multiple biological activities, and both were contenders for interleukin-4 (refs 4, 5, 11). As complementary DNA for BSF-1 was cloned first, this factor will retain that designation, and BCGF-II/TRF/EDF will presumably become interleukin-5 (as proposed by Kinashi *et al.*[1]). These designations, however, have yet to be officially ratified.

Does our current knowledge about these factors produce a coherent scheme of growth and differentiation control in antigen-stimulated B cells? The answer, unfortunately, is not yet. In murine B lymphocytes it is an attractive idea that resting cells become activated by the synergistic action of antigen plus BSF-1 produced by the cooperating T cell, and then become responsive to BCGF-II later in their cycle. Perhaps the balance between these two factors, in conjunction with unknown microenvironmental influences, will then determine which classes of antibody are secreted by the clonal progeny of a particular B cell, or if these progeny will instead revert to the resting state of memory B cells. It is significant that both BSF-1 and BCGF-II are growth and differentiation factors, suggesting that clonal expansion and maturation are coordinately regulated.

Unfortunately, what we know of human B cells does not fit this scheme. First, the genetic homologue of murine BSF-1 has not yet been shown to activate resting human B cells, but rather stimulates proliferation of pre-activated cells[6]. Second, it is likely that there is yet another type of B-cell growth factor for human cells (distinct from interleukin-2). Finally, the factor described by Kishimoto *et al.*[9] has no growth-promoting activity, suggesting compartmentalization of growth and differention in human B cells.

In conclusion, there still may be too many factors in the arena for comfort. Nevertheless, given the availability of the recombinant molecules, various questions can now readily be answered. For instance, are there functional B-cell subpopulations responsive to different factors? Do mixtures of individual lymphokines produce synergistic effects? The answers should not now take long to emerge. □

1. Kinashi, T. *et al. Nature* **324**, 70 (1986).
2. Hirano, T. *et al. Nature* **324**, 73 (1986).
3. Dutton, R.W. *et al. Prog. Immun.* **1**, 355 (1971).
4. Noma, Y. et al. *Nature* **319**, 640 (1986).
5. Lee, F. *et al. Proc. natn. Acad. Sci. U.S.A.* **83**, 2061 (1986).
6. Yokota, T. *et al. Proc. natn. Acad. Sci. U.S.A.* **83**, 5894 (1986).
7. Swain, S.L. & Dutton, R.W. *J. exp. Med.* **156**, 1821 (1982).
8. O'Garra, A. *et al. Proc. natn. Acad. Sci. U.S.A.* **83**, 5228 (1986).
9. Hirano, T. *et al. Proc. natn. Acad. Sci. U.S.A.* **82**, 5490 (1984).
10. Mosmann, T.R. *et al. Proc. natn. Acad. Sci. U.S.A.* **83**, 5654 (1984).
11. Sanderson, C.J., O'Garra, A., Warren, D.J. & Klaus, G.G.B. *Proc. natn. Acad. Sci. U.S.A.* **83**, 437 (1986).
12. Meidema, F. & Melief, C.J.M. *Immun. Today* **6**, 258 (1985).

Gerry G.B. Klaus is in the Division of Immunology, National Institute for Medical Research, London NW7 1AA, UK.

Neurobiology

Questions of taste and smell

Gordon M. Shepherd, Thomas V. Getchell and Charlotte M. Mistretta

RECEPTOR mechanisms in olfaction and taste have been tough nuts to crack for traditional methods of biochemistry and electrophysiology. The advent of molecular neurobiology and patch-clamp recordings is therefore most welcome, as was evident at a recent meeting*.

In olfaction, biochemical and molecular biological studies were made much easier by the development of isolated olfactory ciliary preparations containing enriched membrane fractions. Several molecular components localized in the fractions are believed to be associated with sensory transduction. The proposed sequence is initiated by binding of odour molecules (odogens) to membrane glycoproteins, such as gp95 (Chen, Z. & Lancet, D. *Proc. natn. Acad. Sci. U.S.A.* **81**, 1859; 1985), located in the cilia. The odogen–receptor complex is believed to activate the stimulatory GTP-binding protein (G_s) (D. Lancet, The Weizmann Institute). Although they appear to be less abundant, G_i and G_o binding proteins have also been identified in olfactory cilia using monospecific antisera (R.R.H. Anholt, Johns Hopkins University). Their functions may be related to receptor 'inhibition', or to neuromoldulatory effects of compounds such as substance P (J.F. Bouvet, Université Claude Bernard) or luteinsing hormone-releasing hormone (C.R. Wirsig and T.V.G., Wayne State University). G_s-deficient pseudohypoparathyroid patients have impaired olfactory perception compared with individuals with normal G_s activity (H.N. Wright, State University of New York).

Cyclic AMP is believed to be a second messenger that is activated during olfactory transduction and leads to excitation of receptor neurones. The activity of cyclic AMP in the olfacotry cilia preparations is 15 times that in the brain, and is increased substantially by GTP, its analogue GTPγS and forskolin, which indicates that the cyclase is activated by a G protein (P.B. Sklar, Johns Hopkins University). Certain molecules evoking different odour sensations also markedly increase cyclase activity. Others, which evoke putrid or solvent odours, do not stimulate this enzymatic activity. This observation suggests that parallel, non-adenylate cyclase-dependent transduction mechanisms are operable. For example, isolated olfactory ciliary preparations also exhibit increased phosphodiesterase activity when stimulated with L-alanine and GTP (R.C. Bruch and T. Huque, Monell Chemical Senses Center); this suggests that certain odogens stimulate phosphoinositide turnover by a G-protein-dependent mechanism.

A major question is to determine if cyclic AMP directly activates membrane channel proteins associated with the ion conductance changes responsible for the receptor potential, or if the effect is mediated by phosphorylation of specific proteins by phosphokinases in the cilia. Protein kinase C has been identified by phorbol ester binding and monospecific antisera (R.H. Anholt), suggesting that phosphorylation of the ion channels may be associated directly with conductance changes.

Patch-clamp recordings demonstrate that olfactory receptor neurones have interesting passive membrane properties that include high input resistances (2–6 GΩ) and low input capacitances 2.6–5 pF) (S. Firestein and F. Werblin, University of California, Berkeley; N. Suzuki, Hokkaido University). Membrane depolarizations are associated with a rapid inward Na^+ current followed by several outward K^+ currents (V.E. Dionne, University of California, San Diego; S. Firestein and F. Werblin). Near-threshold concentrations of odour molecules delivered by pressure injection elicit a 6-pA generator current that depolarizes the cell by 15 mV. There is a systematic relationship between the concentration of the odogen, the magnitude of the generator current and the number of action potentials initiated (S. Firestein and F. Werblin). These results support previous evidence that there is relatively close coupling between the conductance sites associated with ligand binding and those associated with impulse initiation (L. Masukawa, *J. Neurosci.* **5**, 128; 1985).

The relationship of the intermediate molecular stages of transduction and ion conductance changes has been investigated using G protein and cAMP analogues (D. Trotier and P. MacLeod, Laboratoire de Neurobiologie Sensorielle), which enhance conductive charges, supporting the biochemical evidence for an enzymatic cascade leading to the generator current. Single channel conductances in functionally reconstituted membrane proteins isolated from olfactory cilia incorporated in bilayer lipid membranes are enhanced by odour molecules and cyclic AMP (V. Vodyanoy and I. Vodyanoy, University of California, Irvine).

A protein of relative molecular mass 20,000 in the olfactory mucosa (J. Pevs-

**IX Symposium on Olfaction and Taste* and *8th Annual Meeting of the Association for Chemoreception Sciences* Snowmass Village, Colorado, 20–24 July 1986.

ner, Johns Hopkins University) binds several types of odour molecules with micromolar and millimolar affinities, is localized in olfactory glands and is released into the surface mucus when the glands are stimulated pharmacologically. The protein may facilitate diffusion of odour molecules through the mucus to receptor sites, or it may inactivate and clear odorants from the active sites. Odour molecules also stimulate secretion from olfactory glands by a cholinergic sensitive pathway, which may provide another mechanism by which odour molecules are cleared from olfactory receptor neurones (M.L. Getchell, Wayne State University).

Immunocytochemical techniques can help to elucidate the location of antigenic molecules in olfactory receptor neurones, which will help further studies on the coding of odour quality and the developmental sequences in neuronal maturation. A neurone-specific antigen (RB-8) in the rat has been characterized as a membrane-associated protein with a relative molecular mass of 125,000 (J.E. Schwob and D.I. Gottlieb, Washington University). In contrast to other regions of the nervous system, RB-8 stains the receptor neurone population nonhomogeneously: the axons of receptor neurones in the ventro-lateral region of the olfactory epithelium to the olfactory bulb are RB-8 positive, whereas axons from neurones with apparently identical morphology in the dorso-medial region of the olfactory epithelium are RB-8 negative. There is heterogeneity in cytochrome oxidase staining of olfactory receptor neurones during the development of normal and odour-deprived neonatal rat pups (P.E. Pedersen, Yale University). The further use of these two techniques should provide a clearer understanding of first principles of the functional organization of the peripheral olfactory system and its primary projections to the olfactory bulb, particularly as it relates to the coding of odour quality. Finally, monoclonal antibodies have been developed as specific probes to identify the emergence of membrane antigens during the development of olfactory receptor neurones (A.I. Farbman, Northwestern University; P.E. Pedersen). Two antibodies, Neu-5 and Neu-9, first bind on embryonic day 13 and stain the developing olfactory nerve bundles as well as the soma and dendrites. Another antibody, Neu-4, binds on embryonic day 14, the earliest time at which an odour-evoked response can be recorded from the olfactory mucosa. Further studies should lead to identification of specific membrane antigens that occur in associated with the development of odogen- and voltage-gated channels in receptor cell membranes.

In the taste field, there is particular interest in whether Na^+ channels are involved in transduction mechanisms for salt taste sensation, mainly deriving from studies where amiloride at least partially blocks the response to NaCl and LiCl but not to other salts.

Amiloride is now thought to block the sodium taste response completely, in contrast to previous reports of only partial blockade. Taste responses to sodium acetate and sodium bicarbonate are suppressed by 95–100 per cent after amiloride application on the tongue, whereas responses to NaCl and NaBr are suppressed by 65–90 per cent (B.K. Formaker and D.L. Hill, University of Toledo). Responses to NH_4Cl and ammonium acetate are not affected. Bretylium tosylate, an antifibrillary drug that opens amiloride-sensitive Na^+ channels, potentiates the taste of NaCl and LiCl, but has no effect on KCl or $CaCl_2$ when applied to the human tongue. The bretylium potentiation is inhibited by amiloride.

Other questions arise, such as why the monoclonal antibody 5B4 stains some, but not all, of the taste-bud cells in a bud. Could the antibody be binding a receptor protein that is present in cells only at certain stages of the turnover cycle? □

Gordon M. Shepherd is in the Section of Neuroanatomy, Yale University School of Medicine, New Haven, Conneticut 06510; Thomas V. Getchell is in the Depatment of Anatomy, Wayne State University, Detroit, Michigan 48021; Charlotte M. Mistretta is in the Department of Oral Biology, University of Michigan School of Dentistry, Ann Arbor, Michigan 48109, USA.

Geophysics

New radiocarbon dating system

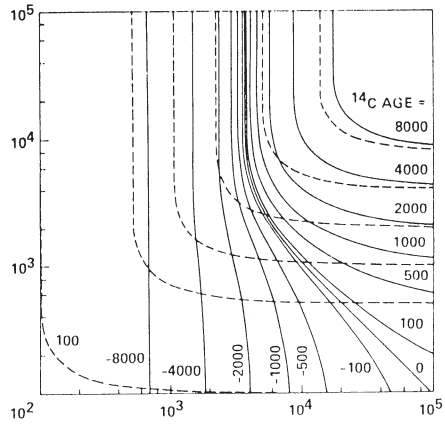
Roy Switsur

THE closest terrestrial analogue to martian conditions probably occurs in the arid valleys of southern Victoria Land, Antarctica; hypotheses suggesting that life exists on Mars are often based on this comparison. The discovery of cryptoendolithic microorganisms that survive in this inhospitable environment without completely adapting to its extremes add to this speculation. Recent studies of these microorganisms by McKay, Long and Friedmann[1] have led to a new approach to radiocarbon dating which is applicable to systems slowly exchanging carbon with the atmosphere, and which relates the true age to the apparent radiocarbon age and to the carbon-exchange rate.

Dry katabatic winds descend from the Antarctic ice plateau to create a lifeless desert where extensive areas of rock lie devoid of all snow or ice cover. The endolithic microorganisms colonize a narrow zone just beneath the surface of the porous granitic translucent rocks. Because of the hostile environment, photosynthesis can occur during only a few hours each year when conditions of moisture and light are suitable. A detailed analysis of this microbial ecosystem suggests that the organisms have very low rates of metabolism and may be very old[2].

The method of dating dead organic matter through its residual radiocarbon content, developed 40 years ago by W.F. Libby[3], is based on a closed system in which the carbon is unchanged through time apart from that lost by radioactive decay. The initial activity is produced through a chain of natural processes: a constant flux of primary cosmic rays impinging on the outer layers of the Earth's atmosphere generate secondary showers with high neutron content. These neutrons lose energy in elastic collisions as they descend until, at a height of about 12 km, they react with stable atmospheric ^{14}N nuclei to produce the radioactive ^{14}C isotope $^{14}N(n,p)^{14}C$.

Following rapid oxidation the radioactive CO_2 is mixed thoroughly, in a very short time compared with the half-life of the ^{14}C, with the existing CO_2 in the lower atmosphere. Most of the radiocarbon enters the oceans and becomes precipitated



True age in years (vertical scale) against mixing time-constant in years (horizontal scale). Solid line, with bomb effect; broken line, without bomb effect (from ref. 1.)

as a calcium carbonate ooze on the ocean floor. Part of the remainder becomes incorporated into plants through photosynthetic reactions. Of some 80 tons of the ^{14}C isotope that exists on the earth only approximately 3 tons remains in the biospheric reservoir, mainly in the form of photosynthetically produced cellulose. The carbon compounds thus produced by the green leaves of plants form the base of the food net for the animal life of the planet and their natural metabolism results in carbon exchange in equilibrium with the