# Mortalin in Cellular Senescence and Immortalization

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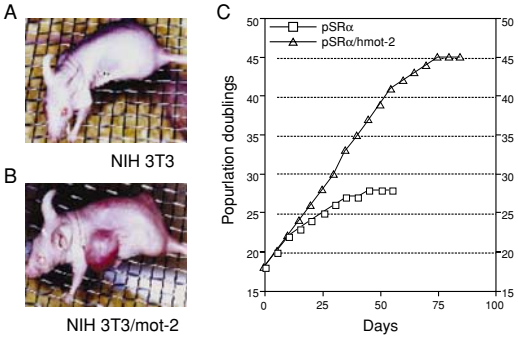
We have first cloned mortalin, a novel member of hsp 70 family of proteins and demonstrated that it is differentially distributed in cells with normal and immortal phenotypes. It is involved in pathways to cellular senescence and transformation. The mouse mot-1 cDNA that encodes cytoplasmically distributed protein caused cellular senescence in NIH 3T3 cells. In contrast, mot-2 cDNA encoding the perinuclear protein resulted in malignant transformation of NIH 3T3 (Figs. A & B) and lifespan extension of normal human fibroblasts (Fig. C). It was demonstrated that mot-2 interacts with p53 in cell cytoplasm and inactivates its function by nuclear exclusion mechanism. Other functions of mortalin include its chaperone activity, intracellular trafficking and mitochondrial import. These are expected to be mediated by its dynamic cellular localizations and its binding partners. Elucidation of such functional aspects of mortalin is extremely important to use it in biotechnology and tumor therapy.




(A) Nude mouse injected with control (NIH 3T3) cells did not result in tumor formation. (B) Tumor formation by NIH 3T3/mortalin (mot-2) transfectants. (C) In vitro population doublings of normal human lung fibroblasts transfected with empty vector (pSRα) and with human mortalin (pSRα/hmot-2) cDNAs.

# Representation of Biological Processes: Signal Transduction Pathway Database Development

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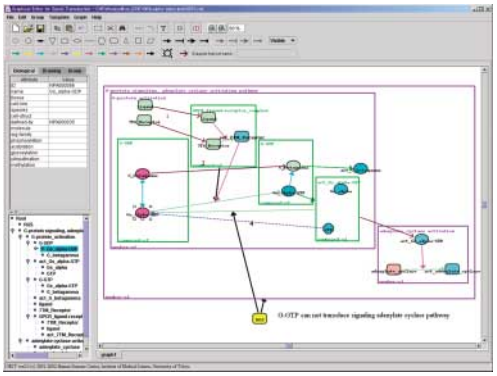
Signal transduction pathways (STPs) explain the underlying mechanisms of various biological phenomena in terms of interactions of bio-processes and bio-molecules.

Since most of the knowledge is represented in the form of text by natural language, a knowledge representation model for STPs that is as readily processed by a computer as it is easily understood by humans is required.

A hierarchical and recursive data model that is able to handle the diversity of molecules and the hierarchical structure of bio-processes in pathways has been developed.



Screenshot of our pathway editor GEST