the *ras* proto-oncogene family also encode similar proteins with respect to size (p21), localization (cytoplasmic membranes), and biochemical properties (binding of guanine nucleotides) (*19*). Functional studies done with the c-*myc* protein have shown it to have a binding affinity for DNA (*17, 20*). It seems likely that N-*myc* also will have an affinity for DNA, based on the numerous basic amino acids found in its COOH terminus. Antibody reagents generated to defined regions of the N-*myc* protein such as those described in this study could prove useful in identifying functional domains.

In addition, antisera to N-*myc* may also have potential clinical utility. The two N-*myc*–specific antisera (II and III) identified for use in histochemical analyses in this study proved to be highly specific for neuroblastoma cells. This could be useful in the sometimes difficult task of differential diagnosis in patients having one of the small round cell tumors of childhood. This group of tumors includes neuroblastomas, neuroepitheliomas, Ewing sarcomas, rhabdomyosarcomas, and lymphomas (*21*). The clinical treatment of these tumors differs greatly; neuroblastomas are not treated in the same manner as lymphomas or Ewing sarcomas. There is evidence that Ewing sarcomas and neuroepitheliomas do not express appreciable levels of N-*myc* (*22*). This is also likely to be true for rhabdomyosarcomas and lymphomas as they are not of neural origin. Thus, a specific histochemically reacting antibody for N-*myc* might be a possible diagnostic reagent. Also, the intensity with which neuroblasts are stained could prove useful in identifying micrometastases in nonprimary sites such as lymph nodes or bone marrow. Finally, correlation of expression of amount of a given proto-oncogene protein with ultimate disease prognosis may be possible with an antibody reagent. Precedent for this already exists with staining for the *ras* gene product in prostatic cancer (*23*).

The identification of the N-*myc* protein and the generation of defined and specific antisera to it should prove helpful in elucidating the role of this gene in human malignancies such as neuroblastoma and small cell lung carcinoma.

REFERENCES AND NOTES

1. M. Schwab *et al.*, *Nature (London)* **305**, 245 (1983).
2. N. E. Kohl *et al.*, *Cell* **35**, 359 (1983).
3. M. Schwab, H. E. Varmus, J. M. Bishop, *Nature (London)* **316**, 160 (1985).
4. J. L. Biedler and B. A. Spengler, *J. Nat. Cancer Inst.* **57**, 683 (1976).
5. J. L. Biedler *et al.*, in *Advances in Neuroblastoma Research*, A. E. Evans, Ed. (Raven, New York, 1980), pp. 81–96.
6. G. M. Brodeur *et al.*, *Science* **224**, 1121 (1984).
7. W. H. Lee, A. L. Murphee, W. F. Benedict, *Nature (London)* **309**, 458 (1984).
8. R. C. Seeger *et al.*, *N. Engl. J. Med.* **313**, 1111 (1985).
9. H. Okayama and P. Berg, *Mol. Cell. Biol.* **2**, 161 (1982).
10. N. E. Kohl *et al.*, *Nature (London)* **319**, 73 (1986).
11. D. J. Slamon *et al.*, *Science*, in press.
12. D. J. Slamon *et al.*, *ibid.* **228**, 1427 (1985).
13. D. J. Slamon, unpublished data.
14. S. R. Hann and R. N. Eisenman, *Mol. Cell. Biol.* **4**, 2486 (1984).
15. A. L. Goldberg and A. C. St. John, *Annu. Rev. Biochem.* **45**, 747 (1976).
16. W. J. Boyle *et al.*, *Mol. Cell. Biol.* **5**, 3017 (1985).
17. R. N. Eisenman *et al.*, *ibid.* p. 114.
18. M. M. Nau *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **83**, 1092 (1986).
19. J. M. Bishop, *Annu. Rev. Biochem.* **52**, 301 (1983).
20. H. Persson and P. Leder, *Science* **225**, 718 (1984).
21. A. J. Triche and F. B. Askin, in *Pathology of Neoplasia in Children and Adolescents*, M. Feingold, Ed. (Saunders, Philadelphia, in press).
22. M. Israel, personal communication.
23. M. V. Viola *et al.*, *N. Engl. J. Med.* **314**, 133 (1986).
24. D. J. Slamon *et al.*, *Science* **224**, 256 (1984).
25. D. J. Slamon *et al.*, *ibid.* **226**, 61 (1984).

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Activation of Mouse T-Helper Cells Induces Abundant Preproenkephalin mRNA Synthesis

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Antigenic or mitogenic stimulation of T cells induces the secretion of an array of protein hormones that regulate immune responses. Molecular cloning has contributed strongly to our present understanding of the nature of this regulation. A complementary DNA (cDNA) library prepared from a cloned concanavalin A–activated mouse T-helper cell line was screened for abundant and induction-specific cDNA's. One such randomly chosen cDNA was found to encode mouse preproenkephalin messenger RNA (mRNA). Preproenkephalin mRNA represented about 0.4 percent of the mRNA in the activated cell line but was absent in resting cells of this line. Other induced T-helper cell lines have 0.1 to 0.5 percent of their mRNA as preproenkephalin mRNA. Induced T-helper cell culture supernatants have [Met]enkephalin-immunoreactive material. The production by activated T cells of a peptide neurotransmitter identifies a signal that can potentially permit T cells to modulate the nervous system.

HELPER T CELLS CAN INDUCE B cells to secrete antibody and can stimulate monocytes, mast cells, and cytotoxic T cells to divide or differentiate. Such T cells, when activated by an antigen or lectin, produce an array of secreted proteins known as lymphokines, which have immunoregulatory activities. Examples of such proteins in the mouse immune system are γ-interferon (γ-IFN), interleukin-2 (IL-2), interleukin-3 (IL-3), and granulocyte-macrophage colony-stimulating factor (GM-CSF) (*1*).

Radiolabeling experiments have shown that, on activation of resting T-helper cells, about 15 percent of newly synthesized proteins appear as secreted products (*2*). In such experiments more secreted protein species are detected than can be accounted for by previously characterized lymphokines. We reasoned that it was important to clone and characterize genes encoding secreted proteins of unknown identity in the hope that they have an as yet undiscovered role in T cell–mediated immune responses. We used a complementary DNA (cDNA) library prepared from the messenger RNA (mRNA) of concanavalin A (Con A)–induced C1.Ly1$^+$2$^-$/9 mouse T-helper cells (*3*). When induced, this cloned T cell line produces secreted activities that regulate the growth and differentiation of lymphoid and myeloid cells (*4*). The cDNA library was probed with ^{32}P-labeled cDNA prepared from oligodeoxythymidine-primed poly(A) mRNA from both resting and induced cells. Approximately 10 percent of the clones hybridized strongly with induced cell probe, but not with resting cell probe. This report describes the characterization of TY3, one such randomly chosen clone.

Clones hybridizing to induction-specific cDNA clone TY3 accounted for about 0.4 percent of the total cDNA's in the library. Hybridization experiments with known lymphokine probes established that TY3 cDNA's do not encode γ-IFN, GM-CSF,

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IL-2, or IL-3. DNA sequence analysis of the TY3 cDNA revealed 475 residues proximal to a poly(A) tail. The 5′ part of this sequence has two open reading frames of 55 and 26 amino acids, respectively. Given the shortness of these potential coding regions, we rescreened the cDNA library for TY3-related clones with larger inserts. Two such clones were characterized. Clone TY3.2 has a 680–base pair (bp) cDNA insert whose 3′ end has complete homology to the TY3 sequence. The sequence of the TY3.2 cDNA shows a 126-residue open reading frame that extends the 55-residue coding region of TY3 (Fig. 1). Another clone, TY3.9, has a 1025-bp cDNA insert whose 3′ end has complete homology to the TY3 and TY3.2 sequences. This longest clone shows a 241-residue open reading frame that extends the TY3 and TY3.2 open reading frames (Fig. 1). The coding region has 97 percent amino acid and 93 percent nucleotide sequence homology to a previously determined rat brain preproenkephalin mRNA sequence (*5*).

Rat brain preproenkephalin, like the bovine and human proteins, is a secreted protein [the primary translation product has a 24-residue leader (*5*)] and encodes seven enkephalin units. The TY3.9 cDNA, by comparison with the rat sequence, lacks 28 codons of the coding region. The amino acid sequence changes between rat and mouse do not affect the postulated proteolytic cleavage sites or the [Met]enkephalin, [Leu]enkephalin, or [Met]enkephalin-Arg^6-Phe^7 products, but the [Met]enkephalin-Arg^6-Gly^7-Leu^8 product is [Met]enkephalin-Arg^6-Ser^7-Leu^8 in the mouse (Fig. 1). This last difference may be the first reported heterogeneity among the enkephalins, since all the enkephalin units are conserved among humans, cows, and rats (*5*).

Figure 2 shows an RNA blot of T cell mRNA with TY3.2 cDNA used as a probe. The estimated size of mouse T cell preproenkephalin mRNA is 1300 residues. As expected from the procedure used for selecting TY3, this mRNA is undetectable in resting T cells and is extremely abundant in induced T cells.

These results demonstrate that stimula-

```
          asp cys ala lys cys ser try arg leu val arg pro gly asp
GGGGGGG GAC TGC GCT AAA TGC AGC TAC CGC CTG GTT CGC CCA GGC GAC
        1                                       a   t   c

ile asn phe leu ala cys thr leu glu cys glu gly gln leu pro ser
ATC AAT TTC CTG GCG TGC ACA CTG GAA TGT GAA GGA CAG CTG CCT TCT
    c           a           c                   g

                                                        lys
phe lys ile trp glu thr cys lys asp leu leu gln val ser arg pro
TTC AAA ATC TGG GAG ACC TGC AAG GAT CTC CTG CAG GTG TCC AGG CCC
            100                                         A

glu phe pro trp asp asn ile asp met tyr lys asp ser ser lys gln
GAG TTC CCT TGG GAT AAC ATC GAC ATG TAC AAA GAC AGC AGC AAA CAG


asp glu ser his leu leu ala lys lys TYR GLY GLY PHE MET lys arg
GAT GAG AGC CAC TTG CTA GCC AAG AAG TAC GGA GGC TTC ATG AAA CGG
                200                   t       g
                                                  val
TYR GLY GLY PHE MET lys lys met asp glu leu tyr pro met glu pro
TAC GGA GGC TTC ATG AAG AAG ATG GAC GAG CTA TAT CCC ATG GAG CCA
  t                             t       t   c     G

glu glu glu ala asn gly gly glu ile leu ala lys arg TYR GLY GLY
GAA GAA GAA GCG AAC GGA GGA GAG ATC CTT GCC AAG AGG TAT GGC GGC
          g   c   t   300 c                                 t

PHE MET lys lys asp ala asp glu gly asp thr leu ala asn ser ser
TTC ATG AAG AAG GAT GCA GAT GAG GGA GAC ACC TTG GCC AAC TCC TCC


asp leu leu lys glu leu leu gly thr gly asp asn arg ala lys asp
GAT CTG CTG AAA GAG CTA CTG GGA ACG GGA GAC AAC CGT GCG AAA GAC
  c                         400   a                         t
                                                  ser thr
ser his gln gln glu ser thr asn asn asp glu asp     met ser lys
AGC CAC CAA CAA GAG AGC ACC AAC AAT GAC GAA GAC     ATG AGC AAG
              g   a                   t         AGC  C
                                GLY
arg TYR GLY GLY PHE MET ARG SER LEU lys arg ser pro gln leu glu
AGG TAT GGG GGC TTC ATG AGA AGC CTC AAA AGA AGC CCC CAA CTG GAA
                          G       500             G

asp glu ala lys glu leu gln lys arg TYR GLY GLY PHE MET arg arg
GAT GAA GCA AAA GAG CTG CAG AAG CGC TAC GGG GGC TTC ATG AGA AGG
  c         g                       t

val gly arg pro glu trp trp met asp tyr gln lys arg TYR GLY GLY
GTG GGA CGC CCC GAG TGG TGG ATG GAC TAC CAG AAG AGG TAT GGG GGC
  c   g                           t   600     a   c   a

PHE LEU lys arg phe ala glu ser leu pro ser asp glu glu gly glu
TTC CTG AAG CGC TTT GCT GAG TCT CTG CCC TCT GAT GAA GAA GGC GAA
                                  a       g
ser                               met
asn tyr ser lys glu val pro glu ile glu lys arg TYR GLY GLY PHE
AAT TAC TCG AAA GAA GTT CCT GAG ATA GAG AAA AGA TAC GGG GGC TTT
 G        t               c       G   a       700   g
```

Fig. 1. Nucleotide sequence of TY3.9 cDNA. The sequence is shown as triplets over the preproenkephalin-coding region, and the numbering starts at the first codon. Differences between the TY3.9-coding region and rat preproenkephalin cDNA (*5*) are shown below the sequence, and those that result in coding changes are in uppercase. Amino acids encoded by the triplets are shown above the sequence, as are differences between the rat and mouse sequences. Note that the rat sequence has an additional codon. Enkephalin peptides are in uppercase and boldface. The sequence was determined by a combination of the dideoxy and chemical degradation (*14, 19*) methods.

```
MET ARG PHE
ATG CGG TTC TGA AGCCCTTTTCCAGCAGTGACCCCGACCCCCACTAGCCTGCTCCATCC
           t
CCCATGAGCAACTGCCTTGTCAATGATGTTTCTTGTCACATGCTGCTTTGTGCTGTACAGTTG
                                  800
CCCCCGTGGTCTAGATAACTACACTGCCTGAAAGCTGTGATTTTAGGGTCTGTGTTCTTTTGA

GTCTTGAAGCTCAGTATTGGTCTCTTATGGCTATGTTGTTATCAATAGTTTGTTACCTCATCT
   900
CTCCTGGATGAAACATCAATAAATGCTTATTGTATATAAATATAATAAACCCGTGACCCCAAC
                                        1000
TGCAAAAAAAAAAAAAAAAAAAAAAA
```

Table 1. Frequency of various cDNA's in two activated helper T cell libraries. Total library plasmid DNA's from Con A–activated C1.Ly1^{-}2^{+}/9 (*3*) and LB2-1 (*7*) helper T cells were used to transform JM101 (*12*). The cells were plated on nitrocellulose filters laid on ampicillin selection plates. Colonies were lysed with 0.5*M* NaOH and 1.5*M* NaCl, neutralized with 1*M* tris-HCl (*p*H 8.0) and 1.5*M* NaCl, and immobilized by drying at 37°C. Hybridizations were in 6× NaCl, sodium phosphate, EDTA buffer (SSPE) (*13*), 20% formamide, 0.1% sodium dodecyl sulfate, and transfer RNA (100 μg/ml) for 6 hours at 37°C. Probes were synthetic DNA's labeled with [γ-^{32}P]ATP (*14*). The sequences of the synthetics used were γ-IFN, bp 172 to 222 (*15*); GM-CSF, bp 10 to 35 (*16*); TY3, bp 232 to 282 (Fig. 1); TY5, bp 132 to 185 (*17*); IL-2, bp 254 to 273 (*7*); and IL-3, bp 292 to 339 (*3*). Filters were washed with 1× SSPE and 0.1% sodium dodecyl sulfate at room temperature. Values are based on counts of at least 10,000 cells. TY5 is an induction-specific clone encoding a secreted 8000-dalton protein of no known function (*17*).

Probe	Positive (%)	
	C1.Ly1^{+}2^{-}/9	LB2-1
γ-IFN	<0.005	1.5
GM-CSF	0.01	0.3
TY3	0.4	0.1
TY5	0.7	0.3
IL-2	<0.005	0.3
IL-3	0.1	0.6

tion of a cloned T-helper cell line by a mitogen induces the synthesis of an abundance of preproenkephalin mRNA. We estimate that about four-thousandths of the mRNA's in such a cell encode preproenkephalin. The classical sites of enkephalin synthesis are the adrenal medulla (*6*), where the mRNA frequency is about 1 per 1000, and the brain (less than 1 per 3000) (*5*). Thus the C1.Ly1^{+}2^{-}/9 cell line can synthesize significant amounts of enkephalins.

To determine whether the expression of preproenkephalin mRNA in activated T cells is a more general phenomenon, we examined the frequency of TY3.2 hybridizing clones in cDNA libraries prepared from different T-helper cell lines. Table 1 shows that activated LB2-1 (*7*), which has a pattern of lymphokine induction distinct from that of C1.Ly1^{+}2^{-}/9, made 0.1 percent of its mRNA specific for preproenkephalin. As a point of reference, Table 1 includes a measurement of the frequency of known lymphokines in the two cDNA libraries tested. The frequency of preproenkephalin mRNA is within the range of known and characterized lymphokines present in these libraries. We also determined that cDNA libraries prepared from two other activated T-helper cell lines, C1.Ly1-T1 and C1.Ly1-N5 (*8*), contained, respectively, 0.5 and 0.1 percent TY3.2 hybridizing clones.

The abundant synthesis of preproenkephalin mRNA by activated T-helper cells indicates that such cells secrete proenkephalin or processed derivatives such as the enkephalins. We assayed the culture supernatants of various T-helper cell lines to determine if they contain materials that are recognized by antibody to [Met]enkephalin in radioimmunoassays (Table 2). Immunoreactive material was not present in significant amounts in the culture supernatant of uninduced C1.Ly1^{+}2^{-}/9, but was present in culture supernatants of all four induced T-helper cell lines tested. Our cDNA analysis and [Met]enkephalin assays show that all six independently derived T-helper cell lines examined can synthesize enkephalins.

Much interest has been focused on the relation between the immune and nervous systems, with many reports showing interactions between the two systems (*9*). Not only have various neurotransmitters been shown to have diverse regulatory effects on lymphocytic cells (*9, 10*), but lymphocytes are now known to have receptors for many

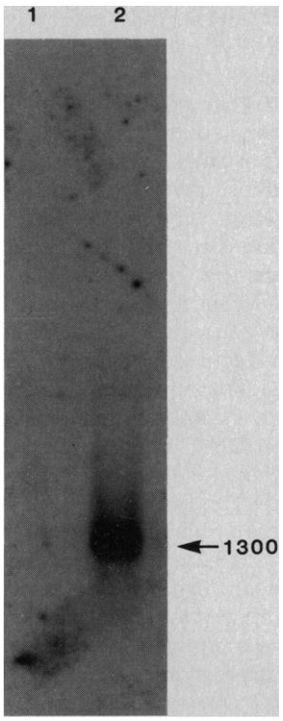

Fig. 2. RNA blot analysis of T cell preproenkephalin mRNA induction. A Pst I subclone of TY3.9 cDNA was labeled with ^{32}P by nick translation (*13*). Ten micrograms of poly(A)-selected mRNA from uninduced (lane 1) and Con A–induced C1.Ly1^{+}2^{-}/9 cells (lane 2) were denatured with formaldehyde and separated on a 1% agarose-formaldehyde gel, transferred to nitrocellulose, and hybridized to the nick-translated probe (*3*).

neurotransmitters (*9, 11*). Our results establish that T cells accumulate preproenkephalin mRNA on activation and that the preproenkephalin gene of T cells is induced along with lymphokines and unidentified proteins synthesized in response to a lectin activation signal. It will be important to demonstrate that physiologically relevant antigenic signals also activate preproenkephalin mRNA synthesis in cloned T-helper cell lines. An understanding of the role of enkephalin released by activated T-helper cells in immune responses will also depend on defining the target cells for this hormone. Enkephalin may simply be serving as another lymphokine and be targeted toward other lymphocytic cells in, for example, a site of inflammation. But it is equally likely that enkephalin may be serving as a signal mediating interactions between the immune and neuroendocrine systems.

Table 2. Assay for [Met]enkephalin in various Con A–induced T cell supernatants. T cells at the indicated concentrations were incubated in medium (*18*) containing Con A at 37°C. The MB2-1 and M264-39 T-helper cell lines have been described elsewhere (*18*). Before radioimmunoassay for [Met]enkephalin (Immuno Nuclear Corporation), 2-ml supernatant samples were acidified with 75 μl of 1*M* HCl and extracted with Sep-Pak C-18 reverse-phase cartridges (Waters Associates). The columns were washed with 20 ml of 4% acetic acid and eluted with 4 ml of methanol. Duplicate samples of dried eluates resuspended in bovine serum albumin–phosphate buffer were then assayed. Predicted concentrations for the unknown samples and their 95% fiducial limits were calculated with SAS programs (SAS Institute). The [Met]enkephalin values represent the concentration of immunoreactive material assumed to be [Met]enkephalin in the supernatants.

Cell line	Cells per milliliter (×10^{6})	Con A (μg/ml)	Time (hours)	[Met]enkephalin (pg/ml) (95% fiducial limits)
C1.Ly1^{+}2^{-}/9	0.2			11 (9 to 13)
C1.Ly1^{+}2^{-}/9	0.2	4	24	175 (149 to 206)
LB2-1	5	6	24	63 (53 to 73)
MB2-1	5	6	24	499 (420 to 596)
M264-39	0.5	10	28	589 (494 to 706)
Medium				12 (10 to 14)
Medium		4		7 (5 to 8)

REFERENCES AND NOTES

1. J. J. Oppenheim, S. Cohen, M. Landy, Eds., *Proceedings of the Third International Lymphokine Workshop* (Academic Press, New York, 1983).
2. T. R. Mosmann *et al.* unpublished manuscript.
3. T. Yokota *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **81**, 1070 (1984).
4. G. Nabel *et al.*, *ibid.* **78**, 1157 (1981).
5. R. D. Howells, *ibid.* **81**, 7651 (1984).

6. M. Noda *et al.*, *Nature (London)* **295**, 282 (1982).
7. T. Yokota *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **82**, 68 (1985).
8. G. J. Freeman *et al.*, *ibid.* **80**, 4094 (1983).
9. E. J. Goetzel, *J. Immunol.* **135**, 739s (1985).
10. D. G. Payan, J. D. Levin, E. J. Goetzl, *ibid.* **132**, 1601 (1984).
11. P. M. Mathews *et al.*, *ibid.* **130**, 1658 (1985).
12. J. Messing, R. Crea, P. H. Seeburg, *Nucleic Acids Res.* **9**, 309 (1981).
13. T. Maniatis, E. F. Fritsch, J. Sambrook, *Molecular Cloning: A Laboratory Manual* (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1982).
14. A. W. Maxam and W. Gilbert, *Methods Enzymol.* **65**, 499 (1980).
15. P. W. Gray and D. V. Goeddel, *Proc. Natl. Acad. Sci. U.S.A.* **80**, 5842 (1983).
16. N. M. Gough *et al.*, *Nature (London)* **309**, 763 (1984).
17. G. Zurawski, M. Benedik, T. R. Mosmann, B. J. Kamb, unpublished manuscript.
18. T. R. Mosmann *et al.*, *J. Immunol.*, in press.
19. F. Sanger, S. Nicklen, A. R. Coulson, *Proc. Natl. Acad. Sci. U.S.A.* **74**, 5463 (1977); C. M. Rubin and C. W. Schmid, *Nucleic Acids Res.* **8**, 4613 (1980).
20. We thank T. Yokota for cDNA libraries; T. R. Mosmann for his continuing encouragement and interest in T cell proteins with no known function; J. A. Zahner, B. Lewis, and G. Burget for help in preparing the manuscript; K. Pope for the excellent synthetic DNA's; A. Londhe for help in statistical treatment of radioimmunoassay data; and the DNAX staff and A. Goldstein for helpful comments.

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Geographic Origin of Benthic Foraminiferal Species

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Museum collections were used to document the worldwide Pliocene and Pleistocene fossil record of 59 species that now occur on the Atlantic continental margin of North America. Tabulation of these data indicates that benthic foraminifera evolve at all latitudes and in all parts of the world ocean rather than from some center or centers of origin. Dispersal in geologic time is very rapid.

THE CENTERS OF ORIGIN OF SPECIES have been discussed in the literature of biogeography and evolution for over a century. The classic scenario maintains that species evolve in the tropics and then disperse toward the higher latitudes (*1*). Recently, the Arctic and Antarctic were invoked as possible centers of origin (*2*). Much of this research centered on the origination of higher taxonomic units. In this report we examine the concept of centers of origin at the species level for benthic foraminifera.

The benthic foraminifera are abundant and ubiquitous and have an excellent fossil record. Thus they are ideal for biogeographic and evolutionary studies. Moreover, they have been the subject of intense study for over a century. The collection at the U.S. National Museum of Natural History contains about a half million identified slides of foraminifera. This collection and 11 others (*3*) are the basis for the data presented here.

The geographic distribution of over 800 species has been documented on the Atlantic continental margin of North America (*4*). These species also often occur elsewhere, and many benthic foraminiferal species are distributed worldwide (*5*). About one third of the modern species have a fossil record. Using collections, we documented the species durations for benthic foraminifera that occur on the Atlantic continental margin of North America (*6*). Our observations indicate that those species with a fossil record extending to the Miocene or older occur in sediments over a wide geographic area. Consequently, at our level of stratigraphic resolution, the geographic origination of a species cannot be determined. Attempting to minimize this difficulty, we examined the worldwide fossil record of species currently occurring on the Atlantic continental margin of North America and originating in the Pleistocene and Pliocene.

Table 1 shows the present distribution on the Atlantic continental margin and the fossil localities of species originating in the Pleistocene. Most of the sediments are late Pleistocene (younger than 12,000 years), and, even so, three species have their first fossil occurrence in both Alaska and Maine. Actually, the simultaneous recording of species from widely separated geographic areas is more common than the table shows because some of the species recorded in Alaska, Vancouver, and Maine have also been reported from Scandinavia and Baffin Island (*7*). (We have not included them in the table because we have not seen the specimens.) We do not, however, doubt that many of the species occur in North America as well as on the European continent, testifying to the rapid dispersal ability of benthic foraminifera. Of the 23 species that today are restricted to the north of Cape Hatteras, 22 were first recorded in the higher latitudes (Table 1). The three species restricted to the south of Cape Hatteras were first recorded in the lower latitudes. The three species that today occur from Florida to Newfoundland

Table 1. Modern distribution of benthic foraminifera on the Atlantic continental margin of North America and Pleistocene fossil localities. Abbreviations: CH, Cape Hatteras; NF, Newfoundland; FL, Florida; *n*, number of species.

Modern distribution	First fossil occurrence	*n*
CH–NF	Alaska	9
CH–NF	Netherlands	1
CH–NF	Alaska, Maine	3
CH–NF	Germany	2
CH–NF	Vancouver	2
CH–NF	Montreal	1
CH–NF	Maine	1
CH–NF	Massachusetts	2
CH–NF	Long Island	1
CH–NF	Southern California	1
FL–NF	Alaska	1
FL–NF	Vancouver	1
FL–NF	Maine	1
FL–CH	Southern California	1
FL–CH	Aruba	1
FL–CH	Northern Australia	1

Table 2. Modern distribution of benthic foraminifera on the Atlantic continental margin of North America and Pliocene fossil localities. For abbreviations used, see Table 1.

Modern distribution	First fossil occurrence	*n*
CH–NF	Netherlands	1
CH–NF	Northern California, Georges Bank	1
CH–NF	Italy	1
CH–NF	Southern California	2
CH–NF	Okinawa	1
CH–NF	Jamaica	1
FL–NF	Alaska	1
FL–NF	Georges Bank	1
FL–NF	Italy	1
FL–NF	Southern California	2
FL–NF	Jamaica	1
FL–NF	Dominican Republic	1
FL–CH	Italy	2
FL–CH	Southern California	1
FL–CH	North Carolina	1
FL–CH	Japan	1
FL–CH	Isle of Rhodes	1
FL–CH	Okinawa	1
FL–CH	Jamaica	5
FL–CH	Jamaica, Dominican Republic	1
FL–CH	Dominican Republic	2
FL–CH	Nicobar Island	1

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