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PATENT APPLICATION SERIAL NO.

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE FEE RECORD SHEET

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LICENTA NO.

PTO-1556 (5/87)



Enclosed are:  [X] Declaration and Power of Attorney form(s)  [X] Three (3) sheets of drawings and two sets of soft copies  [X] Assignment(s) of the invention to Clontech Laboratories. Inc.						
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<del></del>	CLAIMS AS FILED  Number filed Number Ex	The second second second second	Fee			
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Name of person mailing paper

Sir:

DESCRIPTION

METHOD FOR FUNCTIONALIZING AND LABELING
THE 3' TERMINUS OF A SYNTHETIC OLIGONUCLEOTIDE USING
A UNIQUE MULTIFUNCTIONAL CONTROLLED PORE GLASS

(MF-CPG) REAGENT IN SOLID PHASE
OLIGONUCLEOTIDE SYNTHESIS

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## Background of the Invention

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Single base substitutions in human genes are the cause or are strongly associated with a variety of human diseases such as the hemoglobinopathies (Saiki, R.K., S. Scharf, F. Faloona, K.B. Mullis, G.T. Horn, H.A. Erlich, and N. // Arnheim [1985] Science 230:1350-1354; Embury, S.H., S.J. Scharf, R.K. Saiki, M.A. Gholson, M. Golbus, N. Arnheim, and H.A. Erlich [1987] N. Engl. J. Med. 316:656-660) and cancer (Liu, E., B. Hjelle, R. Morgan, F. Hecht, and J.M. // Bishop [1987] Nature 330:186-188; Rodenhuis, S., M.L. van de Wetering, W.J. Mooi, S.G. Evers, N. van Zandwijk, and J.L. Bos [1987] N. Engl. J. Med. 317:929-935). Previously, if no convenient restriction sites were altered by the base change, then the only recourse has been to clone and sequence the affected gene. Recently, polymerase chain reaction (PCR) amplification of the DNA segment in question, coupled with hybridization of specific oligonucleotide probes, has allowed sequence determination without the need for molecular cloning. The applicability of the latter technique is dependent on the availability of versatile and inexpensive oligonucleotide probes.

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Methods to covalently attach labels and reporter molecules to oligonucleotides have permitted their use as non-radioactive hybridization probes. New technologies in non-isotopic gene probes (Agrawal, S., C. Christodoulou, and M.J. Gait [1986] Nucl. Acids Res. 14:6227-6245; Connolly, B.A. [1987] Nucl.

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