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ASSIGNEE: Abbott Laboratories, North Chicago, IL
FILING & ISSUING DATA:
U.S. Patent No.: 4,370,417
Date Issued: January 25, 1983

This patent describes a modified plasmid with inserted DNA that codes for a plasminogen activator that is related to human urokinase. The modified plasmid can be introduced into a bacterium or other microorganism (e.g. *Escherichia coli, Saccharomyces cerevisiae, Bacillus subtilis,* or *Neurospora crassa*), which can then be cultured to produce urokinase-like material. Urokinase is a complex protein of unknown structure that is found in human urine in trace amounts. It promotes the dissolution of blood clots when injected in amounts far greater than those normally found in the blood. The *E. coli* plasmid pBR322 can be cleaved by a restriction enzyme and the 4 200 base pair plasminogen activator gene inserted. *E. coli* Transformant X1776 (pABB26), which produces the urokinase-like plasminogen activator protein, has been deposited with the ARS Culture Collection, U.S. Department of Agriculture, Peoria, IL (No. B12122).

*Country Codes:
Au = Australia
GB = Great Britain
DE = Federal Republic of Germany
DK = Denmark
HU = Hungary
US = United States
JP = Japan

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PATENT ANALYSIS

by Oskar R. Zaborsky

TITLE: Extrachromosomal Regulation of Expression
INVENTORS: John J. Sninsky, Mountain View, CA, and Stanley N. Cohen, Portolla Valley, CA
ASSIGNEE: The Board of Trustees of the Leland Stanford Jr. University, Stanford, CA
FILING AND ISSUING DATA:
U.S. Patent No.: 4,374,927
Date Issued: February 22, 1983

University professors are continuing to obtain patents with rather broad claims. This patent describes a method for producing poly(amino acids) using extrachromal elements such as linear or circular DNA segments which may change form in the cell. The elements may become circularized and supercoiled, and they are capable of replication in a host cell. The extrachromosomal element has a gene to produce the expression product (control factor), and this gene is controlled by an external modulator. The change in concentration of the control factor enhances the expression of a second gene that is involved with the production of the desired poly(amino acids) in the host microorganisms. This enhanced expression is accompanied by amplification of the poly(amino acid) producing gene. In this way, enhanced production of a peptide or protein is realized as a result of the change in concentration of the control factor and also because of the increase in the copy number of the product-producing gene.

The external modulator is a chemical or physical means external to the host cell for regulating the expression of a gene which produces the control factor. "Physical means" can include changes in temperature or light; "chemical means" can include a variety of effectors, some of which are known as inducers or corepressors. The preferred mode of activation of the runaway replication vector on the extrachromosomal element is by a change in temperature.

This patent addresses the important problems associated with the production of peptides and proteins when the microbial-produced product is detrimental to the growth of the host microorganism or when the rate of production of the desired product is offset by the rate of its degradation. Also, this method should be beneficial when the product of interest is only made in minute amounts compared to other proteins in the cell, and when isolation and separation become major barriers to economic viability.

An interesting side note to this patent is that the principals of the Cohen-Boyer patent application now being contested by Stanford University are also involved in this issuance: Stanley N. Cohen, the inventor, Bertram I. Rowland, the attorney representing the university, and Alvin E. Tanenholtz, the primary examiner at the U.S. Patent and Trademark Office. The patent application was filed on February 24, 1981.

TITLE: Process for Thymosin a_1
INVENTOR: Bernard L. Horecker, New York, NY
ASSIGNEE: Hoffman-La Roche, Inc., Nutley, NJ
FILING AND ISSUING DATA:
U.S. Patent No.: 4,374,197
Date Issued: February 15, 1983

This invention describes a method for the amino-terminal acetylation of a completed chain of a hormonal protein by ribosomal preparations having transacetylase activity. The selected amino terminus acetylation of desacetyl thymosin a_1 to thymosin a_1 is achieved in 15% conversion. Although the extent of conversion is low, process improvement should certainly increase this level.

Sources for the ribosome preparation include animal tissue such as thymus gland, liver, reticulocytes, pituitary gland, muscle, heart, kidney, brain, and skin. Plant cells such as wheat germ can also be employed. The preferred sources of ribosome preparations are the thymus gland and wheat germ. The acetylating agent is acetyl-Coenzyme A.

As pointed out in the patent, this method for acetylating the amino terminus of the desacetyl thymosin a_1 complements the solid state synthesis of this compound reported by Wong and Merrifield (1980) in Biochemistry **19:**3233–3239. Thymosin a_1 is useful in increasing T-cell numbers and normalizing immune function in patients with thymic-dependent primary immunodeficiency diseases and in cancer patients who are immunodepressed.

Oskar R. Zaborsky, Ph.D., is program director at the National Science Foundation and founding editor of Biotechnology Patent Digest.