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Gout manifests as recurrent episodes of acute joint inflammation and pain due to the deposition of monosodium urate (MSU) crystals within the affected tissue in a process dependent on NLRP3 inflammasome activation. The synthesis, activation, and release of IL-1β are crucial for MSU-induced inflammation. The current study evaluated the mechanism by which TNF-α contributed to MSU-induced inflammation. Male C57BL/6J or transgenic mice were used in this study and inflammation was induced by the injection of MSU crystals into the joint. TNF-α was markedly increased in the joint after the injection of MSU. There was inhibition in the infiltration of neutrophils, production of CXCL1 and IL-1β, and decreased hypernociception in mice deficient for TNF-α or its receptors. Pharmacological blockade of TNF-α with Etanercept or pentoxyfylline produced similar results. Mechanistically, TNF-α blockade resulted in lower amounts of IL-1β protein and pro-IL-1β mRNA transcripts in joints. Gene-modified mice that express only transmembrane TNF-α had an inflammatory response similar to that of WT mice and blockade of soluble TNF-α (XPro™1595) did not decrease MSU-induced inflammation. In conclusion, TNF-α drives expression of pro-IL-1β mRNA and IL-1β protein in experimental gout and that its transmembrane form is sufficient to trigger MSU-induced inflammation in mice.