

ADAM-10

A Disintegrin and [metalloproteinase](#) domain-containing protein 10, also known as ADAM10 or CDw156 or CD156c is a protein that in humans is encoded by the ADAM10 gene.

Members of the ADAM family are cell surface proteins with a unique structure possessing both potential adhesion and protease domains. Sheddase, a generic name for the ADAM metallopeptidase, functions primarily to cleave membrane proteins at the cellular surface. Once cleaved, the sheddases release soluble ectodomains with an altered location and function.

Although a single sheddase may “shed” a variety of substances, multiple sheddases can cleave the same substrate resulting in different consequences. This gene encodes an ADAM family member that cleaves many proteins including TNF-alpha and E-cadherin.

[Disintegrin](#) and [metalloproteinases](#) (ADAMs) 10 and 17 can release the extracellular part of a variety of membrane-bound proteins via ectodomain shedding important for many biological functions. So far, substrate identification focused exclusively on membrane-anchored ADAM10 and ADAM17. However, besides known shedding of ADAM10, we identified ADAM8 as a protease capable of releasing the ADAM17 ectodomain. Therefore, we investigated whether the soluble ectodomains of ADAM10/17 (sADAM10/17) exhibit an altered substrate spectrum compared to their membrane-bound counterparts. A mass spectrometry-based N-terminomics approach identified 134 protein cleavage events in total and 45 common substrates for sADAM10/17 within the secretome of murine cardiomyocytes. Analysis of these cleavage sites confirmed previously identified amino acid preferences. Further in vitro studies verified fibronectin, [cystatin C](#), sN-cadherin, PCPE-1 as well as sAPP as direct substrates of sADAM10 and/or sADAM17. Overall, we present the first degradome study for sADAM10/17, thereby introducing a new mode of proteolytic activity within the protease web ¹⁾.

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 ²⁾.

¹⁾

Scharfenberg F, Helbig A, Sammel M, Benzel J, Schlomann U, Peters F, Wichert R, Bettendorff M, Schmidt-Arras D, Rose-John S, Moali C, Lichtenthaler SF, Pietrzik CU, Bartsch JW, Tholey A, Becker-Pauly C. Degradome of soluble ADAM10 and ADAM17 metalloproteases. *Cell Mol Life Sci*. 2019 Jun 17. doi: 10.1007/s00018-019-03184-4. [Epub ahead of print] PubMed PMID: 31209506.

²⁾

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.

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