New England Deaconess Hospital

Harvard Medical School

August 17, 1990

A.J. Melaragno
Captain, Medical Corps
United States Navy
Director of Research and Development
National Naval Medical Center
Bethesda, Maryland 20814-5044

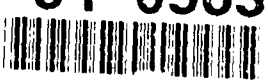
RE: Status Report for Grant # N00014-90-J-1847
Entitled "Development of Hematopoietic Growth Factors for Use in Military Personnel"

Dear Dr. Melaragno:

This grant was started on April 15, 1990. The present report delineates progress through May 31, 1990.

Project I: Human Erythropoietin

Prior to the start date of this grant, we were able to initiate some of the proposed studies on a very small scale. We have now begun to expand these studies as delineated in the grant proposal. Specifically, we have developed seven mutants of human erythropoietin in order to identify the active site of the hormone. Mutation of amino acids 99-109 of the hormone drastically alters the hormone's biological activity. Our preliminary conclusion is that amino acids 99-109 are very important for biological activity. We are now initiating a new series of mutations designed to focus on individual amino acids in this domain. The goal of these studies is to design new erythropoietin molecules with increased biological activity in vivo.



Project II: Erythroid Burst Promoting Activity

The goal of this project is to purify the B cell derived burst promoting activity (B-BPA) growth factor in order to obtain amino acid sequence, clone and express the gene, and initiate *in vivo* trials of this agent. We have begun to develop an animal model for the human B-BPA by testing conditioned medium from lymphocyte cultures of mice. At present we are developing the *in vitro* assays of mouse erythroid progenitor cells necessary to measure murine B-BPA. As soon as we are confident in our ability to carry out these assays, we will be able to begin to identify and characterize murine and other animal B-BPAs and initiate a purification program.

Sincerely yours,

Arthur J. Sytkowski, M.D.

AJS:rck

cc: Dr. Feldman
Research Administration

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