Metalloproteinase

A metalloproteinase, or metalloprotease, is any protease enzyme whose catalytic mechanism involves a metal. An example of this would be meltrin which plays a significant role in the fusion of muscle cells during embryo development, in a process known as myogenesis.

Most metalloproteases require zinc, but some use cobalt. The metal ion is coordinated to the protein via three ligands. The ligands co-ordinating the metal ion can vary with histidine, glutamate, aspartate, lysine, and arginine.

The fourth coordination position is taken up by a labile water molecule.

Treatment with chelating agents such as EDTA leads to complete inactivation. EDTA is a metal chelator that removes zinc, which is essential for activity. They are also inhibited by the chelator orthophenanthroline.

see Matrix metalloproteinase.

In a study, Sanz et al. identified a metalloproteinase-dependent mechanism necessary to promote growth in embryonic dorsal root ganglion cells (DRGs).

Treatment of embryonic DRG neurons with pan-metalloproteinase inhibitors, tissue inhibitor of metalloproteinase-3, or an inhibitor of ADAM Metallopeptidase Domain 10 (ADAM10) reduces outgrowth from DRG neurons indicating that metalloproteinase activity is important for outgrowth.

The IgLON family members Neurotrimin (NTM) and Limbic System-Associated Membrane Protein (LSAMP) were identified as ADAM10 substrates that are shed from the cell surface of Dorsal root ganglion (DRG) neurons. Overexpression of LSAMP and NTM suppresses outgrowth from DRG neurons. Furthermore, LSAMP loss of function decreases the outgrowth sensitivity to an ADAM10 inhibitor. Together this findings support a role for ADAM-dependent shedding of cell surface LSAMP in promoting outgrowth from DRG neurons [1].

1)
Sanz RL, Ferraro GB, Girouard MP, Fournier AE. Ectodomain shedding of Limbic System-Associated Membrane Protein (LSAMP) by ADAM Metallopeptidases promotes neurite outgrowth in DRG neurons. Sci Rep. 2017 Aug 11;7(1):7961. doi: 10.1038/s41598-017-08315-0. PubMed PMID: 28801670.