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Titel des Beitrags:
TNF-alpha-converting enzyme (TACE/ADAM17) inactivation in mouse myeloid cells prevents lethality from endotoxin shock

Abstract:
TNF-alpha, a potent proinflammatory cytokine, is synthesized as a membrane-anchored precursor and proteolytically released from cells. Soluble TNF is the primary mediator of pathologies such as rheumatoid arthritis, Crohn's disease, and endotoxin shock. The TNF-alpha converting enzyme (TACE), a disintegrin and metalloprotease 17 (ADAM17), has emerged as the best candidate TNF sheddase, but other proteinases can also release TNF. Because TACE-deficient mice die shortly after birth, we generated conditional TACE-deficient mice to address whether TACE is the relevant sheddase for TNF in adult mice. In this study, we report that TACE inactivation in myeloid cells or temporal inactivation at 6 wk offers strong protection from endotoxin shock lethality in mice by preventing increased TNF serum levels. These findings corroborate that TACE is the major endotoxin-stimulated TNF sheddase in mouse myeloid cells in vivo, thereby further validating TACE as a principal target for the treatment of TNF-dependent pathologies.

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