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The soluble cytoplasmic tail of CD45 (ct-CD45) in human plasma contributes to keep T cells in a quiescent state

A. Puck1, S. Hopf1, M. Modak1, O. Majdic1, P. Cejka1, S. Blu¨ml2, K. Schmetterer1, C. Arnold-Schrauf1, J. G. Gerwien3, K. S. Frederiksen3, E. Thell4, J. Leitner1, P. Steinberger1, R. Aigner1, M. Seyerl-Jiresch1, G. J. Zlabinger1, J. Sto¨ckl1;

1 Institute of Immunology, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria,
2 Department for Rheumatology, Medical University of Vienna, Vienna, Austria,
3 Novo Nordisk A/S, Biopharmaceuticals Research Unit, Ma¨løv, Denmark,
4 Department for Gynecology, St. Josef Hospital, Vienna, Austria.

The cytoplasmic tail of CD45 (ct-CD45) is proteolytically cleaved and released upon activation of human phagocytes. It acts on T cells as an inhibitory, cytokine-like factor in vitro. Here we show, that ct-CD45 is abundant in human peripheral blood plasma from healthy adults compared with plasma derived from umbilical cord blood and plasma from patients with rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE). Plasma depleted of ct-CD45 enhanced T-cell proliferation, while addition of exogenous ct-CD45 protein inhibited proliferation and reduced cytokine production of human T lymphocytes in response to TCR signaling. Inhibition of T- cell proliferation by ct-CD45 was overcome by co-stimulation via CD28. T-cell activation in the presence of ct-CD45 was associated with an upregulation of the quiescence factors Schlafen family member 12 (*SLFN12*) and Krueppel-like factor 2 (*KLF2*) as well as of the cyclin-dependent kinase (CDK) inhibitor *p27kip1*. In contrast, positive regulators of the cell cycle such as cyclin D2 and D3 as well as *CDK2* and *CDK4* were found to be downregulated in response to ct-CD45. In summary, we demonstrate that ct-CD45 is present in human plasma and sets the threshold of T cell activation.