More recently it has become possible to search for suppressor mutations in higher organisms by combining developments in the genetics of these organisms with advances in molecular biology that enable the precise nature of many structural gene mutations to be determined. In this way it is possible to show whether unlinked mutations that revert a particular genetic phenotype represent informational suppression or merely the activation of silent genes. Only a limited number of selective systems exist for the isolation of variant clones from mammalian cell cultures and as a result mutant cell lines can only be obtained with mutations at a small number of genetic loci.

One locus that has been extensively studied is that coding for hypoxanthine-guanine phosphoribosyl-transferase (HGPRT). Clones partially or completely deficient in HGPRT can be isolated by selecting cells resistant to certain purine derivatives such as 8-azaguanine (8AG) or 6-thioguanine (6TG). Good evidence exists that mutations in the gene for HGPRT are the basis of the changes in cell phenotype (C. T. Caskey, University of Texas, Austin; M. R. Capecchi, University of Utah, Salt Lake City). From these variants it is possible to isolate revertants that have regained the enzyme activity by selecting cells growing in medium containing hypoxanthine, aminopterin and thymidine (HAT) although this procedure only selects revertants having more than 40% of normal HGPRT activity, as shown by autoradiographic analysis of ^{3}H-hypoxanthine incorporation (J. E. Celis, Aarhus). As such it is not suitable for obtaining informational suppressors of mutations that inactivate the HGPRT gene, since these are unlikely to be able to restore the enzyme activity to such a high percentage of its normal level and not disrupt protein synthesis to a degree lethal to the cell. To be compatible with viability they will probably only restore the enzyme level to less than 20% of its normal value (Celis). The cell lines that can be shown to produce an altered HGPRT are only a small fraction of the variant clones resistant to 8AG and 6TG, and therefore this selection is not very efficient for isolating lines in which to study the process of mutation in animal cells or the structure-function relationship of HGPRT (Caskey).

Until recently it was impossible to verify the nature of the alteration in HGPRT defective clones, and so to classify these as missense, nonsense, frameshift or deletion mutants. However, this problem may soon be overcome. It has recently become possible to screen clones for the presence of nonsense mutations in the HGPRT gene by introducing nonsense supressing tRNAs from yeast into the variant cells. These tRNAs are isolated from specific nonsense-suppressing yeast strains and have been characterised by their ability to suppress nonsense codons in *in vitro* protein synthesising systems (R. Gesteland, University of Utah, Salt Lake City). They can be introduced into mammalian cells either by direct microinjection using glass capillaries (Graessman & Graessman *Proc. natn. Acad. Sci. U.S.A.* **73,** 366; 1976) or, on a much larger scale, by being trapped within red blood cells which are then fused to the recipient cells (Kaltoft *et al. Proc. natn. Acad. Sci. U.S.A.* **73,** 2793; 1976). Preliminary experiments using the first procedure have shown, by autoradiographic measurement of ^{3}H-hypoxanthine incorporation combined with videotape recording of which cells were injected, that yeast nonsense suppressors cause a temporary phenotypic reversion when introduced into certain HGPRT-deficient cell lines (Celis). The second procedure can also be used to bring about *in vitro* suppression of nonsense codons (Capecchi) but is less readily applicable to the screening of many clones for nonsense mutants. It should also be possible to introduce frameshift suppressor tRNAs, isolated from frameshift suppressing strains of yeast, into variant cells, but these tRNAs may be too specific in their action to provide a selective system for the majority of frameshift mutants.

By fusing two mammalian cell lines, each carrying the same type of mutation but in different structural genes, it will be possible to isolate a hybrid cell carrying two identical mutations. In such a cell there will be a very low rate of simultaneous spontaneous reversion to the wild-type phenotype in both genes and the stage will be set for isolating the first true suppressor mutations of mammalian cells. Informational suppressors in higher organisms are already being characterised in *Drosophila melanogaster* and the nematode *Caenorhabditis elegans*. In the latter, Waterston and Brenner (*Nature* **275,** 715; 1978) have described a suppressor of the paralysed paramyosin-deficient E1214 mutant that acts on a range of alleles and partially restores paramyosin in worms homozygous for the mutation. The paramyosin synthesised as a result of the action of this suppressor seems to be identical to the wild-type protein. In *Drosophila* the existence of informational suppression is well characterised genetically, although in no single specific instance is the biochemical mechanism established.

Some disorganised muscle mutants of the nematode *Caenorhabditis elegans* produce a shorter myosin heavy chain than normal (A. R. MacLeod *et al. J. molec. Biol.* **114,** 133; 1977). After cyanylation of the wild-type and mutant proteins with ^{14}C-labelled cyanide, a reaction which breaks the myosins at their very infrequent cysteines and labels the N-termini of the fragments with ^{14}C, and gel fractionation of the products of partial cleavage of each of these fragments with cyanogen bromide, it is possible to distinguish nonsense and deletion mutants. In a nonsense mutant only the largest labelled fragment from one of the cyanylation products will have a reduced mobility relative to the fragments from the wild-type myosin, whereas in most deletion mutants several fragments show a diminution in size corresponding to the size of the deletion (S. MacLeod, University of Cambridge). Besides providing a way of mapping deletion mutants within the coding region, this approach can also be used to detect suppression of nonsense mutations in the genes for the heavy chain of myosin. □

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A hundred years ago

NEWS from Panama states that the volcano Cotopaxi is in a state of violent activity. Its crater is surrounded by ice and snow but the clouds of ashes and smoke rising from it can be seen even at Guayaquil on the shores of the Pacific.

A VIOLET coloured meteor, with a reddish train, was seen at Stanislas, Austria, on the evening of the 24th in the Great Bear and moving in a northerly direction. It is described as thrice the size of Jupiter.

. . . it is stated that carrier pigeons are "being turned to useful account" in a new direction in Germany, for Consul Ward writes to the Foreign Office "that the successful results attained by the establishment of communication between the two Eider lightships and the Port of Tonning, in Schleswig, by these means has led to its organisation" elsewhere. This mode of communication is, however, not new, as carrier pigeons were employed early in this country as a means of communication with the Bell Rock Lighthouse, as mentioned in my late father's "Account" of that work. The pigeons passed between the lighthouse and the shore—a distance of eleven miles in eleven minutes. The employment of these birds, however, was, I suppose, found to be more curious than convenient for they have long since ceased to be employed.

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