

# EXHIBIT A

(12) **United States Patent**  
**Engelhardt et al.**

(10) **Patent No.:** **US 6,992,180 B1**  
 (45) **Date of Patent:** **Jan. 31, 2006**

(54) **OLIGO- OR POLYNUCLEOTIDES  
 COMPRISING PHOSPHATE-MOIEITY  
 LABELED NUCLEOTIDES**

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(Continued)

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(73) Assignee: **Enzo Life Sciences, Inc. c/o Enzo  
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(\* ) Notice: Subject to any disclaimer, the term of this  
 patent is extended or adjusted under 35  
 U.S.C. 154(b) by 0 days.

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 Bogdanos

(21) Appl. No.: **08/479,997**

(57) **ABSTRACT**

(22) Filed: **Jun. 7, 1995**

The present invention provides a nucleotide having the  
 formula,

**Related U.S. Application Data**

Sig-PM-SM-BASE

(60) Continuation of application No. 08/046,004, filed on  
 Apr. 9, 1993, now abandoned, which is a continuation  
 of application No. 07/532,461, filed on May 31, 1990,  
 now abandoned, which is a division of application  
 No. 07/140,980, filed on Jan. 1, 1988, now aban-  
 doned, which is a continuation of application No.  
 06/674,352, filed on Nov. 21, 1984, now abandoned,  
 which is a continuation of application No. 06/391,  
 440, filed on Jun. 23, 1982, now abandoned.

wherein PM is a phosphate moiety, SM is a sugar moiety and  
 BASE is a pyrimidine, purine or 7-deazapurine moiety. PM  
 is attached to the 3' or the 5' position of the sugar moiety  
 when the nucleotide is a deoxyribonucleotide and at the 2',  
 3' or 5' position when the nucleotide is a ribonucleotide.  
 BASE is attached to the 1' position of SM from the N<sup>1</sup>  
 position when BASE is a pyrimidine or the N<sup>9</sup> position when  
 BASE is a purine or 7-deazapurine. Sig is covalently  
 attached to PM directly or via a chemical linkage, and  
 represents a detectable moiety covalently attached to SM  
 directly or through a linkage group. Also provided are an  
 oligo- or polynucleotide comprising at least one such phos-  
 phate-moiety labeled nucleotide, and other compositions  
 including those wherein a polypeptide is terminally ligated  
 or attached to the oligo- or polynucleotide. The phosphate-  
 moiety labeled nucleotide, and the oligo- or polynucleotides  
 and other compositions comprising such phosphate-moiety  
 labeled nucleotides, are useful as diagnostic tools for detect-  
 ing analytes and as therapeutic agents.

(51) **Int. Cl.**  
**C12N 15/11** (2006.01)

(52) **U.S. Cl.** ..... **536/23.1**; 536/25.32

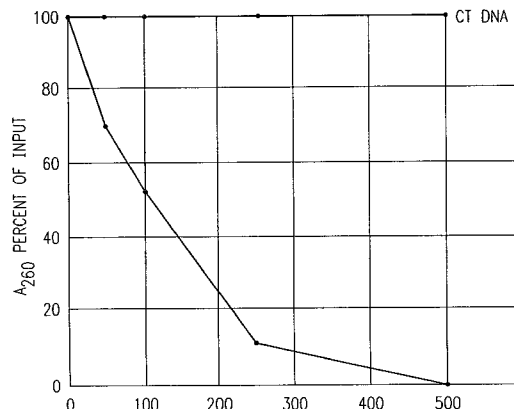
(58) **Field of Classification Search** ..... 435/6,  
 435/7.1; 536/26.6, 25.31, 25.32, 23.1  
 See application file for complete search history.

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**116 Claims, 4 Drawing Sheets**



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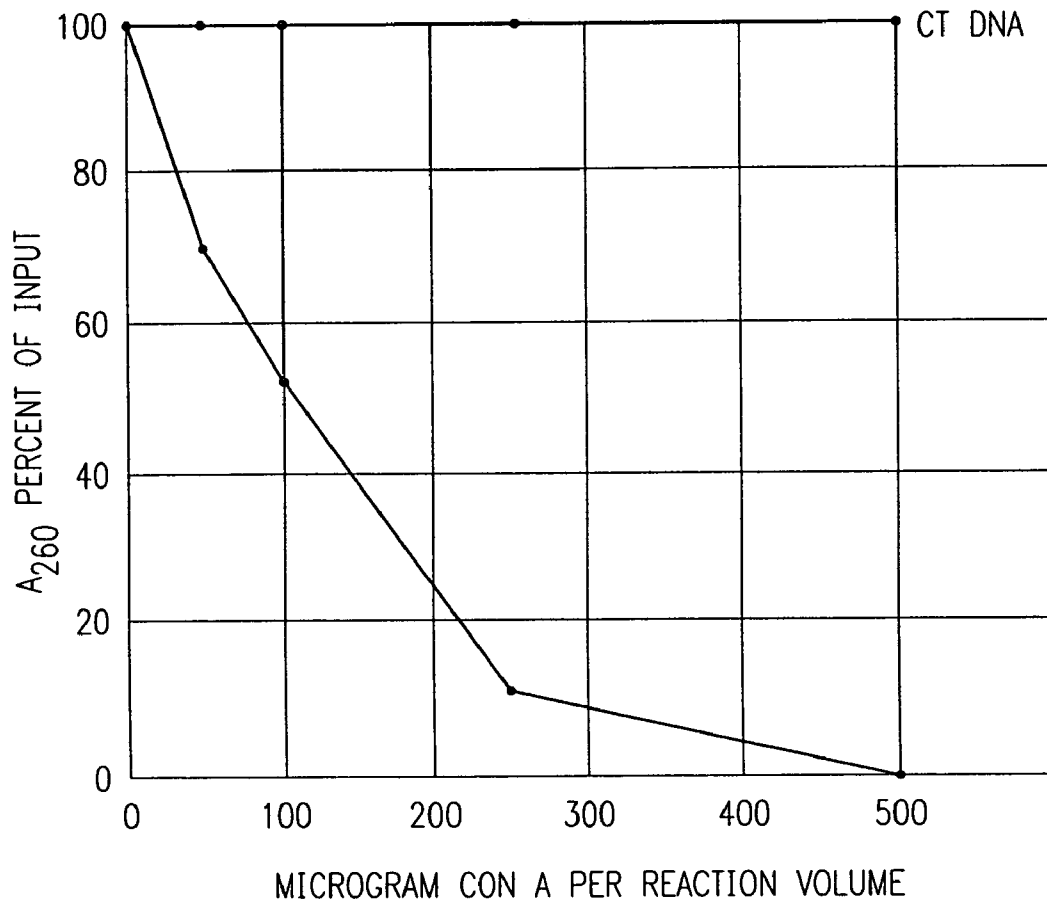
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FIG. 1



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