CALIFORNIA STATE SCIENCE FAIR
2008 PROJECT SUMMARY

Name(s)

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Project Number

S0417

Project Title

Construction of an IGF-NAGLU Fusion Protein for Treatment of Sanfilippo B Syndrome

Abstract

Objectives/Goals

Mucopolysaccharidosis Type IIIB, also known as Sanfilippo B Syndrome, is a genetic disorder resulting from a deficiency of the enzyme alpha-N-Acetylglucosaminidase (NAGLU). Synthetic NAGLU has not effectively corrected this deficiency because it has poor cell uptake. Attaching an insulin-like growth factor II (IGF-II) tag to synthetic NAGLU may allow the enzyme to enter cells using the mannose-6-phosphate receptor. The goal of this project was to use recombinant DNA techniques to create a plasmid that coded for a NAGLU protein with an IGF-II tag.

Methods/Materials

IGF-II DNA was inserted into an initial plasmid pCI-Neo to produce pCI-IGF-II plasmids. Isolated NAGLU fragments were then inserted into this plasmid to create pIGF-NAGLU plasmids. At each step, the products yielded were verified and purified using gel electrophoresis.

Results

The intact pIGF-NAGLU plasmid underwent transformation and amplification using E. coli cells. About 700 colonies were produced, each containing a possible pIGF-NAGLU. Plasmids were extracted from the E. coli colonies, double digested, and screened using gel electrophoresis. Out of the 40 colonies already screened, none of the plasmids appear to have the exact configuration needed. More colonies will be screened to find the correct pIGF-NAGLU.

Conclusions/Discussion

This project has created a new plasmid, pCI-IGF-II. Preliminary evidence suggests that this plasmid can be used to produce a pIGF-NAGLU plasmid. Much work remains to identify the pIGF-NAGLU plasmid with the correct configuration to make the protein needed for effective enzyme replacement therapy for Sanfilippo B disease. The new plasmid pCI-IGF-II is an IGF-II tagging vector. It may allow the IGF-II tag to be attached to other synthetic enzymes besides NAGLU, to facilitate their entry into cells. This step could speed the development of effective enzyme replacement therapies for other diseases.

Summary Statement

This project used recombinant DNA techniques to create a plasmid coding for the NAGLU enzyme with an IGF-II tag which could be used to treate Sanfilippo B syndrome.

Help Received

Work performed under the supervision of Patricia Dickson, M.D. and Brigette Tippin, Ph.D., at Harbor-UCLA Medical Center.