

[54] INSULINOTROPIC HORMONE

[75] Inventor: Joel F. Habener, Newton, Mass.

[73] Assignee: The General Hospital Corporation,
Charlestown, Mass.

[21] Appl. No.: 532,111

[22] Filed: Jun. 1, 1990

Related U.S. Application Data

[63] Continuation of Ser. No. 148,517, Jan. 26, 1988, abandoned, which is a continuation-in-part of Ser. No. 859,928, May 5, 1986, abandoned.

[51] Int. Cl.⁵ A61K 37/02; A61K 37/28;
C07K 7/10; C07K 7/34

[52] U.S. Cl. 514/12; 514/866;
530/308; 530/324

[58] Field of Search 530/324, 303, 308;
514/12, 866

[56] References Cited

FOREIGN PATENT DOCUMENTS

0044168 1/1982 European Pat. Off. .

OTHER PUBLICATIONS

Uttenthal et al., J. Clin. End. Metab. 61=472-479 (1985).

Ghiglione et al., Diabetologia, 27=599-600 (1984).

Rudinger, Peptide Hormones, Parsons (Ed.) U. Park Press, Baltimore, pp. 1-7 (1976).

Schmidt et al., Diabetologia 28=704-707 (1985).

Bell et al., Nature, 302=716-718 (1983).

Andrews et al., J. Biol. Chem. 260=3910-3914.

Houghten, R. A. et al., *Biotechniques* 4:522-524, 526, 528 (Jul. 1986).

Meienhofer, J., In: *Peptides 1984*, Ragnarsson, U. (ed.) Almquist & Wiksell International, Stockholm (1984).

Sarson, D. L. et al., *Diabetologia* 22:33 (1982).

Hauner, H. et al., *Ann. Nutr. Metab.* 32:282-288 (1989).

Ganong, W., *Review of Medical Physiology*, 9th Ed., Lange Medical Publications, Los Altos, CA (1979) pp. 257-276.

Drucker, D. J. et al., *Proc. Natl. Acad. Sci. USA* 84:3434-3438 (1987).

Mojsov, S. et al., *J. Clin. Invest.* 79:616-619 (1987).

Holst, J. J. et al., *FEBS Lett.* 211:169-174 (1987).

Kreymann, B. et al., *The Lancet*, Dec. 5, 1987, pp. 1300-1304.

Weir, G. et al., *Diabetes* 38(3):338-342 (Mar. 1989).

Gefel, D. et al., *Endocrinology* 126 (4):2164-2168 (1990).

Primary Examiner—John Doll

Assistant Examiner—Christina Chan

Attorney, Agent, or Firm—Sterne, Kessler, Goldstein & Fox

[57] ABSTRACT

Derivatives of glucagon-like peptide I (GLP-1) have been found to have insulinotropic activity. The invention pertains to such derivatives, and to the use of such derivatives as a potential therapy for *Diabetes Mellitus*.

21 Claims, 6 Drawing Sheets

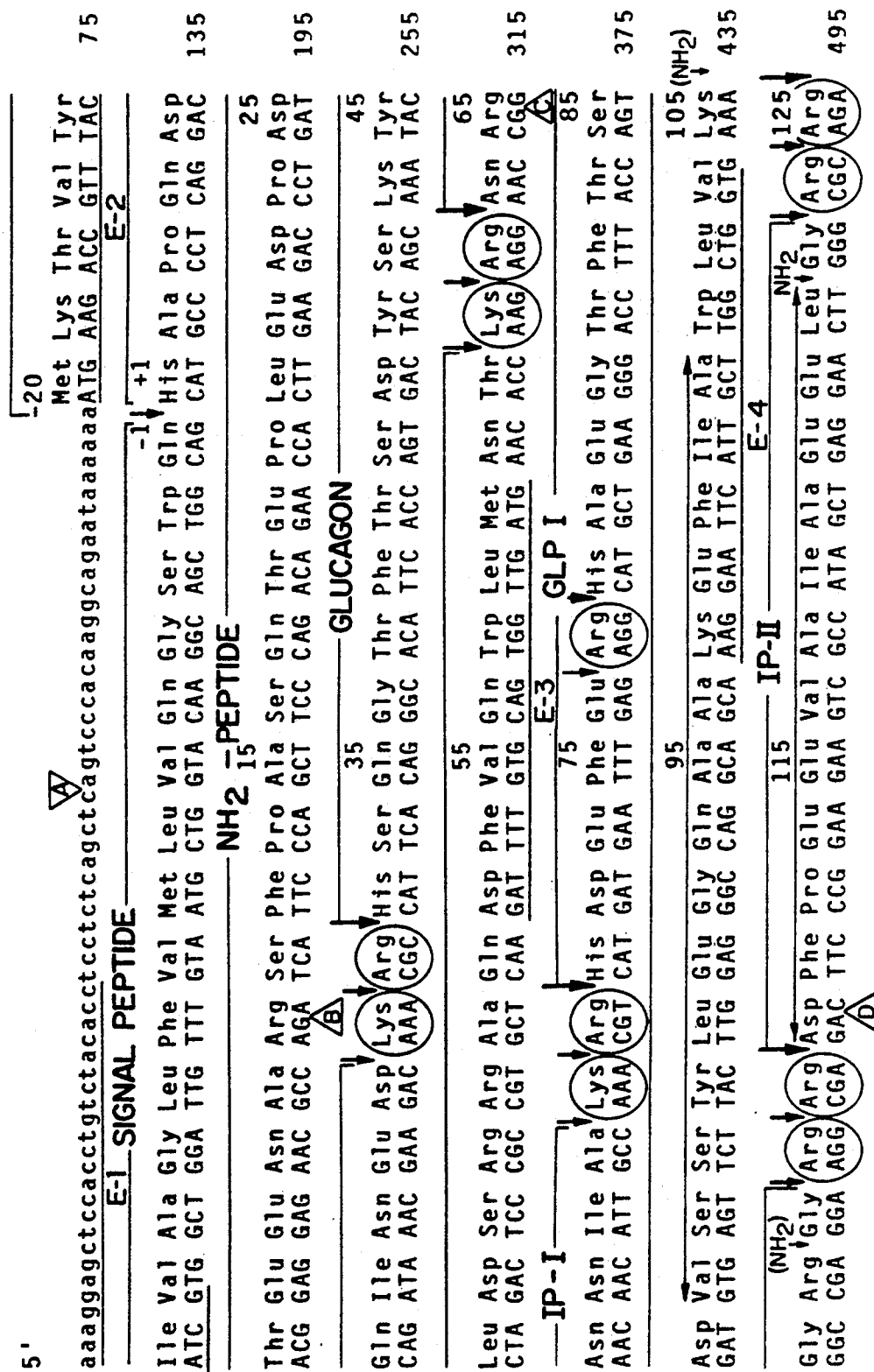


FIG. 1

135 GLP II 145
 His Ala Asp Gly Ser Phe Ser Asp Glu Met Asn Thr Ile Leu Asp Asn Leu Ala Thr Arg
 CAT GCT GAT GGA TCC TTC TCT GAT GAG ATG AAC ACG ATT CTC GAT AAC CTT GCC ACC AGA 555
 E-5
 Asp Phe Ile Asn Trp Leu Ile Gln Thr Lys Ile Thr Asp Lys Lys End
 GAC TTC ATC AAC TGG CTG ATT CAA ACC AAG AAG ATC ACT GAC AAG AAA TAG gaatatttcaccatt 618
 cacaaccatcttcacaacatctcctgcccagtcactgggatgtacatttgagagcgcataatccgaagctatactgcttgc 697
 atgcggaacgaatacatttccctttagcgttggtgaacccaaagggtgtaaatggaataaagttttccagggtgtgat 776
 aaagtaacaaactttacagtatgaaaaatgctggattctcaaatgtctcctcgttttgaagttaccgccctgagattact 855
 tttctgtggtataaaattgtaaattatcgcagtcacgcacacctggattacaacaacagaaacacatggtaacctggttaacc 933
 gtagtggtagaacctggaaagagaacttctccttgaaccctttgtcataaatgcgctcagcttcaatgtatcaagaat 1012
 agatttaataataatctcat 1024
 3'

FIG. 1 CONT.

STIMULATION OF cAMP IN RIN 1046-38

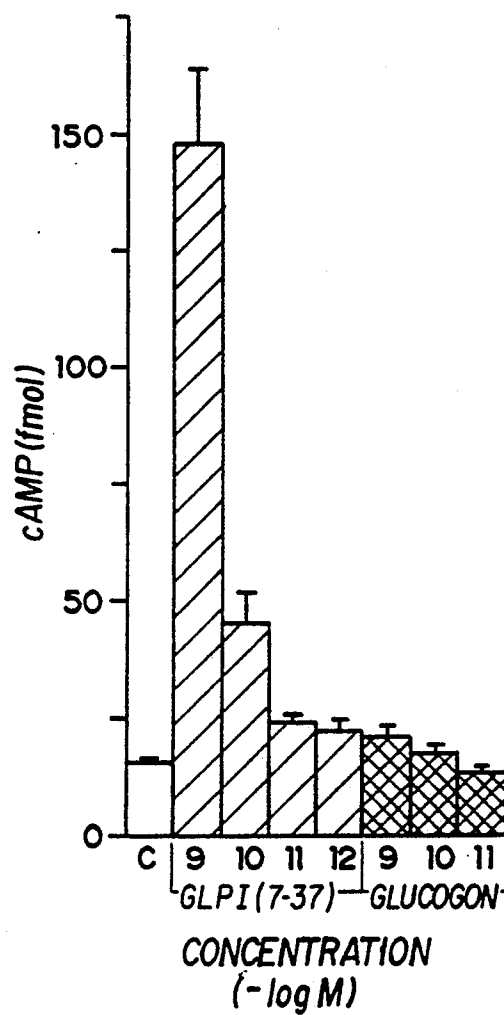


FIG. 2

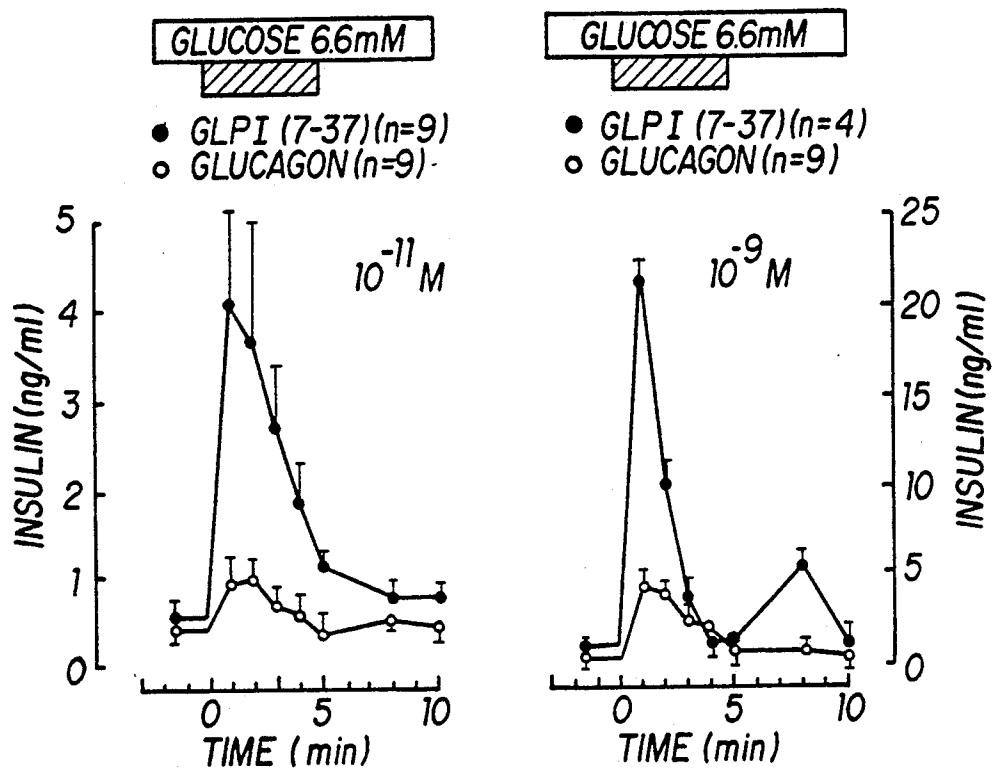


FIG. 3



Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.