# SUMO PROTEINS: GUARDIANS OF IMMUNE SYSTEM

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**Introduction:** Small ubiquitin-like modifier (SUMO) proteins belong to the ubiquitin-like family and act to change the function of target proteins through post-translational modifications. SUMO is involved in the innate immune response through their role in NF-kB and interferon pathways. In the NF-κB pathway, for example, SUMO-3binds IKK-γ (NEMO) which forms a complex with IKKα and IKKβ kinases, that then phosphorylate IκBα, an inhibitor of NF-κB, leading to its degradation and subsequent NF-κB activation. SUMO-1also negatively regulates this pathway through binding and protecting dephosphorylated IκBα from degradation, thus keeping NF-κB in an inactive state. In the interferon pathway, IRF3sumoylation inhibits the IRF3-dependent transcription of IFNβ, whereas desumoylation, by SENP2, results in ubiquitination and proteasomal degradation of IRF3, thus removing the IRF3-SUMO-dependent inhibition of IFNβ transcription. SUMO is involved also in the IFNs signaling pathways, since STAT1sumoylation completely blocks the IFN-γ pathway through inhibiting phosphorylation of the sumoylated STAT1homodimer. That SUMO proteins are important in avoiding excessive immune response and subsequent autoimmunity is demonstrated by their involvement in both the regulation of Treg cell and the development of autoimmune diseases such as type 1diabetes, Bechet's disease, Rheumatoid arthritis, gammopathies, Wiskott-Aldrich syndrome. On the other hand, the importance of sumoylation in the immune response during infection is highlighted by the development of pathogen strategies that aim to evade host defense by impairing the sumoylation in host cells.

**Materials and methods:** Animals. C57BL/6mice and caspase-8-floxed mice were used. Cell harvesting and cell culture. Thymocytes were counted by hemocytometer and single cell suspensions were cultured in flat-bottomed 96-well plates. Western blot analysis. Cells were lysed in RIPA buffer. Total proteins were separated using 12or 15% SDS polyacrylamide gel electrophoresis (SDS-PAGE). In vitro protein-binding assay. Pull-down assay were performed by incubating the GST-Gilz fusion protein, loaded onto gluthatione-sepharose beads, with cellular lysates in binding buffer. Statistical analysis. Data represent the mean ± 1SEM.

**Results:** Along with bone marrow, the thymus is the primary lymphoid organ where T lymphocyte maturation is completed. Therefore, the thymus plays an important role in the defense against pathogens. During infections, the thymus undergoes reversible involution. Glucocorticoids are involved in thymic involution by triggering massive thymocyte apoptosis. To this end, glucocorticoids stimulate the transcription of glucocorticoid-induced leucine zipper (Gilz) and the activation of caspase-8, which, in turn, co-activate each other. Gilz activates caspase-8and activated caspase-8sumoylates Gilz, allowing the prolongation of Gilz expression by inhibiting ubiquitin-mediated Gilz proteasomal degradation. The final result of this process is apoptosis of thymocytes.

**Discussion and conclusion:** In conclusion, the importance of sumoylation in immunity is highlighted by the involvement of SUMO proteins in the development of different autoimmune diseases and its importance in defense against pathogens. For example, bacteria, viruses, and parasites interfere with the sumoylation of host cells by exploiting the host system to enable sumoylation of their own proteins and by interfering with sumoylation of host proteins. Both strategies lead to a decreased immune defense or detection, which increase the infective potential. The pivotal role of SUMO in modulation of the immune system suggests that new therapeutic strategies for treating autoimmune diseases and infections that target SUMO are warranted, especially the latter given the rapid increase in microbial resistance to antibiotics. Therefore, SUMOs could be a novel target in the fight against infectious and autoimmune diseases.