METHODS FOR ALZHEIMER'S DISEASE TREATMENT AND COGNITIVE ENHANCEMENT

The present invention relates to compositions and methods to modulate e-secretase and/or to improve cognitive ability. The invention further relates to the improved/enhanced cognitive ability in diseased individuals, particularly Alzheimer's Disease patients, and treatment thereof through increased sAPP production. Macrocyclic lactones (i.e., brostatin class and neristatin class) are compounds preferred for use with the present composition. The present invention also provides methods for increasing the generation of non-amyloidogenic soluble APP comprising the activation of protein kinase C (PKC) by administering an effective amount of PKC activator(s).
A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : A61K 31/35, 31/335
US CL : 514/450, 451, 449
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
U.S. : 514/450, 451, 449

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAS ONLINE MEDLINE BIOSIS search terms: bryostatin, neristatin, PKC activator, Alzheimer, dementia

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y</td>
<td>US 6,080,784 A (DRIEDGER et al) 27 June 2000 (27.06.2000), column 2, line 47 to column 3, line 4, and the claims.</td>
<td>1-36</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C. See patent family annex.

Date of the actual completion of the international search: 23 August 2003 (23.08.2003)

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Form PCT/ISA/210 (second sheet) (July 1998)