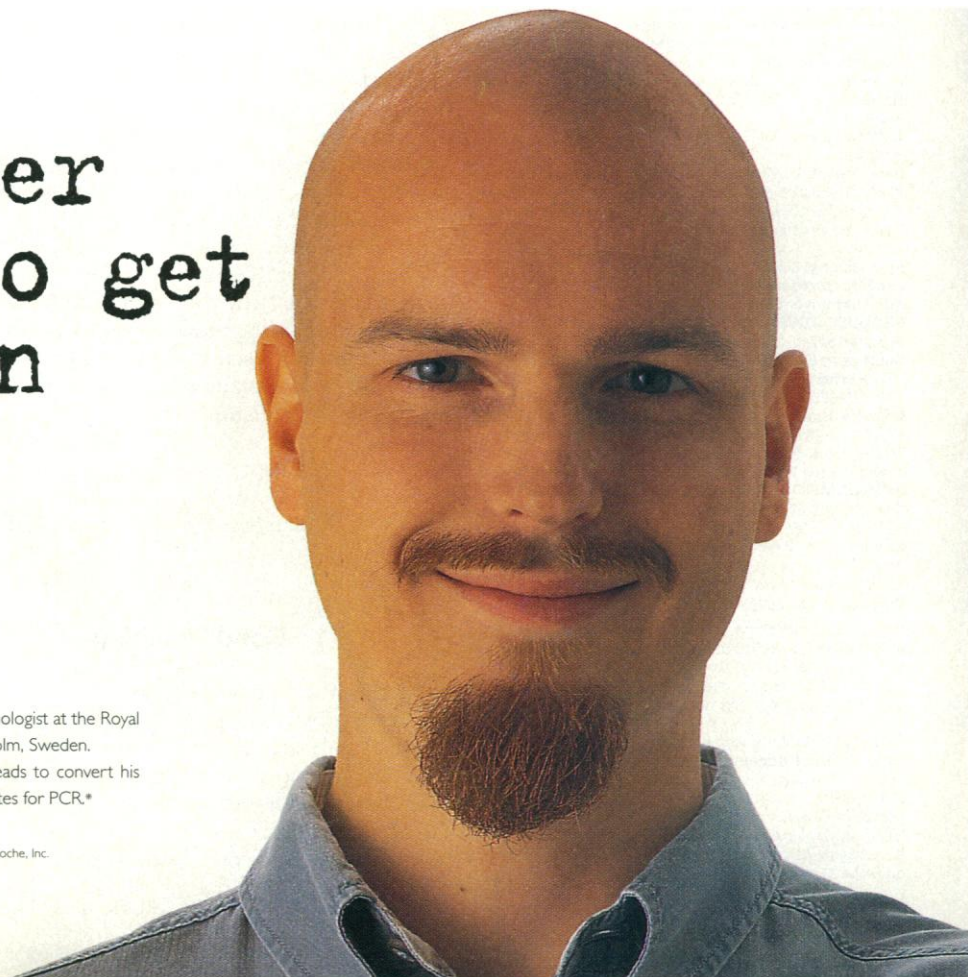
Candidate human anti-AIDS vaccines should be safe and effective. In their report "Genomic structure of an attenuated quasi

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Patrik Samuelson is a molecular biologist at the Royal Institute of Technology in Stockholm, Sweden.

Patrik uses Ready-To-Go beads to convert his RNA samples into cDNA templates for PCR.\*

\* PCR is a patented process of Hoffmann-La Roche, Inc.



species of HIV-1 from a blood transfusion donor and recipients" (10 Nov., p. 988), N. J. Deacon *et al.* state (p. 991)

The strain of [human immunodeficiency virus-type 1] HIV-1 that infected the eight members of the Sydney Bloodbank cohort has not caused disease, even in the members affected by the immunosuppressive effects of age, drug therapy, and [systemic lupus erythematosus] SLE. This attenuated strain of HIV-1, therefore, could perhaps be the basis for a live attenuated vaccine.

We would like to state two caveats about this proposal.

The death of the HIV-infected patient C83, who died with *Pneumocystis carinii* pneumonia (1), is attributed to her underlying autoimmune disease, SLE, which required immunosuppressive therapy. However, neither CD4<sup>+</sup> T cell counts nor data on viral load are provided in the report. Deacon *et al.* mention that DNA extracted from the only blood sample of patient C83 available did not yield HIV *nef* gene sequences, even though single copy cellular genes could be amplified. The sensitivity of the polymerase chain reaction (PCR) assays is not given in the report. As patient C83 died with an opportunistic infection, readers need to see all CD4<sup>+</sup> T cell counts available, more information regarding the in-

tactness of this DNA sample, and the time of its collection during the patient's illness. Thus, the data presented by Deacon *et al.* for patient C83 are inconclusive and do not exclude the possibility that *nef*-deleted HIV contributed significantly to her death.

The pathogenicity observed in infant macaques infected with SIVΔ3, a mutant of the simian immunodeficiency virus (SIV) containing large deletions in the *nef* and *vpr* genes and in the negative regulatory element of the long terminal repeat (2), is not discussed by Deacon *et al.* Two of the original four SIVΔ3-infected macaque infants have died of AIDS, and the survivors now have high viral loads.

Although we have concerns regarding the safety and efficacy of the proposed use of *nef*-deleted viruses as anti-AIDS vaccines, *nef*-deleted, live attenuated viruses still could play a major role in determining the correlates of immune protection in animal models, which could contribute to the design of safer, more effective vaccines.

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## References

1. J. Learmont *et al.*, *Lancet* **340**, 863 (1992).
2. T. W. Baba *et al.*, *Science* **267**, 1820 (1995); T. W. Baba *et al.*, *ibid.* **270**, 1220 (1995).

**Response:** Ruprecht and her collaborators state two caveats regarding our recent report. Our response follows.

Patient C83 died with SLE only 4.25 years after infection and 8 days after HIV seropositivity was reported to the New South Wales Red Cross Bloodbank. This was 2 years before the initial discovery of the first two long-term "nonprogressors" was made and before our undertaking any laboratory studies. A single lymphocyte subset analysis was performed shortly before death at a time when she had active SLE nephritis and was being treated with large doses of glucocorticoids, azathioprine, and cyclophosphamide. She had a CD4<sup>+</sup> lymphocyte count of 91 per microliter (CD4:CD8 = 0.15) (1). This would be compatible with either advanced HIV-1 infection, severe immunosuppression resulting from drug therapy, or the patient's underlying disease.

The information on viral load was based on a small sample of DNA extracted from unfractionated peripheral blood mononuclear cells (PBMCs) obtained 2

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years before the patient's death (with an unknown CD4<sup>+</sup> cell count). The sensitivity of the *nef*-LTR region PCR method was determined to be 1 to 10 copies of HIV-1 DNA per 10<sup>5</sup> CD4<sup>+</sup> T cells (with the use of a dilution series of 8E5 cells) (2). That we could not amplify HIV DNA from this PBMC DNA sample, therefore, suggests that the patient's viral load was very low; the data on successful amplification of a single-copy gene were provided to show that the DNA sample had not been degraded. We agree that while the possibility that patient C83 died of progressive HIV infection cannot be completely excluded, we believe it is highly unlikely.

We agree that Ruprecht's data on infection of infant macaques with multiply deleted SIV raises concerns about the use of similar strains of HIV as vaccines in human infants. However, these data apply to SIV with a different constellation of genomic defects than the HIV strain described in our report; the effect of the latter mutations on pathogenicity of SIV for infant macaques is unknown. Further studies of the transmission of different doses of *nef*-defective SIV from mother to offspring are required. In addition, infants are not the most logical target population for an HIV vaccine.

We share the concern of Ruprecht and her colleagues about the safety and efficacy of live attenuated HIV-1 vaccines, and we thank them for raising some important issues in this regard. However, we stand behind our original contention that "This attenuated strain of HIV-1 ... could perhaps be the basis for a live attenuated vaccine." All live attenuated vaccines currently licensed are pathogenic in at least some immunocompromised individuals; that has not precluded their widespread use, nor has it vitiated their efficacy.

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## References

1. R. Garsia, personal communication.
2. A. Solomon and N. J. Deacon, unpublished data.

## Structural Change Mechanisms in Regulatory Proteins

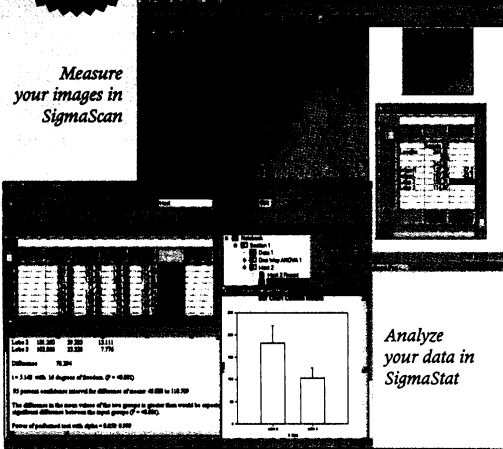
The Research News article "Flexing muscle with just one amino acid" (R. F. Service, 5 Jan., p. 31) describes recent work by Sykes and colleagues and correctly emphasizes the fundamental importance of discovering that a single amino acid plays a key role in controlling structural changes in calcium (Ca)-binding regulatory proteins like troponin-C. Earlier observations indicate that single amino acid residues can control large shape changes in troponin-C and calmodulin. These two Ca-binding proteins have similar molecular architectures but different functional properties. Yet a combination of mutational and simulation studies have shown that replacement of one amino acid, the arginine in position 11 (Arg 11) of skeletal troponin-C by alanine, conferred calmodulin-like functional and dynamic behavior on the mutant (1). The analysis from molecular dynamics simula-



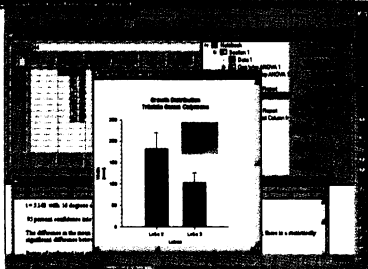
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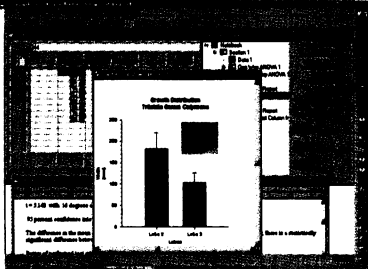
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