Letters

Nucleotide Sequence of a Gene: First Complete Specification

Readers of *Science* should have their attention called to the fact that the marvelous achievement of Holley *et al.* (*1*) in determining the complete nucleotide sequence of an alanine transfer RNA isolated from yeast probably reveals for the first time the complete primary structure of a gene, an implication which is doubtless taken for granted by many who are familiar with the field, but which may not be immediately evident to others. Previous work (*2*) has shown that s-RNA molecules have base sequences complementary to those of DNA of the same organism. This is virtually equivalent to saying that cistrons or genes make s-RNA, and that the base sequence in one strand (*3*) of the genic DNA is complementary to the base sequence in its s-RNA product. Current knowledge (*4*) further indicates that the methylated bases in s-RNA acquire their modifications after transcription from their DNA gene. It is assumed that other modified bases in s-RNA are also modified after transcription. Hence, we may write out in full from Holley *et al.*'s base sequence of their alanine RNA the base sequence of the yeast cistron or gene that produced it, as in Fig. 1.

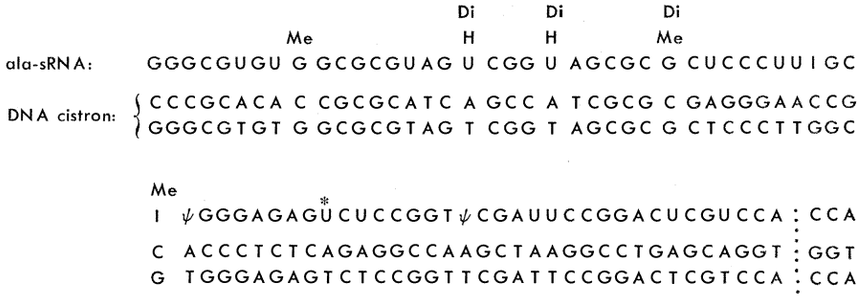

Fig. 1. Primary structure of an alanine transfer RNA (from Holley *et al.*) and of the gene from which it was obtained. Symbols in ala-sRNA represent the 3′-phosphates of: G, guanosine; C, cytidine; U, uridine; MeG, 1-methylguanosine; A, adenosine; DiHU, 5,6-dihydrouridine; DiMeG, N^2-dimethylguanosine; I, inosine; MeI, 1-methylinosin; ψ, pseudouridine; T, ribothymidine. U* is a mixture of U and DiHU. The A, C, G, and T in the DNA cistron have the standard meanings of deoxyadenylate, deoxycytidylate, deoxyguanylate, and deoxythymidylate, respectively.

Whether the terminal CCA is coded by the cistron is doubtful since this can be enzymatically added to or removed from s-RNA in general (*5*). Hence the last three nucleotide pairs, those to the right of the dotted line, probably do not belong on the gene. There are of course some assumptions as to generality underlying the preceding argument.

All of the supplementary evidence referred to in the citations above is based on studies of viruses and bacteria which are, of course, simpler than the eucaryotic yeast. If we may assume that these discoveries on viruses and bacteria are applicable to yeast, then the formula for the DNA cistron given above is the formula for the first fully specified cistron or gene.

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Stratigraphy and Evolution

Edward S. Deevey, in his review (5 Feb., p. 592) of *Approaches to Paleoecology* (J. Imbrie and N. Newell, Eds., Wiley, New York, 1964), says: "In stratigraphy, for example, the classical or evolutionary work being largely finished. . . ." A most amazing statement. This kind of study has hardly begun. The following basic problems, among others, are virtually unexplored: (i) evolution of taxa in samples obtained in direct superposition, that is, in one continuous section; (ii) quantitative assessment of how many forms in an assemblage show directional evolution, any evolution, or none at all; (iii) under what circumstances (factual, not theoretical) evolution (rapid, directional, otherwise) takes place; (iv) whether direction of evolution and direction of natural selection coincide (Kurtén method).

Deevey's sentence continues: ". . . the problems of correlation that remain are ecological problems. . . ." The complete confusion existing with regard to correlation within the Tertiary is occasioned, in my opinion, by a lack of sufficient data on the role played by parallel evolution proceeding at different rates in different lineages.

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I am sorry that Mac Gillavry has taken my innocent statement as indicating either ignorance of or animus against evolutionary studies. I agree that evolutionary work of many exciting kinds is just beginning, now that classical stratigraphy has provided the temporal framework. Confusing as it must sometimes be to those who practice both, paleontology and stratigraphy are different subjects, and my reference was to stratigraphy in the narrow, literal sense—the recording of strata. Evolutionary change offers the best basis for ordering strata, and the stratigraphic units—stages, series, and systems—that can be ordered in evolutionary time are the classical ones. A different methodology is required, however, for unfossiliferous rocks, and for units that are too short to have witnessed appreciable evolutionary change. It is for these shorter or fossil-poor units, and especially for correlation between coeval units of different lithology *and* fossil content, that ecological insight is proving most useful. That is

why I think of paleoecology as a post-classical development in stratigraphy. There are, of course, two other antonyms of *classical* that may have echoed in the minds of some readers; but if some paleoecology is *modernistic* or *baroque*, so, I think, are several of the basic evolutionary problems listed by Mac Gillavry, notably those posed by Kurtén.

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VA Hospitals

I am glad to see from your news report of 19 March (p. 1426) that the postwar improvement in Veterans Administration hospitals is continuing. But an experience leads me to believe that the general concept of budgeting for government hospitals may be responsible for a form of social entropy —effort entailing a measurable dissipation of energy that cannot be transformed into useful work.

On my first assignment as a ward medical officer in a military hospital, I inherited about 100 patients, many of whom had been on the sick list for many months. Fresh from a very active surgical internship in a private university hospital, I carried my customary level of activity into this ward and soon had all but 15 or 20 patients back to duty. I reduced significantly the hospital census and the average length of stay. The only reward for this was to be assigned additional duties. I later came to appreciate that the budgeting of government hospitals is based largely on patient-day occupancy. If a hospital is budgeted for 36,500 patient-days of care, it is immaterial to the budgeting authority or the hospital administration whether 100 patients occupy the hospital for 365 days each or 1000 patients for 36.5 days each. The entropy lies in the fact that the hospital has the same physical plant, personnel, patient-care costs, and upkeep whether the 100 or the 1000 patients are attended. The patient-day cost will be higher in the more efficient hospital because of the increase in medical, laboratory, and clerical work.

From the figures in your news account it may be calculated that in 1964 the average stay of patients in all VA hospitals was about 56 days. The figure is skewed by the inclusion of patients in the 5 tuberculosis and 39 psychiatric hospitals, but a figure for the short-stay hospitals is available in statistics for 1958–60, which show that the mean length of stay in the 124 general VA hospitals was 41.2 days, in federal hospitals other than VA 11.9 days, in nonfederal hospitals 8.1 days, and in all short-stay hospitals combined 8.4 days ["Hospital Discharges and Length of Stay: Short-Stay Hospitals, United States 1958-60," *Dept. Health Educ. Welfare Series B, No. 32* (1962)]. What the optimum length of stay in a VA hospital is I do not know. If it should be 20 days, for example, then only 50,587 beds would have been required (on the basis of 80-percent occupancy) for the 738,583 admissions reported for 1964, instead of the 121,000 beds the VA now maintains.

Dissatisfaction with the availability of all types of medical technology in the average general hospital is reflected in the report of the President's Commission on Heart Disease, Cancer, and Stroke [*A National Program to Conquer Heart Disease, Cancer and Stroke*, vols. 1 and 2 (Government Printing Office, Washington, D.C., 1964, 1965)]. The commission has recommended the establishment of high-quality treatment centers to be constructed and supported for the *quality of patient care*. These centers will need to justify sustained support on the basis of reduced morbidity and improved results, not upon bed occupancy. Quality of care for many less frequent diseases is dependent upon the proficiency of the staff. The level of proficiency is a function of the number of cases managed per unit time as well as of the training of the staff. The incidence of a disease in a given population and the number of cases that a staff must manage per unit time in order to remain proficient should be the fundamental determinants of the number of treatment centers of different types. The assumption that equality in the number of beds available per unit population assures equal distribution in the quality of care is archaic. Society cannot support exhaustive treatment centers for every disease just at the patient's doorstep, and to try to do so in the presence of a good transportation system is wasteful. The Veterans Administration is correct in closing its smaller and more remote general hospitals. I only wonder if it should not close additional hospitals as rapidly as Congress will permit and concentrate even more intensely on the development of high-caliber treatment centers, quality control in therapy, and research in expeditious patient care.

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Committee for Professional Opportunity

Last summer a group of scientists at the Marine Biological Laboratory at Woods Hole formed a Committee for Professional Opportunity on the basis of the following declaration:

Negroes constitute a minute fraction of the American scientific community. The waste of Negro talent, originating in racial discrimination, deprives American science of its full potential. This inequity is a social and moral challenge to the humanizing and liberating spirit of science. A basic cause of the under-participation of the Negro in science is the lack of adequate educational opportunity, beginning with the earliest levels of schooling, in North as well as South. To make opportunities equal in fact as well as in theory will require an extended period of time. We believe that it is time for scientists themselves to take positive action and make special efforts now to accelerate the entry of Negroes into all aspects of scientific work.

Educational institutions throughout the country are beginning to undertake measures which will help improve the quality of education for small numbers of Negroes. Examples of activities being currently discussed or initiated are: (a) An examination of ways and means for helping to bring Negroes into the stream of American technological and scientific professional life; (b) Promoting the entry of Negro students by providing special preparation prior to college entrance, and special financial and tutorial aid to matriculated students; (c) Extramural activities, such as summer programs for teachers in Negro high schools, and programs to improve educational method and content in Negro colleges and universities.

Recognizing our responsibilities as individual scientists:

We welcome and will actively solicit applications from Negro science students and from scientists who seek to work in our laboratories or departments as technicians, graduate students, research assistants, or staff members.

We will endeavor to help in securing loans, scholarships, fellowships, time-off for course work, free or reduced tuition, for those applicants who wish to continue with course work or graduate studies.

If an applicant for graduate study does not satisfy certain requirements of our respective institutions, but is otherwise an individual with potential for successful