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A Historical View of Nonsense Triplets

MEMOIRS ARE A TRICKY LITERARY GENRE, EVEN for towering figures such as Sydney Brenner (*1*) ("A scientific kokopelli," B. Edgar, Books *et al.*, 7 Dec., p. 2103). His accomplishments are so extensive that a small correction of the record on nonsense triplets and their suppressor genes might be excused as a concession to the historical accuracy and completeness that Sydney espouses. He summarizes the entire history of nonsense triplets as follows: "And so putting all this together I worked out that the most likely sequence for the three nonsense codons was UAG, UAA and UGA." And later, "I've had many different kinds of achievement... And the two things here are the triplet nature of the genetic code and the decoding of suppression triplets." In this case, Sydney has swept too much under the carpet with his "Occam's broom."

In our rash youth, Sydney and I competed in a dash to identify nonsense triplets that acted as translation-terminating signals in the genetic code and the suppressor genes that enabled nonsense triplets to become sense triplets (*2*). The existence of nonsense triplets was first deduced in 1962 from the experiments of Benzer and Champe on the rII genes of coliphage T4 (*3*) and the experiments of Obaid Siddiqi and myself on the alkaline phosphatase gene of *Escherichia coli* (*4*). Direct evidence that nonsense triplets generated truncated protein fragments was first reported by Sydney's laboratory for coliphage T4 (*5*) and later for coliphage f2 (*6*), beta-galactosidase (*7*), and alkaline phosphatase (*8*). To identify the three nonsense triplets indicated by the patterns of nonsense suppression (*9*), Sydney's laboratory and mine chose different approaches, which had to be indirect because DNA sequencing methods were still in the future. Sydney and his colleagues chose to analyze specific base changes in T4 DNA generated by chemical mutagenesis, while Martin Weigert and I chose to analyze amino acid changes in revertants of alkaline phosphatase nonsense mutants and to deduce the nonsense triplet from the sequence relationships of the revertant codons. The first nonsense triplet identified was UAG (*10*, *11*). The remaining nonsense triplets, UAA and UGA, were identified by Sydney's laboratory (*11*, *12*) and mine (*9*, *13*), using our respective approaches.

The next goal was to identify suppressor genes for nonsense triplets. Active suppressor genes, called Su+, enable a cell to translate a nonsense triplet and thereby reverse the premature termination effect of the triplet on translation (*3–5*). Sydney's laboratory and mine identified and mapped several suppressor genes for the nonsense triplets (*14–17*). The search for the amino acids incorporated into the nonsense sites of a protein by the Su+ genes occupied several years, culminating in the identification of the amino acids associated with all of the known Su+ genes for the three nonsense triplets (*17–27*).

For those who wish to delve further into this chapter of early molecular genetics, my review, written while memories were fresh (*2*), might serve as a counterbalance to Sydney's remembrances of things long past. His memoir remains a fitting tribute to a remarkable protean scientist and colleague.

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Wetware Problem, Not a Software Problem

THE TITLE OF THE ARTICLE "SOFTWARE GLITCH threw off mortality estimates" (News of the Week, J. Kaiser, 14 June, p. 1945) is misleading. There was no software glitch involved—the tool worked exactly as specified. The scientists overestimated the risks of fine particles in the air because they specified incorrect parameters for the algorithm. That the scientists misused their tool is not the fault of the tool. This is a blunder on the part of the scientists, not the software.

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CORRECTIONS AND CLARIFICATIONS

NEWS FOCUS: "The battery: not yet a terminal case" by J. Alper (17 May, p. 1224). The name of one of Quallion's collaborators in developing a new solid polymer electrolyte battery was omitted from this article. Argonne National Laboratory is also taking part in the research.

NEWS OF THE WEEK: "U.S. science academy elects new members" (10 May, p. 1001). In the list of new foreign members elected to the U.S. National Academy of Sciences, countries printed in parenthesis indicate the nationality of each newly elected member, not the country in which the individual's current institution is located.

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.