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Glucocorticoid (GC)-induced leucine zipper (GILZ) has been shown to mediate or mimic several actions of GC. This study assessed the role of GILZ in self-resolving and GC-induced resolution of neutrophilic inflammation induced by LPS in mice. GILZ expression was increased during the resolution phase of LPS-induced pleurisy, especially in macrophages with resolving phenotypes. Pretreating LPS-injected mice with trans-activator of transcription peptide (TAT)-GILZ, a cell-permeable GILZ fusion protein, shortened resolution intervals and improved resolution indices. Therapeutic administration of TAT-GILZ induced inflammation resolution, decreased cytokine levels, and promoted caspase-dependent neutrophil apoptosis. TAT-GILZ also modulated the activation of the survival-controlling proteins ERK1/2, NF-κB and Mcl-1. GILZ deficiency was associated with an early increase of annexin A1 (AnxA1) and did not modify the course of neutrophil influx induced by LPS. Dexamethasone treatment resolved inflammation and induced GILZ expression that was dependent on AnxA1. Dexamethasone-induced resolution was not altered in GILZ(-/-) mice due to compensatory expression and action of AnxA1. Our results show that therapeutic administration of GILZ efficiently induces a proapoptotic program that promotes resolution of neutrophilic inflammation induced by LPS. Alternatively, a lack of endogenous GILZ during the resolution of inflammation is compensated by AnxA1 overexpression.