Interleukin-1α (IL-1α) is a multifunctional cytokine. The most explored function of IL-1α is activation of proinflammatory signalization via its membrane-bound receptor. There are, however, also noncanonical functions of IL-1α independent on the receptor signalization, which are the topic of the presented thesis. The evolutionary conserved N-terminal domain of IL-1α is responsible for both the noncanonical functions in nucleus and for anchoring IL-1α to the plasma membrane.

In nucleus, IL-1α activates expression of proinflammatory genes regulated by NF-κB, binds to histone acetyltransferase complexes and induces apoptosis in malignant cells. The catalytic core module of SAGA and ADA histone acetyltransferase complexes was identified to bind IL-1α in yeast, while the homologous STAGA complex and p300 bind IL-1α in human cells.

Anchoring of IL-1α to the plasma membranes limits the ability of IL-1α to signal solely to the cells in direct physical contact. The N-terminal domain of IL-1α is required for membrane anchoring; however, neither the mechanism of IL-1α externalization nor the mechanism of IL-1α anchoring are well understood.

The thesis explores both the nuclear functions and the membrane association of IL-1α. IL-1α is able to partially rescue growth defects of yeast cells harboring deletion of Snf1 under conditions regulated by Snf1-dependent derepression of SAGA complex. The association of IL-1α with tumor suppressor p53 following genotoxic stress is further described in human cell lines. Also, IL-1α colocalize with membrane-binding protein annexin A2 at the plasma membrane in response to oxidative stress.