1. Title

2. Research Term
   FY 2000 ~ 2001 ISAS Grant for Basic Study oriented to utilization of Space station
   FY 2002 Ground-based Research Announcement for Space Utilization

3. Research Fields
   Biomedical Science

4. Research Categories
   ISAS Grant for Basic Study oriented to utilization of Space station

5. Research Theme
   Signal transduction of mechanical stress through ASK1-MAP kinase system

6. Investigators
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8. Summary of Research
   ASK1 was originally identified and cloned by us in 1997 as a gene encoding the cytoplasmic
   signal transducer of physico-chemical stress-induced cell death. ASK1 activates the JNK and p38
   MAP kinases in response to environmental stress. In this research project, a potential role of
   ASK1 in the signal transduction of mechanical stress was investigated in order to understand the
   molecular mechanisms of biological activities induced by the mechanical stress.
To analyze the specific requirement of ASK1 for various physico-chemical stress, ASK1 knock-out mice were generated; ASK1 was thus found to be required for TNF-, oxidative stress- and Endoplasmic Reticulum (ER) stress-induced JNK/p38 activation and apoptosis. ASK1 was also found to form an oligomeric complex upon stress stimulation, followed by an autophosphorylation of activation loop in the kinase domain. Moreover, we found that mechanical stress generated by cell stretching activated p38 through Rap1 activation. All together, these results suggest that ASK1-MAP kinase system may be a potential therapeutic target for the space-associated diseases, and development of such drugs may significantly contribute to the space utilization and development.

9. Publication List


