AEG3482 is an antiapoptotic compound that inhibits Jun kinase activity and cell death through induced expression of heat shock protein 70.

Salehi AH, Morris SJ, Ho WC, Dickson KM, Doucet G, Milutinovic S, Durkin J, Gillard JW, Barker PA. ***Chem Biol.*** 2006 Feb;13(2):213-23.

We describe a group of small-molecule inhibitors of Jun kinase (JNK)-dependent apoptosis. AEG3482, the parental compound, was identified in a screening effort designed to detect compounds that reduce apoptosis of neonatal sympathetic neurons after NGF withdrawal. We show that AEG3482 blocks apoptosis induced by the p75 neurotrophin receptor (p75NTR) or its cytosolic interactor, NRAGE, and demonstrate that AEG3482 blocks proapoptotic JNK activity. We show that AEG3482 induces production of heat shock protein 70 (HSP70), an endogenous inhibitor of JNK, and establish that HSP70 accumulation is required for the AEG3482-induced JNK blockade. We show that AEG3482 binds HSP90 and induces HSF1-dependent HSP70 mRNA expression and find that AEG3482 facilitates HSP70 production while retaining HSP90 chaperone activity. These studies establish that AEG3482 inhibits JNK activation and apoptosis by a mechanism involving induced expression of HSP proteins.