Title: INCREASING LIFE SPAN BY MODULATION OF SMEK

Abstract: The Smek (Suppressor of mek null) gene is described and characterized. Smek acts in the stress response pathway of animals by binding to and enhancing the transcription of FOXO, thereby providing the link between the stress response pathway and the insulin/IGF-1 pathway. Given the link between both the stress response pathway and the insulin/IGF-1 pathway and longevity, Smek represents an essential target for modulation of life span and the stress response. Methods of increasing life span and stress tolerance by modulation of Smek activity are disclosed, as are screening methods for identifying compounds that modulate Smek activity. In addition, recombinant animals expressing the Smek gene that have a longer life span and enhanced stress tolerance, and methods of using the Smek gene to modulate both longevity and stress tolerance, are described.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC: A61K 48/00 (2006.01); A01N 37/18 (2006.01)

USPC: 514/44; 514/2
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. : 514/44; 514/2

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)
EAST/STN bioscience cluster database

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>
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</table>

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

Date of the actual completion of the international search: 24 June 2006 (24.06.2006)

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