Abstract

T lymphocytes specifically recognize and promote immune response against pathogenic agents, which endanger health of host organism. However, this ability must be tightly controlled to prevent response against innocuous or self-tissue antigens, which would unnecessarily damage an organism. For a maintenance of this tolerance, there is a number of molecular mechanisms regulating T lymphocytes. The protein NDFIP1 is important component of these mechanisms. This transmembrane adaptor protein binds to E3 ubiquitin ligases from the NEDD4 family, which are under normal circumstances in inactive state. Binding of NDFIP1 leads to their activation and facilitates regulation of T cell behaviour by these ligases. NDFIP1 deficiency in mice causes the development of inflammatory disease affecting the skin, lungs and gastrointestinal tract. It is characterized by increased numbers of activated $CD4^+$ T lymphocytes and eosinophils, which infiltrate the affected tissues. The disease is ultimately fatal. The aim of this work is to describe the function of the NDFIP1 protein in T lymphocytes, which are essential for the development of this pathology. The absence of NDFIP1 in T cells disrupts several molecular mechanisms, including the degradation of the transcription factors JUNB and RORγT and the regulation of mTOR pathway activity. These and probably other hitherto unknown molecular events then contribute to increased activation and proliferation of T lymphocytes, increased differentiation of Th2 and Th17 lymphocytes, overproduction of IL-4 and destabilization of Treg lymphocytes. The result is the development of pathological inflammation.

Key words: NDFIP1, ITCH, NEDD4, T lymphocytes, JUNB, E3 ubiquitin ligases, IL-4