Title (en)

SAG: SENSITIVE TO APOPTOSIS GENE

Title (de)

SAG: SENSITIVE-TO-APOPTOSIS GENE (APOPTOSIS INDUZIERBAR GEN)

Title (fr)

SAG: GENE SENSIBLE A L'APOPTOSE

Publication

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Application

EP 98963962 A 19981215

Priority

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- US 6817997 P 19971219
- US 9984098 P 19980911

Abstract (en)

[origin: WO9932514A2] The present invention provides novel genes and polypeptides derived therefrom encoding a redox-sensitive protein that promotes cell growth, protects cells from apoptosis, scavenges oxygen radicals and can be used for the reversion of a tumor phenotype. In an attempt to identify gene(s) responsible for 1,10-phenanthroline (OP)-induced apoptosis in tumor cells we have used the differential display technique and cloned an OP-inducible gene, SAG (Sensitive to Apoptosis Gene). SAG encodes a novel, redox-sensitive, heme-binding protein with a zinc RING finger domain. The SAG protein consists of 113 amino acids with a calculated molecular weight of 12.7 kDa. Sequence homology searches reveal that SAG is highly conserved among species, suggesting its functional importance. This suggestion is demonstrated by the finding that SAG disruption in yeast is lethal. Two SAG deletion mutants have been detected in human cancer cell lines originating from colon and testis, suggesting its possible role in human carcinogenesis. Overexpression of SAG protein in a human colon carcinoma line, DLD1, and a human neuroblastoma line, SY5Y, protects cells from apoptosis induced by OP, zinc and copper ions. Furthermore, antisense SAG transfection inhibits certain tumor cell phenotypes in DLD1 human cell line and microinjection of SAG RNA stimulates cell growth. We propose that SAG protein is a cellular protective molecule functioning as a redox sensor to buffer oxidative-stress induced damage as well as a growth factor to stimulate cell growth. SAG protein will be an ideal molecular target in the development of drugs against neurodegenerative disorders, cancers, muscle dystrophy, and promoting wound healing.

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