the specific case of *lacZ* bacteria, for example, the leakiness will generate functional LacZ which will break down lactose and release energy for growth and DNA replication. There will then be a whole range of fidelity errors associated with that process.

This is relevant to the controversial issue of DNA turnover in nondividing cells. Recent experiments with *mutT* bacteria indicated that there is far more such DNA synthesis than had been supposed (*11*). Could this be due to leakiness resulting from misincorporation during transcription? In principle the answer must be yes at least in part, although the strains used in those experiments (*trpE* and *tyrA* auxotrophs with ochre mutations) do not demonstrate any of the leakiness for growth seen with the *lacZ* amber strain. The consequences for cellular physiology of the leakiness of *mutT* bacteria must be determined by whether the particular protein produced is present in sufficient quantity to have a detectable effect.

It is indeed surprising that such a small amount of 8-oxo-rGTP in the pool should lead to so much leakiness of the *lacZ* amber mutation. Perhaps this apparent contradiction arises because *lacZ* is strongly induced by lactose and its analogs, generating more transcription than expected. Even so, the arithmatic is against so little rGTP having an effect. The content of 8-oxo-G in DNA of *mutT* bacteria due to incorporation of 8-oxo-dGTP has been estimated to be about four per 10^6 guanine residues (*4*), and about half of the 8-oxo-G will presumably be mispaired with adenine. There is no reason to believe that the relative incorporation into RNA will be grossly different, which means that half a million transcripts of *lacZ* would have to be made to get one that will produce functional protein. So a culture of *mutT* bacteria ought to have only about 2×10^{-6} the enzyme activity of a lac^+ culture. This seems hardly compatible with the reported value of about 10^{-4}. Maybe *lacZ* is special in some unknown way in its response to *mutT*, in which case it may be premature to draw general conclusions about the extent of transcriptional leakiness in *mutT* bacteria.

One other aspect of the new results, touched on but not explained by Taddei *et al.*, shows that all is not yet understood. They observed that anaerobic conditions reduced transcriptional leakiness in their strain by a factor of 22, entirely consistent with the involvement of active oxygen species. Under similar conditions, however, others have found that the mutator effect of *mutT* is not affected by anaerobic conditions (*12*). Since both effects have been ascribed to 8-hydroxynucleoside triphosphates, this discrepancy clearly requires further study.

Taddei *et al.* look beyond their immediate results and point out that it is in nondividing cells that RNA metabolism and fidelity are likely to be most critical. Such cells include not only growth-restricted bacteria, but also a wide variety of mammalian cells including neurons, heart muscle, and ova. Is the effect of the MutT pool–cleansing enzyme merely the tip of an iceberg of mechanisms for maintaining the accuracy of RNA processes—not only transcription but also editing and splicing?

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NOTA BENE: NEUROBIOLOGY

Unconscious Odors

As connoisseurs of perfumes or wines will attest, there are thousands of distinguishable odors that together lend a unique identity to a fragrant event. But a special subset of olfactory signals, the pheromones, are not perceived consciously—or as widely appreciated. These molecules, often fatty acids or steroids, are secreted by animals, then detected by other animals of the same species, where they regulate such basic functions as mating, the timing of the estrous cycle, and aggressiveness.

Unlike odorants, which are initially detected deep within the nasal cavities in the olfactory epithelium, pheromones are perceived chiefly by the vomeronasal organ, located in rodents within the nasal septum. The pheromone binds to a receptor on the neuron surface and triggers a signal that goes via the accessory olfactory bulb through nonolfactory pathways, bypassing higher cognitive centers, to the amygdala and the hypothalamus, brain structures that govern emotional and neuroendocrine responses.

A new family of about 100 genes that likely encode pheromone receptors in the vomeronasal organ has now been identified and analyzed in the mouse (*1*) and in the rat (*2, 3*). This family joins two others already known to receive olfactory signals: one that perceives garden-variety odorants in the olfactory epithelium (*4*) and one that encodes vomeronasal receptors (*5*), likely also responsible for the perception of pheromones. Like the genes for the olfactory receptors, both pheromone receptor families encode proteins with seven transmembrane domains, which convey their signals via heterotrimeric GTP-binding proteins (G proteins).

Nevertheless, the 550–amino acid extracellular domains of the new receptor family are considerably larger than the ~20 amino acids typical of the other two. The unusual structure of this domain suggests that it may be responsible for ligand binding, like that of the similar metabotropic receptor for glutamate. This sort of domain structure for binding would allow more rapid evolution of receptor specificity than is possible for the ligand-binding sites of the other olfactory receptors, which are pockets formed by several transmembrane domains.

The previously described gene family of pheromone receptors is expressed only in the apical portion of the vomeronasal organ, where it is colocalized with a $G\alpha_{i2}$ protein (*5*). The new family (*1–3*) is found in the basal region, where it is colocalized with a different G protein, $G\alpha_o$. The rough apical-basal subdivision in the vomeronasal organ may represent specializations for the perception of different types of molecules, such as pheromones with and without accessory binding proteins or pheromones that trigger short-term behavioral responses and long-term physiological adaptation. Indeed, the segregation of these two sets of signals is maintained as the information travels further into the brain.

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