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May 27, 2004

Dr. Grant A. Krafft, Ph.D.
Chairman and Chief Scientific Officer
Acumen Pharmaceuticals, Inc.
1309 Evergreen Court
Glenview, Illinois 60025

Re: Japanese Patent Application No.: 10-533262
National Stage of International Patent App. No.: PCT/US98/02426
MBHB Ref. No.: 97-002-H

Grant:

We are pleased to report that the Japanese Patent Office has granted the patent application identified above and accorded it Japanese Patent Registration No. 3512815.

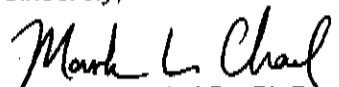
Enclosed please find an original Certificate of Patent as well as a copy of the issued patent. This patent will expire on February 5, 2018, provided that all annuities are timely paid. The next annuity for this patent will be due on January 16, 2007, and yearly thereafter. We will keep you apprised of these dates as they approach.

Also enclosed please find an English translation of the claims that were allowed. You may recall that in order to expedite prosecution of the present patent application, we cancelled the rejected claims that were directed to "compounds that block the formation of ADDLs" (in view of the disclosure of gossypol and tryptic peptides) as well as claims directed to the "treatment of Alzheimer's disease, etc." (in view of Japanese patent policy regarding medical treatment claims).

Please note, however, that we re-filed these rejected claims in a divisional patent application. We are considering alternative claim language for these claims in the divisional application; language that will be acceptable to the Japanese Patent Office. We will forward the particulars for the divisional application as they become available.

Please let me know if you need additional information or have any questions regarding this matter.

Sincerely,

A handwritten signature in black ink that reads "Mark L. Chael". The signature is written in a cursive style with a large, stylized "M" and "C".

Mark L. Chael, J.D., Ph.D.

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Enc.

Cc: Ms. Barbara Spiegel
Dr. John J. McDonnell, Esq.

TRANSLATION OF AMENDED CLAIMS

Filed: October 1, 2003

1. An isolated, soluble, non-fibrillar amyloid β protein assembly comprising 3 to 12 amyloid β proteins, wherein the amyloid β protein is the β 1-42 protein and wherein the assembly is neurotoxic.
2. The protein assembly according to claim 1 wherein the assembly comprises trimer, tetramer, pentamer, and hexamer aggregates of amyloid β protein.
3. The protein assembly according to claim 1 or 2 wherein the assembly has a molecular weight of about 26 kD to about 28 kD as measured by non-denaturing gel electrophoresis.
4. The protein assembly according to any of claims 1 to 3 wherein the assembly has a molecular weight of about 22 kD to about 24 kD or about 18 kD to about 19 kD as determined by electrophoresis on a 15% SDS-polyacrylamide gel.
5. The protein assembly according to any of claims 1 to 4 wherein the assembly has comprises globules with dimensions of about 4.7 nm to about 6.2 nm as measured by atomic force microscopy.
6. The protein assembly according to any of claims 1 to 5 wherein the assembly comprises globules with dimensions of about 4.9 nm to about 5.4 nm as measured by atomic force microscopy.

7. The protein assembly according to any of claims 1 to 5 wherein the assembly comprises globules with dimensions of about 5.7 nm to about 6.2 nm as measured by atomic force microscopy.

8. The protein assembly according to any of claims 1 to 5 wherein about 40% to about 75% of the assembly comprises globules with dimensions of about 4.9 nm to about 5.4 nm and dimensions of about 5.7 nm to about 6.2 nm, as measured by atomic force microscopy.

9. A method for assaying the effects of the protein assembly according to any of claims 1 to 8, the method comprising:

(a) administering the protein assembly to the hippocampus of an animal excluding human;

(b) applying an electrical stimulus; and

(c) measuring the cell body spike amplitude over time to determine the long-term potentiation response,

with the proviso that administration of the protein assembly is not done for therapy.

10. The method of claim 9, wherein the long-term potentiation response of the animal is compared to the long-term potentiation response of another animal treated in the same fashion except having saline administered instead of the protein assembly prior to application of the electrical stimulus.

11. A method for detecting in a test material the protein assembly of any of claims 1 to 8, the method comprising:

(a) contacting the test material with β amyloid specific antibody; and

(b) detecting binding of the antibody to the protein assembly.

12. A method for detecting in a test material the protein assembly of any of claims 1 to 8, the method comprising:

(a) contacting the test material with serum-starved neuroblastoma cells; and

(b) measuring morphological changes in the cells by comparing the morphology of the cells against neuroblastoma cells that have not been contacted with the test material.

13. A method for detecting in a test material the protein assembly of any of claims 1 to 8, the method comprising:

(a) contacting the test material with brain slice cultures; and

(b) measuring brain cell death as compared against brain slice cultures that have not been contacted with the test material.

14. A method for detecting in a test material the protein assembly of any of claims 1 to 8, the method comprising:

(a) contacting the test material with neuroblastoma cells; and

(b) measuring increases in Fyn kinase activity by comparing Fyn kinase activity in the cells against Fyn kinase activity in neuroblastoma cells that have not been contacted with the test material.

15. A method for detecting in a test material the protein assembly of any of claims 1 to 8, the method comprising:

(a) contacting the test material with cultures of primary astrocytes; and

(b) determining activation of the astrocytes as compared to cultures of primary astrocytes that have not been contacted with the test material.

16. A method for detecting in a test material the protein assembly of any of claims 1 to 8, the method comprising:

(a) contacting the test material with cultures of primary astrocytes; and

(b) measuring in the astrocytes increases in the mRNA for proteins selected from the group consisting of interleukin-1, inducible nitric oxide synthase, Apo E, Apo J, and α 1-antichymotrypsin by comparing the mRNA levels in the

astrocytes against the corresponding mRNA levels in cultures of primary astrocytes that have not been contacted with the test material.

17. A method for identifying compounds that modulate the effects of the protein assembly according to any of claims 1 to 8, the method comprising:

(a) administering either saline or a test compound to the hippocampus of an animal;

(b) applying an electrical stimulus;

(c) measuring the cell body spike amplitude over time to determine the long-term potentiation response; and

(d) comparing the long-term potentiation response of animals having saline administered to the long-term potentiation response of animals having test compound administered,

with the proviso that administration of the test compound is not done for therapy.

18. The method of claim 17 which further comprises administering the protein assembly to the hippocampus either before, along with, or after administering the saline or test compound, with the proviso that administration of the protein assembly is not done for therapy.

19. A method for identifying compounds that block the neurotoxicity of the protein assembly of any of claims 1 to 8, the method comprising:

