Programmed cell death protein 4 affects translation termination and undergoes proteolysis in cell lysate

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E. Shuvalova *[I], A. Ivanov *[I], A. Shuvalov[I], N. Biziaev[I], N. Pustogarov[I], I. Terenin[II], T. Egorova[I], E. Alkalaeva[I]

[I]Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, Russia, [II]Belozersky Institute of Physico-Chemical Biology, Moscow, Russia

Programmed cell death 4 (PDCD4) was originally identified as a gene whose expression was increased during apoptosis. The PDCD4 expression decrease accompanied the development of a number of malignant tumors, including lungs, colon, liver, breast cancer, and glioblastoma. PDCD4 encodes a highly conserved phosphoprotein, which subcellular localization (in the nucleus or cytoplasm) is controlled by the protein kinase. PDCD4 also affects two stages of translation: cap-dependent initiation and elongation of oncogenic mRNAs: c-myb and a-myb. PDCD4 prevents initiation by binding to eukaryotic initiation factor 4A via MA3 domains located in the middle and C-terminal part of the protein. Elongation of c-myb and a-myb is thought to be affected by the interaction of PDCD4 with the N-terminal domain of poly(A)-binding protein (PABP). We previously showed that PABP is able to stimulate translation termination by recruiting the release factor 3a (eRF3a). After that, we found that PDCD4 binds to the release factors independently of PABP and observed stimulation of termination activity by PDCD4. Thus, PDCD4 increased the termination efficiency by stabilizing termination complex formation and stimulating the GTPase activity of eRF3a. In addition, we found out that PDCD4 is proteolyzed in a cell-free translation system based on rabbit reticulocytes lysate. This fact suggests the presence of a mechanism for the PDCD4 regulation modulated by proteases.
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* The authors marked with an asterisk equally contributed to the work.