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

Notch-3/Fc Chimera
Mouse, Recombinant
Expressed in insect cells

Product Number **N 8911**

Product Description

Recombinant Mouse Notch-3/Fc Chimera is produced from a DNA sequence encoding the first eleven EGF repeats of mouse Notch-3 (amino acid residues Met 24-Glu 468),[1] fused to the Fc region of human IgG1 via a polypeptide linker. The fusion protein is expressed in an insect cell line. Recombinant mouse Notch-3/Fc, generated by the proteolytic removal of the signal peptide, is a disulfide-linked homodimeric protein. Based on N-terminal sequencing, the mature protein starts at Ala 40. The calculated molecular mass is 71.5 kDa. As a result of glycosylation, the recombinant protein migrates as a 90-95 kDa protein in SDS-PAGE under reducing conditions. Mouse Notch3 shows 90% amino acid sequence identity to human Notch3 and 96% amino acid identity to rat Notch3 over the entire protein.

Mouse Notch-3 is a member of Notch family of type I transmembrane glycoproteins involved in a number of early-event developmental processes.[2] Notch signaling is important for specifying cell fates and for defining boundaries between different cell types. The molecule is synthesized as a 2318 amino acid precursor that contains a 39 amino acid signal sequence, a 1603 amino acid extracellular region, a 20 amino acid transmembrane segment, and a 655 amino acid cytoplasmic domain. The large Notch extracellular domain has 34 EGF-like repeats followed by three notch/Lin-12 repeats (LNR).[1] Of the 34 EGF-like repeats, the 11th and 12th are necessary and sufficient for binding the ligands Serrate and Delta in *Drosophiia*.[3] The extracellular domain of Notch receptors interacts with the extracellular domain of transmembrane ligands Jagged, Delta, and Serrate.

In mammals, four Notch genes have been identified (Notch1-4) that are expressed in a wide variety of cells and play a crucial role in differentiation and development.[4-6] The Notch protein family is a group of highly conserved proteins important in the determination of cell fate and maintenance of progenitors in many developmental systems. This family of proteins function both as membrane cell receptors and as transcription factors. Activation of Notch by cell-cell interactions causes a transcription inhibitory effect that enables inhibition of differentiation in some cells but not in others. As a consequence, some cells adopt a particular fate while other progenitors remain uncommitted. The Notch protein is important in cell fate during myogenesis, neurogenesis, oogenesis, and wing and eye development in *Drosophila*.

Notch3 is predominantly expressed in the developing central nervous system of mice.[7] Mutations in Notch3 in humans cause an autosomal dominant condition called CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy). This condition is characterized by recurrent ischemic strokes at an early age without any underlying vascular risk and progressive dementia. The mutations leading to CADASIL are clustered in the first 5 EGF repeats of the Notch3 gene.[8]

Reagent

Recombinant Mouse Notch-3/Fc Chimera is supplied as approximately 50 µg of protein lyophilized from 0.2 µm filtered solution in phosphate buffered saline.

Storage/Stability

Prior to reconstitution, store at –20 °C. Reconstituted product (in the presence of a carrier protein) may be stored at 2-8 °C for up to one month. For prolonged storage, freeze in working aliquots. Avoid repeated freezing and thawing.

Preparation Instructions

Reconstitute the contents of the vial using 0.2 µm filtered phosphate buffered saline. Prepare a stock solution of no less than 100 µg/ml. The carrier-free protein should be used immediately upon reconstitution to avoid losses in activity due to non-specific binding to the inside surface of the vial. For long term storage as a dilute solution, a carrier protein such as 0.1% human serum albumin or bovine serum albumin should be added to the vial.

Product Profile
The biological activity of mouse Notch-3/Fc Chimera is measured by its ability to bind Jagged-1. Immobilized recombinant mouse Notch-3/Fc at 5 µg/ml (100 µl/well) can bind recombinant rat Jagged-1/Fc with a linear range of 8-500 ng/ml in an ELISA.

Endotoxin: < 1.0 EU (endotoxin unit)/µg cytokine as determined by the LAL method.

References

1. Lardelli, M., et al., Mech. Dev., **46**, 123 (1994).
2. Weinmaster, G., Curr. Opin. Genet. Dev., **10**, 363, 2000.
3. Rebay, I., et al., Cell, **67**, 687 (1991).
4. Milner, L.A., et al., Proc. Natl. Acad. Sci. USA, **93**, 13014-13019 (1996).
5. Huppert, S.S., et al., Nature, **405**, 966-970 (2000).
6. Milner, L.A., et al., Blood, **93**, 243-248 (1999).
7. Lardelli, M., et al., Mech. Dev., **46**, 123 (1994).
8. Joutel, A., and Tounier-Lasserve, E., Sem. Cell & Dev. Biol., **9**, 619 (1998).

KAA 05/04