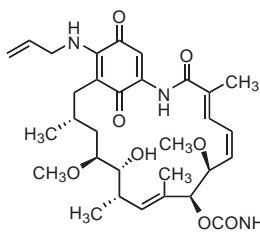


## 17-(Allylamino)-17-dimethoxygeldanamycin (17-AAG): Potent Hsp90 inhibitor

Prod. No. **A 8476**



Heat shock protein 90 (Hsp90) is a molecular chaperone that binds to and enhances stability and function of client proteins (mutated, chimeric and over-expressed signaling proteins) that promote cancer cell growth and/or survival. 17-AAG, an inhibitor of Hsp90 function, induces the selective degradation of several intracellular proteins that regulate multiple signaling pathways.

17-AAG is a less toxic analog of the antibiotic **Geldanamycin** (Prod. No. **G 3381**) [1], which is another potent inhibitor of Hsp90 function.

17-AAG has been shown to inhibit Hsp90 in four human colon adenocarcinoma cell lines, displaying  $IC_{50}$  values of 0.2  $\mu$ M (HT29), 0.8  $\mu$ M (HCT116), 0.9  $\mu$ M (KM12) and 46  $\mu$ M (HCT15), respectively [2]. In other studies, 17-AAG has been shown to deplete client proteins and inhibits the proliferation of various human tumor xenografts grown in immunosuppressed mice, including colon, breast and prostate cancers as well as melanoma [3,4].

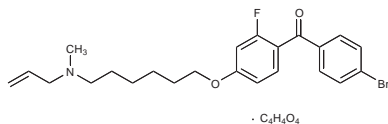
17-AAG will be a useful tool for researchers studying the role of chaperone proteins in cell growth and development.

### References

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## Ro 48-8071: 2,3-Oxidosqualene:lanosterol cyclase inhibitor

Prod. No. **R 2278**



Within the **cholesterol** (Prod. No. **C 8667**) biosynthesis cascade, the enzyme 2,3-oxidosqualene cyclase [EC 5.4.99.7] is of

special interest due to its dual function of both cyclizing 2,3-monoepoxysqualene to **lanosterol** (Prod. No. **L 5768**) and converting 2,3,22,23-diepoxy-squalene to oxysterol. Thus, this enzyme represents a unique target for novel cholesterol lowering drugs.

Ro 48-8071 acts as a 2,3-oxidosqualene:lanosterol cyclase inhibitor and has been shown to block human liver OSC and cholesterol synthesis in HepG2 cells, displaying  $IC_{50}$  values of 6.5 nM and 1.5 nM, respectively [1].

Ro 48-8071 is therefore a valuable tool with which to study and develop novel anti-cholesterol drugs that are safe and effective in lowering cholesterol levels.

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## Anti-FKHR (FOXO1a): Transcription factors controlling life and death

Prod. No. **F 6928**

Clone FKH 117, developed in mouse

Purified mouse immunoglobulin in phosphate-buffered saline *ImmunoGen*: peptide corresponding to human FKHR (amino acids 636-651)

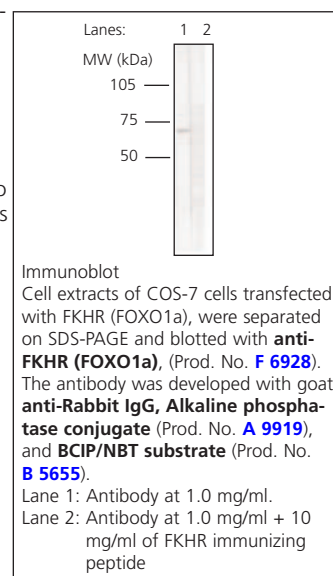
*Isotype*: IgG1

*Species Reactivity*: Human

Forkhead box, class O (FOXO) is a subfamily of the forkhead family of transcription factors. FOXO family members control glucose metabolism, stress response, regulation of cell cycle progression, apoptosis and physiological states varying from aging and cancer to diabetes. The superfamily of forkhead transcription factors consists of more than 100 members with orthologs expressed in a variety of species ranging from yeast to man. A common forkhead box DNA domain (or FOX) characterizes this family of proteins. The FOXO subfamily consists of FKHR (forkhead in rhabdomyosarcoma; FOXO1a), FKHL1 (FKHR-like 1; FOXO3a), and AFX (acute-lymphocytic-leukemia-1; FOXO4) and was first identified at chromosomal breakpoints in human tumors, and consequently it is linked to tumorigenesis.

FKHR, FKHR-L1 and AFX are downstream nuclear components of the PI3K-PKB signaling pathway. In the presence of growth factors, PI3-K activates PKB (Akt) that in turn directly phosphorylates FOXO transcription factors, allowing them to be exported to the cytoplasm and thereby inhibit their ability to induce expression of target genes. The PI3-K-Akt-FOXO pathway is well conserved and has been adapted to control diverse biological functions. Further research is needed to determine how FOXO factors moderate alternative transcriptional programs and how they may affect tumorigenesis and aging.

Immunoblot, using a total extract from COS-7 cells transfected with the FKHD expression plasmid, detected a band at 70-75 kDa. In addition, the antibody may be used for immunoprecipitation and ELISA.



### References

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Related Antibodies and Proteins	Application	Prod. No.
Anti-AFX (rabbit)	Immunoblotting Immunofluorescence	<b>A 8975</b>
Anti-FKHR (rabbit)	Immunoblotting	<b>F 2303</b>
Monoclonal Anti-FKHL1, Clone FR1 (mouse)	(available soon)	<b>F 1304</b>
Anti-FKHL1 (rabbit)	Immunoblotting Immunofluorescence	<b>F 2178</b>