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培養がん細胞内のモータリン分布パターンをもとに同定された抗がん遺伝子標的

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Mortalin is a member of the hsp70 family of proteins and shows differential cellular distribution in human normal and cancer cells; pancytoplasmic in normal and perinuclear in cancer cells. Induction of senescence in cancer cells by a variety of chemicals and stress conditions resulted in the shift of staining pattern from the perinuclear to pancytoplasmic type along with the nuclear translocation and activation of p53 function. Using mortalin staining as a model reporter, we screened human shRNA library for the identification of gene targets for cancer therapy. Cancer cells were stably transfected with the shRNA expressing plasmids in 96-well plates, immunostained with anti-mortalin antibody and screened for mortalin staining pattern. By four rounds of screening, we identified shRNAs that caused shift in mortalin staining from the perinuclear to the pancytoplasmic pattern. In order to validate the selected candidates we undertook three-dimensional approach: (i) genomic analysis by comparative genomic hybridization (CGH) and gene specific genomic PCR analyses (ii) functional analysis by p53 and p16 expression profiles and (iii) pathway analysis by bioinformatics approach. We report DNA damage signaling pathway as a candidate target for cancer therapy.