

In spite of these influences, the MBRS and MARC programs are clearly having a positive impact on the production of Ph.D. minority research scientists.

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Notes

1. Data from the Office of Program Analysis, National Institute of General Medical Sciences, and the National Academy of Sciences, Doctoral Records File.
2. Officials at the National Institute of General Medical Sciences indicate that because social security number data matched to the National Academy of Sciences doctoral record file is incomplete for early participants in the programs, this fraction is an underestimate.

I congratulate *Science* for its 1992 and 1993 issues on Minorities in Science, as I believe that this is the most challenging and important issue facing the biomedical community, now and in the future. The issues addressed, the individuals featured, and the general commentary on this problem were commendably appropriate.

I would like, however, to emphasize the lack of priority of these issues at some of our major institutions (often research universities), most often demonstrated by the lack of recognition of faculty (both tenured and nontenured) who are committed, devoted, and dedicated to these efforts. Although the efforts are not made for recognition, very often they act as an impediment to an individual's career, thereby serving as a disincentive. Most certainly under these conditions, the problem will not be solved, let alone even addressed.

The disappointing aspect of this is two-fold. First it is a fairly well-recognized occurrence and therefore represents an issue that should be addressed. Second, it could be addressed in a straightforward manner if the traditional, change-resistant system in place at our institutions of higher learning were willing to make a change. The system needs to recognize that this is important for our faculty to do, especially when there are those who choose to make the major and important commitment that it takes to address this issue. As such, the presidents (who set the universities' mandates) and the provosts or vice presidents (in charge of academic affairs) must make the academic community, particularly the deans, chairs, and faculty, aware of the importance of this issue by assurances that these efforts will indeed "count" in promotions and other forms of advancement and recognition within the academic system.

LETTERS

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Daniel E. Koshland Jr.'s editorial "Minorities in science" (12 Nov., p. 971) makes two major suggestions: (i) that only a goal of a color-blind recruitment policy for science is ultimately morally justifiable and (ii) that the scientific community will benefit from increased minority representation primarily through an extension of the talent pool.

There is more to be said about the true activity and nature of the scientific community. Science is about vision and direction as much as it is about talent. Individuals who belong to cultural minorities possess slightly different concepts of the world, and these different concepts bring a valuable diversity into the vision of the scientific community.

We must integrate the potential critiques and novel perspectives of those individuals who are members of "marginalized voices" in American society: African Americans, feminists, homosexuals, and others. A diversity of cultural identities in science is invaluable in producing innovative and reliable knowledge.

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Triple Repeat DNA as a Highly Mutable Regulatory Mechanism

In a recent Perspective, "Molecular genetics of neurological diseases" (29 Oct., p. 674), J. B. Martin discusses several human diseases that develop when certain variable-length, repeated trinucleotide DNA sequences exceed their normal range, noting that disease severity and age of onset are correlated with the length of the triple repeat. In effect, the repeat length seems to regulate the expression of a disease state. Possibly this variation in repeat length has no effect unless a critical threshold is exceeded, with disease as its only consequence. But variation *within* the normal range might also be meaningful. What if the length of a triple repeat were correlated with the penetrance of some normal phenotypic trait? Could these diseases be revealing, in deleteriously exaggerated form, the expression of an unsuspected but normally advantageous regulatory mechanism?

If triple repeat length were to regulate the quantitative expression of an associated gene, then spontaneous changes in sequence length (by whatever process this



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¹ *Anal. Biochem.* 179: 37-49

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might occur) would provide generation-by-generation variability in phenotype. The resulting phenotypic variation would be similar to that caused by recombination among multiple loci with many alleles, but would have a more efficient molecular basis. One stable allele associated with a spontaneously variable regulator would enable offspring to display a range of phenotypic values around a parental mean.

Significantly, such a mechanism for spontaneous, site-specific mutagenesis of a regulatory sequence would enable even a small population to extend its range of phenotypic variation, for the affected trait, within a few generations. Natural selection could establish and maintain an optimal trait distribution in a shifting environment, with no delay for the mutation of Mendelian genes or for the elimination of less fit alleles. Yet maladaptive extremes of gene expression would be unlikely to arise except from parents who were themselves far from the population mean, so genetic load would be minimal (unless, of course, the mechanism slipped out of control or exceeded some threshold, as it may have in cases of human neurological disease).

From an evolutionary perspective, non-

standard mutational mechanisms that affect specific loci can offer substantial advantages (1). The triple repeats that are widespread among animal genomes might represent one such mechanism. Testing the hypothesis that variable repeat length may regulate quantitative gene expression will be challenging precisely because such sequences are not stable from one generation to the next. But understanding a mechanism that could generate copious but normally benign mutation might be worth the effort. After all, it's been more than a century since Darwin promised that "a grand and almost untrodden field of inquiry will be opened, on the causes and laws of variation" (2).

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References

1. P. Rainey and R. Moxon, *Science* 260, 1958 (1993); R. E. Lenski and J. E. Mittler, *ibid.*, p. 1959.
2. C. Darwin, *On the Origin of Species* (Harvard Univ. Press, Cambridge, MA, 1964), p. 486.

Genetics and Violent Crime

Peter R. Breggin writes (Letters, 3 Dec., p. 1498) that there are no known biological or genetic factors that contribute to violent crime. Yet it is well known, even by most psychiatrists, that individuals with Y chromosomes commit the overwhelming preponderance of violent crimes.

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Corrections and Clarifications

In the report "DNA sequence determination by hybridization: A strategy for efficient large-scale sequencing" by R. Drmanac *et al.* (11 June, p. 1649), the sequence of clone 8 in figure 2B (p. 1650) was inadvertently shortened by the deletion of "GA" at the seventh position from the right in the second line. In reference 20 of the same report, the probes ATATGGGG and ATGTCCTG should not have been included.

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