(*Z*)-11-Octadecenoate was also abundant in the sex pheromone gland of *T. ni*, and chain-shortened products of this can account for an additional 10 percent of the sex pheromone components known for the Noctuidae (*1*). In a preliminary experiment with *Xestia dolosa*, in which (*Z*)-7-tetradecenyl acetate is the principal sex pheromone component, we have observed that large quantities of the expected precursors (*Z*)-11-octadecenoate and (*Z*)-9-hexadecenoate are present [but (*Z*)-11-hexadecenoate is absent]. In *Argyrotaenia velutinana* (Tortricidae), in which the principal sex pheromone components are (*Z*)- and (*E*)-11-tetradecenyl acetates, we found earlier that hexadecanoate is chain-shortened to tetradecanoate and that this is desaturated to produce (*Z*)- and (*E*)-11-tetradecenoates (*16*). The (*Z*)- and (*E*)-9-dodecenyl moieties are also common as sex pheromone components in many other species in the Tortricidae (*1*), and these may arise as chain-shortened products of (*Z*)- and (*E*)-11-tetradecenoates. The small proportion of (*Z*)-13-octadecenoate found in the gland of *T. ni* may represent a chain-elongated product of (*Z*)-11-hexadecenoate. Combinations of (*Z*)-11-hexadecenyl and (*Z*)-13-octadecenyl moieties are common in sex pheromone blends of many species in the Pyralidae (*1*). The sex pheromone compositions of all these families, together with our present results, indicate that chain-shortening or chain-elongation systems, in conjunction with delta-11 desaturases that react with 18-, 16-, or 14-carbon chain fatty acyl groups, may be involved in the biosynthesis of many of the known lepidopteran sex pheromone components.

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References and Notes

1. Y. Tamaki, in *Chemical Control of Insect Behavior*, H. H. Shorey and J. J. McKelvey, Eds. (Wiley, New York, 1977), p. 253; in *Comprehensive Insect Physiology, Biochemistry and Pharmacology*, G. A. Kerkut and L. I. Gilbert, Eds. (Pergamon, New York, in press).
2. W. Steck, *J. Chem. Ecol.* **8**, 731 (1982).
3. J. J. Volpe and P. R. Vagelos, *Physiol. Rev.* **56**, 339 (1976); S. J. Wakil, *Lipid Metabolism* (Academic Press, New York, 1970).
4. D. K. Bloomfield and K. Bloch, *J. Biol. Chem.* **235**, 337 (1960); P. Strittmatter, *Proc. Natl. Acad. Sci. U.S.A.* **71**, 4565 (1974); E. L. Pugh and M. Kates, *Lipids* **14**, 159 (1979).
5. Glands were dissected from the ovipositors of females (3 to 4 days old) and extracted with 1 ml of a 2:1 mixture of chloroform and methanol [J. Folch, *J. Biol. Chem.* **226**, 497 (1957)]. All fatty acyl moieties were converted to methyl esters by acid methanolysis, and subsequent treatment with acetyl chloride converted fatty alcohols to acetates.
6. Capillary GLC was conducted with a 45-m Carbowax 20-m column used with splitless injection and programmed from 80° to 200°C at 10° per minute after an initial delay of 2 minutes. Packed GLC columns were 3 percent OV-101 (methyl silicone) on 100- to 120-mesh Gas-Chrom Q, 2-m glass column (inside diameter, 4 mm) and 10 percent XF-1150 (50 percent cyanoethyl, methyl silicone) on 100- to 120-mesh Chromosorb W-AW-DMCS, 2-m glass column (inside diameter, 2 mm).
7. R. S. Berger, *Ann. Entomol. Soc. Am.* **59**, 767 (1966); L. B. Bjostad, *J. Chem. Ecol.* **6**, 727 (1980); C. E. Linn, *Environ. Entomol.* **10**, 379 (1981); *ibid.*, p. 751.
8. Precoated TLC plates (Whatman K5, 0.25 mm, 20 by 20 cm) were used to separate gland extracts. Plates were developed for 2 cm with a mixture of chloroform, methanol, and water [62:34:4 (by volume)] to separate ethanolamine phosphatides and choline phosphatides (neutral lipids moved with the solvent front), then developed for 7.5 cm with a mixture of Skelly B, diethyl ether, and acetic acid (80:20:2) to separate diacylglycerols, triacylglycerols, and acetates. These lipid classes were scraped from the plate, methanolyzed, and acetylated for GLC analysis.
9. I. F. Jones and R. S. Berger, *Environ. Entomol.* **7**, 668 (1978).
10. A 5-μl solution of 1 μCi of sodium [1-^{14}C]acetate (Amersham) in a 1:1 mixture of water and dimethyl sulfoxide was applied to the pheromone glands of five female *T. ni* (1 to 2 days old). The glands were held everted by clamping the abdomens with smooth-jawed microalligator clips. The droplets completely absorbed into the gland in about 1 hour, and the clips were removed. After 24 hours, the glands were extracted, and the extract was methanolyzed and treated with acetyl chloride (*5*). The reaction products were separated on XF-1150 at 140°C (*6*). Fractions were collected in 30-cm glass capillary tubes. Compounds were recovered by washing through each tube with scintillation fluid (0.5 percent PPO in toluene) into a scintillation vial. Overall incorporation of ^{14}C into sex pheromone components and fatty acyl moieties was 2.2 percent.
11. Methyl [16-^{3}H](*Z*)-11-hexadecenoate was prepared by adding a dimethyl sulfoxide solution of NaB^3H_4 (Amersham) to methyl [16-tosyl](*Z*)-11-hexadecenoate, and base hydrolysis produced [16-^{3}H](*Z*)-11-hexadecenoic acid. A 5-μl solution of 1 μCi of the acid in dimethyl sulfoxide was applied to the pheromone glands of 19 female *T. ni* (1 to 2 days old). Overall incorporation of ^{3}H into sex pheromone components and fatty acyl moieties [other than the starting material (*Z*)-11-hexadecenoate] was 2.0 percent.
12. Unsaturated compounds were dissolved in Skelly B and added to a solution of ozone in Skelly B in a dry ice–acetone bath. This (0.5 ml) was flushed with N_2 to dispel excess ozone and added to a solution of benzylhydroxylamine hydrochloride (0.5 mg) in pyridine (0.5 ml) in a 4-ml vial with a Teflon-lined lid. The tightly capped vial was heated at 100°C for 16 hours. The products were separated on OV-101 (*6*), programmed from 100° to 225°C at 6° per minute with a 1-minute delay.
13. J. Percy, *Can. J. Zool.* **57**, 220 (1979).
14. P. B. Lazarow and C. de Duve, *Proc. Natl. Acad. Sci. U.S.A.* **73**, 2043 (1976); P. B. Lazarow, *J. Biol. Chem.* **253**, 1522 (1978); *Arch. Biochem. Biophys.* **206**, 342 (1981).
15. P. B. Lazarow, *Science* **197**, 580 (1977); H. Osmundsen, *Int. J. Biochem.* **12**, 625 (1980).
16. L. B. Bjostad and W. L. Roelofs, *J. Biol. Chem.* **256**, 7936 (1981).

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Suppressor T Cell Action Inhibits the Expression of an Excluded Immunoglobulin Gene

Abstract. *Cells of the murine plasmacytoid line MOPC-315 synthesize two distinct immunoglobulin light chains: a normal λ_{II} protein, which is incorporated into secretory and surface-bound immunoglobulin, and a truncated, nonfunctional λ_I protein found only in the cytoplasm. Idiotype-specific suppressor T lymphocytes selectively inhibit the expression of both λ_{II}- and λ_I-specific messenger RNA by MOPC-315 cells. This finding demonstrates that phenotypically excluded light chain genes can be subject to immunoregulatory control and suggests that the expression of divergent λ isotypes may be coordinately regulated in immunoglobulin-secreting cells.*

Immunoglobulin light chain proteins of the mouse occur in four isotypic varieties, designated κ, λ_I, λ_{II}, and λ_{III}, each characterized by a specific amino acid sequence of the constant (C)-region domain (*1*). Each of the four C-region isotypes is encoded by a corresponding C-region gene, present as a pair of alleles in the normal diploid genome. Individual lymphoid cells, however, selectively express only one of these eight available C genes as functional protein; the light chain secreted or displayed as surface-bound immunoglobulin by a given clone is of a single isotype and is exclusively derived from either the maternal or the paternal C-region allele. The remaining allelic and isotypic C genes are said to be excluded.

Molecular analysis of the structure and ontogeny of immunoglobulin genes has begun to clarify the mechanisms by which lymphoid cells select a single C-region gene for expression (*2*). The formation of an active light chain gene requires specific DNA rearrangements that occur at an early stage in commitment to the B lymphocyte lineage (*3*). These rearrangements bring together separate genetic elements that encode the variable and C-region domains and align these elements in a precise manner for transcription and subsequent translation. While rearrangements of this type provide the major source of sequence diversity among immunoglobulin proteins, they are not without genetic risk. Aberrant rearrangements are common (*4*) and can result either in deletion of the affected locus or in the formation of a structurally anomalous gene. Such aberrantly rearranged genes may be transcriptionally silent or may be capable of rudimentary expression, giving rise to inactive transcripts or to transcripts that specify a nonfunctional light chain. One currently held view (*5, 6*) is that the differentiating lymphocyte rearranges its

light chain C genes one at a time, in a process of genetic trial and error, until a successful rearrangement gives rise to a functional light chain protein. Further rearrangements then cease, and the cell and its progeny are committed to the overt expression of this particular light chain gene. The remaining C genes, whether deleted, aberrantly rearranged, or retaining the germ-line configuration, are phenotypically excluded.

In myeloma cells, immunoglobulin synthesis can be suppressed by T lymphocytes directed against the variable region (idiotype) of the secreted immunoglobulin. We have investigated this phenomenon in the BALB/c mouse plasmacytoma MOPC-315. This clonal cell line secretes an immunoglobulin (M315) composed only of α heavy chains and λ_{II} light chains but has also been found to contain substantial quantities of λ_I-specific messenger RNA (mRNA) encoding a truncated, nonfunctional λ_I light chain (*7*). Because the λ_I gene product has no apparent immunologic function in MOPC-315 cells, we sought to determine whether the expression of λ_I mRNA in these cells is affected by immunoregulatory stimuli. We report that idiotype-specific suppressor T lymphocytes, which selectively block the expression of the M315 λ_{II} light chain and its corresponding mRNA, simultaneously inhibit the expression of RNA derived from the excluded λ_I gene.

Immunization of syngeneic BALB/c mice with M315 protein results in the generation of Lyt-1^-2^+ suppressor T cells directed against the M315 idiotype (*8–10*). These cells bear surface membrane binding sites specific for M315 and release soluble factors that reversibly inhibit the biosynthesis and secretion of both α and λ_{II} proteins by MOPC-315 cells. This suppressive action does not affect rates of MOPC-315 cell proliferation or of nonimmunoglobulin protein synthesis, does not require participation of accessory cells (for example, macrophages), and does not affect the secretory activity of closely related plasmacytoma lines lacking the M315 idiotype. The physical and biochemical properties of the suppressive factors are unknown.

BALB/c mice were immunized with purified M315 protein (*9*). Spleen cells were harvested aseptically, suspended briefly in hypotonic ammonium chloride to lyse contaminating erythrocytes, and applied to a column of nylon wool; the nonadherent (T cell) population was collected and used as a source of suppressor cells without further treatment. Control T cells were isolated by the same method from the spleens of unimmunized mice. Such cell preparations typically contained > 90 percent T lymphocytes, as assayed by susceptibility to cytolysis with antiserum to θ and complement.

Plasmacytoma cells from a culture-adapted line of MOPC-315 were grown for 48 hours in the presence of T cells from M315-immune or control mice. These incubations were carried out under two sets of conditions (Table 1). In the first, MOPC-315 cells were combined in direct coculture with a 40-fold numerical excess of T cells. Alternatively, the MOPC-315 cell suspension was physically separated from the T cell population by a porous membrane that prevented direct cell-to-cell contact while permitting the exchange of diffusible chemical mediators having molecular weights of up to 50,000.

At the end of the 48-hour incubation period, the extent of suppression of M315 secretion was determined by an indirect Jerne hemolytic plaque assay specific for M315 (*10*). When grown in the absence of T cells, virtually 100 percent of cells in the cloned MOPC-315 line synthesize immunoglobulin protein (*8*), but only 38 percent secrete sufficient quantities of immunoglobulin to be detectable as plaque-forming cells in this assay. A similar proportion of secretory cells (35 percent) was detected in MOPC-315 populations exposed to con-

Table 1. Inhibition of immunoglobulin secretion in MOPC-315 plasmacytoma cells by idiotype-specific suppressor T lymphocytes. T cells were prepared from the spleens of 100 to 150 BALB/c mice per group. Conditions for culture of MOPC-315 alone and in coculture with T lymphocytes have been described (*8*). For membrane-segregated culture, 2.5×10^6 plasmacytoma cells were enclosed in a Spectra/Por 6 dialysis bag (molecular weight cutoff 50,000) and immersed in the T cell suspension in a 75-cm^2 tissue culture flask. Although the suppressor T cells are not cytostatic in themselves (*8*), net viable MOPC-315 cell concentration increased by not more than 50 percent during the incubation period, probably as a result of the high initial cell density used in these studies. No net proliferation of the T cell populations occurred.

Culture conditions	T cell source	Ratio of T cells to MOPC-315	MOPC-315 cell viability (%)*	Secretory activity (% PFC)†
MOPC-315 alone	None	0	93	38
Coculture	Nonimmune	40:1	89	35
	M315-immune	40:1	86	1
Membrane-segregated	Nonimmune	100:1	78	36
	M315-immune	100:1	76	6

*Assayed by dye exclusion. †Plaque-forming cells as percentage of viable MOPC-315 cells, assayed as described (*10*).

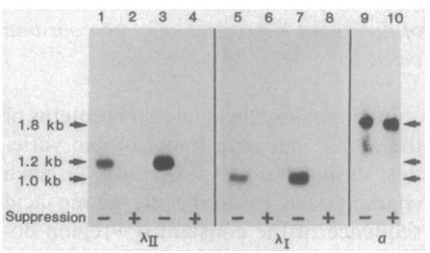

Fig. 1. Idiotype-specific suppression inhibits the expression of immunoglobulin light chain mRNA. MOPC-315 cells incubated for 48 hours in the presence of control or suppressor T lymphocytes were washed, pelleted, and lysed by suspension in a solution containing 5*M* guanidinium thiocyanate, 0.5 percent *N*-lauroylsarcosinate, 50 m*M* tris, *p*H 7.5, and 75 m*M* 2-mercaptoethanol. RNA was isolated by sedimentation through 6*M* CsCl (*17*), and enriched for poly(A) sequences by two successive passes over an oligo-deoxythymidilate affinity column. Samples containing 3 μg of poly(A) RNA were denatured by heating to 65°C for 5 minutes in the presence of 50 percent (weight to volume) formamide and 6 percent formaldehyde, then applied to slab gels containing 6 percent formaldehyde and 1.2 percent agarose (*18*). After electrophoresis at 100 V for 10 hours, the RNA was transferred to nitrocellulose, fixed, and probed with specific labeled DNA restriction fragments (*19*). The λ_I and λ_{II} probes were isolated by combined Pvu II–Xho I or Pst I–Ava I digestion, respectively, of cloned chimeric plasmids (*7*). Each fragment was 250 to 300 base pairs in length and comprised only constant region coding sequences. As noted by others (*7, 12*), the λ_I and λ_{II} probes are each specific for the corresponding isotypic RNA and do not cross-react detectably under the hybridization conditions we used. Cell samples incubated under coculture conditions were partially enriched for MOPC-315 cells by brief low-speed centrifugation before RNA isolation. Because the T cell samples contained few contaminating B cells, of which only a small subpopulation expresses α or λ mRNA, it is unlikely that the T cell population contributed significant quantities of the RNA species detected here. RNA was isolated from MOPC-315 cells grown in coculture with control T cells (lanes 1 and 5), in coculture with suppressor T cells (lanes 2 and 6), in membrane-segregated culture with control T cells (lanes 3, 7, and 9), and in membrane-segregated culture with suppressor T cells (lanes 4, 8, and 10). Autoradiographic exposure times were 4 hours for λ_{II} and 12 hours for λ_I, with probes of equal specific radioactivity. The total RNA content of suppressed MOPC-315 cells was approximately 20 percent less than that of the controls; this disparity may account for the slightly higher relative concentration of heavy chain transcripts in RNA from suppressed cells (*11*).

trol T lymphocytes. In contrast, only 1 percent of plasmacytes grown in coculture with M315-immune T cells showed detectable secretory activity, a 97 percent inhibition of secretion relative to the control. Similarly, under membrane-segregated culture conditions, T cells from M315-immune mice inhibited M315 secretory activity by 83 percent relative to the control. The specificity of this suppressor activity for the M315 idiotype was demonstrated earlier (*8*). As in the earlier studies (*8*), there were only minimal differences in viability between MOPC-315 cells exposed to M315-immune or control T cell preparations under a given set of culture conditions.

To determine the levels of immunoglobulin mRNA underlying these differences in immunoglobulin secretion, polyadenylated [poly(A)] RNA was isolated from MOPC-315 cells in each group, subjected to agarose gel electrophoresis under denaturing conditions, transferred to nitrocellulose membranes, and probed for RNA sequences complementary to specific cloned DNA fragments. When poly(A) RNA from MOPC-315 cells cocultured with control T cells was hybridized to a labeled probe specific for the λ_{II} C-region coding sequence, autoradiography revealed a single λ_{II} transcript 1.2 kilobases (kb) in length, representing mature-sized λ_{II} mRNA (*7*) (lane 1 in Fig. 1). Exposure to suppressor T cells drastically reduced the concentration of this λ_{II} transcript (lane 2). Densitometric analysis of such autoradiograms indicated that the concentration of λ_{II} transcripts in suppressed cells was clearly less than 10 percent of the control value; however, the image density of the λ_{II} band in RNA from suppressed cells was too low for more precise quantification. Similar results were observed in membrane-segregated cultures (lanes 3 and 4), although the inhibition of λ_{II} mRNA expression (like the inhibition of M315 secretion) was less complete than in direct coculture.

Analysis of these same RNA preparations with a hybridization probe specific for the λ_I C region (lanes 5 to 8) also revealed a single complementary species. Because a large portion of the coding sequence for the variable region is absent from this anomalous λ_I transcript (*7*), it was easily distinguished from λ_{II} mRNA by its smaller size (1.0 kb). Changes in the concentration of the λ_I transcript precisely paralleled those observed for λ_{II} mRNA; exposure to either suppressor T cells or soluble suppressor factors resulted in a marked decline in the concentration of RNA derived from the excluded λ_I gene. In contrast, the concentration of α heavy chain mRNA in these cells was not significantly decreased by suppressor T cell action (lanes 9 and 10), implying that the inhibition of light chain RNA expression is relatively selective and is not merely a result of nonspecific RNA degradation. The persistently high levels of α chain mRNA are surprising in view of the absence of heavy chain protein synthesis in suppressed MOPC-315 cells and suggest that heavy and light chain expression may be inhibited through fundamentally different mechanisms. The regulation of heavy chain synthesis during idiotype-specific suppression has been examined (*11*).

Our studies indicate that suppressor T cell action can selectively inhibit the expression of light chain mRNA in immunoglobulin-secreting cells. To produce such an effect, the suppressive factors must either decrease the rate of synthesis of light chain–specific transcripts or enhance the rate of degradation of these transcripts in the nucleus or cytoplasm of the target cell. In addition, we find that suppressor factors directed against the idiotype of a secreted immunoglobulin not only affect the secreted light chain, but can simultaneously block the expression of mRNA representing a different light chain isotype. This coordinate regulation occurs despite the finding that the rearranged λ_I and λ_{II} genes reside on different chromosomes in MOPC-315 (*12*) and demonstrates that excluded light chain genes can be subject to immunoregulatory control.

Our findings can be contrasted with those of Abbas *et al.* (*13*), who have studied the effects of suppressor T cell action on a murine myeloma-myeloma hybrid line (MOPC-315 × MPC-11) secreting both κ and λ_{II} light chains. They report that idiotype-specific suppression of one light chain isotype has no effect on secretion of the other. This apparent discrepancy could be due to anomalous properties of the hybridoma system. An alternative interpretation is that, while the various λ isotypes are coordinately regulated as a group, the control of κ gene expression may be mediated through an independent mechanism (*14*). In this regard, it may be significant that the λ_I and λ_{II} C-region genes show a considerably higher degree of nucleotide sequence homology to each other than to the κ locus (*15*), reflecting a close evolutionary relationship between the λ genes (*16*). The variable region coding elements of λ_I and λ_{II} also exhibit substantial sequence homology; this homology extends several kilobases upstream from the coding regions themselves (*7, 16*). Coordinate regulation of λ_I and λ_{II} gene expression in MOPC-315 may reflect the presence of conserved regulatory sequences common to both genes.

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References and Notes

1. T. Cotner and H. N. Eisen, *J. Exp. Med.* **148**, 1388 (1978); T. Azuma, L. Steiner, H. N. Eisen, *Proc. Natl. Acad. Sci. U.S.A.* **78**, 569 (1981); J. Miller, E. Selsing, U. Storb, *Nature (London)* **295**, 428 (1982).
2. P. Early and L. Hood, *Cell* **24**, 1 (1981).
3. C. Brack, M. Hirama, R. Lenhard-Schuller, S. Tonegawa, *ibid.* **15**, 1 (1978); J. G. Seidman and P. Leder, *Nature (London)* **276**, 790 (1978); P. W. Early, M. M. Davies, D. B. Kaback, N. Davidson, L. Hood, *Proc. Natl. Acad. Sci. U.S.A.* **76**, 857 (1979).
4. P. A. Hieter, S. J. Korsmeyer, T. A. Waldmann, P. Leder, *Nature (London)* **290**, 368 (1981); C. Coleclough, R. P. Perry, K. Karjalainen, M. Weigert, *ibid.*, p. 372.
5. F. W. Alt, V. Enea, A. L. M. Bothwell, D. Baltimore, *Cell* **21**, 1 (1980).
6. S. J. Korsmeyer, P. A. Hieter, J. V. Ravetch, D. G. Poplack, T. A. Waldmann, P. Leder, *Proc. Natl. Acad. Sci. U.S.A.* **78**, 7096 (1981).
7. A. L. M. Bothwell, M. Paskind, R. C. Schwartz, G. E. Sonenshein, M. L. Gefter, D. Baltimore, *Nature (London)* **290**, 65 (1981); R. C. Schwartz, G. E. Sonenshein, A. Bothwell, M. L. Gefter, *J. Immunol.* **126**, 2104 (1981).
8. G. L. Milburn and R. G. Lynch, *J. Exp. Med.* **155**, 852 (1982).
9. J. W. Rohrer, B. Odermatt, R. G. Lynch, *J. Immunol.* **121**, 1799 (1978).
10. J. W. Rohrer, K. Vasa, R. G. Lynch, *ibid.* **119**, 861 (1977).
11. G. L. Milburn, T. G. Parslow, C. Goldenberg, D. K. Granner, R. G. Lynch, *J. Cell. Mol. Immunol.*, in press.
12. N. Hozumi, G. Wu, H. Murialdo, R. Baumal, T. Mosmann, L. Winberry, A. Marks, *J. Immunol.* **129**, 260 (1982).
13. A. K. Abbas, S. J. Burakoff, M. L. Gefter, M. I. Greene, *J. Exp. Med.* **152**, 969 (1980).
14. This hypothesis could not be tested in MOPC-315 cells, which contain no detectable κ genes (*5*); T. Parslow, unpublished manuscript.
15. When aligned for maximal amino acid homology, the nucleotide sequences encoding λ_I and λ_{II} constant regions differ from each other at 26 percent of residues, while each differs from the κ coding sequence at approximately 51 percent of residues. Differences occur uniformly throughout the sequences in each case. M. O. Dayhoff, *Atlas of Protein Sequence and Structure* (National Biomedical Research Foundation, Washington, D.C., 1972); E. E. Max, J. V. Maizel, P. Leder, *J. Biol. Chem.* **256**, 5116 (1981); and (*15*).
16. E. Selsing, J. Miller, R. Wilson, U. Storb, *Proc. Natl. Acad. Sci. U.S.A.* **79**, 4681 (1982).
17. V. Glisin, R. Crkvenjakov, C. Byus, *Biochemistry* **13**, 2633 (1974).
18. N. Rave, R. Crkvenjakov, H. Boedtker, *Nucleic Acids Res.* **6**, 3559 (1979).
19. P. S. Thomas, *Proc. Natl. Acad. Sci. U.S.A.* **77**, 5201 (1980).
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