

A5 Substrate specificity and inducibility of TACE revisited: the Ala-Val preference, and induced intrinsic activity
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The TNF-alpha converting enzyme (TACE/ADAM-17) releases from the cell surface the extracellular domains of TNF and several other proteins. Previous studies have found that while TACE preferentially cleaves peptides representing the processing sites in TNF and TGF-alpha, it nonetheless sheds proteins with divergent cleavage sites very efficiently. More recent work, identifying the cleavage site in the p75 TNF receptor, quantitating the susceptibility of additional peptides to TACE, and identifying additional protein substrates, underlines the complexity of TACE:substrate interactions. In addition to substrate specificity, the mechanism underlying the increased rate of shedding caused by agents that activate cells is poorly understood. Recent work in this area, utilizing a peptide substrate as a probe for cellular TACE activity, indicates that the intrinsic activity of the enzyme is somehow increased, while localization of TACE and its substrates is not appreciably changed.