3050 Spruce Street
Saint Louis, Missouri 63103 USA
Telephone (800) 325-5832 (314) 771-5765
Fax (314) 286-7828
email: techserv@sial.com
sigma-aldrich.com

ProductInformation

Fas (CD95, Apo-1)/Fc CHIMERA
Human, Recombinant
Expressed in mouse NSO cells

Product Number **F 8674**

Product Description

Recombinant human Fas (CD95, Apo-1)/Fc Chimera is a transmembrane glycoprotein receptor expressed in mouse NSO cells. The DNA sequence encoding the extracellular domain (aa 1-173) of human Fas antigen[1] is fused to the Fc portion of human IgG1. The recombinant protein is a disulfide-linked dimer with a blocked amino terminus. The mature monomer of recombinant human Fas/Fc, generated after the removal of the predicted 16 amino acid signal peptide, has a molecular mass of 45 kDa. Human Fas is a type 1 membrane protein belonging to the TNF and NGF receptor family.

Homeostasis of multicellular organisms is controlled not only by the proliferation and differentiation of cells but also by cell death. The death of cells during embryogenesis, metamorphosis, endocrine-dependent tissue atrophy or death due to a variety of pathologic conditions and normal tissue turnover is called programmed cell death (PCD). Most of PCD proceeds by apoptosis, a process that includes condensation and segmentation of nuclei, condensation and fragmentation of the cytoplasm, and often extensive fragmentation of chromosomal DNA into nucleosome units.[2] Many cells can be activated to undergo apoptosis following the interaction of selected ligands with cell surface receptors.

The cellular pathways that control apoptosis are critical to the maturation, selection, and survival of lymphocytes. Apoptosis is the physiological mode of lymphoid cell death in the negative selection of T cells in the thymus, ligation of CD4 and CD3 in mature T cells, down-regulation of the immune response, clonal deletion of B cells, death of killer cell targets, cytokine-mediated killing, and tumor regression.

The most studied receptors involved in apoptosis are CD95/Fas/Apo-1 (apoptosis inducing protein 1) and TNF receptor I (TNF RI). Apoptosis mediated by both signaling cascades results in activation of a family of cysteine proteases known as caspases. However, Fas-mediated death occurs much more rapidly than that triggered by the TNF RI. Engagement of Fas by its ligand (Fas ligand, FasL, CD95L), or by an appropriate antibody, results in the rapid induction of PCD in susceptible cell lines. This process bypasses the usual long sequence of signaling enzymes and immediately activates preexisting caspases.[3]

The action of Fas is mediated via FADD (Fas-associated death domain)/ MORT1, an adapter protein that has a death domain at its C-terminus and binds to the cytoplasmic death domain of Fas. Primary sequence analysis of the extracellular portion of CD95/Fas/Apo-1 reveals strong homologies with the extracellular domain of receptors belonging to the TNF receptor family. This family includes TNF receptor types I and II, the low affinity nerve growth factor receptor, and lymphocyte receptors such as CD27, CD30, CD40, and OX40.[1,4] An integral membrane protein, with strong homology to TNF-α and TNF-β, has been identified as the Fas ligand (CD95L/FasL).[1]

A moderate degree of homology (26% identity in a stretch of 65 amino acids) between the intracellular portion of the human CD95 (Fas) and the 55 kDa TNF RI, has been observed. Mutational analysis of this domain has revealed its involvement in the generation of the apoptotic signal from both Fas and TNF RI.[1] Thus, a common effector may transduce the apoptotic signal from both receptors.

Fas is highly expressed in epithelial cells, hepatocytes, activated mature lymphocytes[5], virus-transformed lymphocytes, and tumor cells. It is found on a number of lymphoma cell lines. Upon contact with an anti-Fas antibody, some lymphocytes expressing Fas antigen undergo apoptosis.[6,7] Fas is also expressed in mouse thymus, liver, heart, lung, kidney and ovary. A soluble form of Fas has been detected that plays a role in regulating certain aspects of immune system function. Elevated levels of soluble Fas have been detected in sera from patients with leukemic diseases, as well as in patients with systemic lupus erythematosus. Therefore, altered levels of secreted Fas protein are likely to be involved in the abnormal growth regulation of lymphoid cells. The production of excess soluble Fas protein prevents cells from undergoing Fas ligand induced apoptosis and thereby permits tumor cells to escape immunosurveillance. Antibodies reacting specifically with CD95 (Fas, Apo-1) are useful tools in the study of the intracellular pathways leading from membrane

receptor engagement to apoptotic cell death, the tissue distribution and developmental expression pattern of Fas, and its essential role in mammalian development especially in immune system homeostasis.

Reagent
Recombinant human Fas is supplied as an approximately 50 µg of protein lyophilized from a 0.2 µm filtered solution of phosphate buffered saline (PBS) containing 2.5 mg bovine serum albumin.

Preparation Instructions
Reconstitute the contents of the vial using sterile phosphate-buffered saline (PBS). Prepare a stock solution of no less than 10 µg/ml.

Storage/Stability
Store at –20 °C. Upon reconstitution, store at 2-8 °C for up to one month. For extended storage, freeze in working aliquots. Repeated freezing and thawing is not recommended.

Product Profile
Recombinant human Fas is measured by its ability to inhibit FAS-ligand induced apoptosis of Jurkat cells.[8] The ED_{50} for this effect is generally 0.01-0.04 µg/ml in the presence of 2 ng/ml of recombinant human Fas ligand.

The ED_{50} is defined as the effective concentration of growth factor that elicits a 50% increase in cell growth in a cell based bioassay.

Purity: >97% as determined by SDS-PAGE, visualized by silver stain.

Endotoxin: < 0.1 ng/µg of protein, determined by the LAL (Limulus amebocyte lysate) method.

References

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