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Inflammation is a physiological response of the immune system to injury or infection but may become chronic. In general, inflammation is self-limiting and resolves by activating a termination program named resolution of inflammation. It has been argued that unresolved inflammation may be the basis of a variety of chronic inflammatory diseases. Resolution of inflammation is an active process that is fine-tuned by the production of proresolving mediators and the shutdown of intracellular signaling molecules associated with cytokine production and leukocyte survival. Apoptosis of leukocytes (especially granulocytes) is a key element in the resolution of inflammation and several signaling molecules are thought to be involved in this process. Here, we explore key signaling molecules and some mediators that are crucial regulators of leukocyte survival in vivo and that may be targeted for therapeutic purposes in the context of chronic inflammatory diseases.