Aleksander Roszczyk Zakład Immunologii Klinicznej WUM

Streszczenie w języku angielskim

Introduction: Research over the last twenty years has shown that mushrooms are a valuable source of many bioactive substances. Fungal-derived polysaccharides are the best-known constituents with documented immunomodulatory and anticancer properties. One of the most thoroughly studied compounds is lentinan, β -1,6: β -1,3-glucan extracted from the fruiting bodies of *Lentinula edodes*, which has immunostimulatory properties. Se-Le-30 tested in this study is a selenium-enriched mixture of linear 1,4- α -glucans, linear 1,3- β - and 1,6- β -glucans, isolated from *L. edodes* mycelium. The aim of the study was to evaluate the immunomodulatory properties of Se-Le-30 in relation to human T lymphocytes.

Materials and methods: Peripheral blood mononuclear cells (PBMCs) and T lymphocytes were isolated from peripheral blood or buffy coats obtained from healthy blood donors. Next, the effect of Se-Le-30 in in vitro culture was analyzed: the expression of activation markers (CD25 and CD69), the effect on the proliferation of lymphocytes stimulated with mitogens: SAC (Staphylococcus aureus Cowan), PHA (phytohemagglutinins), alloantigens, anti-CD3 (OKT3) and anti-CD3/CD28 antibodies, influence on the production of cytokines (IL-2, -4, -6 -10, TNF- α , IFN- γ) and on the phosphorylation of pathway proteins CD3/TCR-related signaling: ZAP70, Lck, LAT and SLP76.

Results: It was shown that Se-Le-30 has an inhibitory effect on the proliferation of human T cells stimulated with anti-CD3 antibody and alloantigens and promoted T cell division when cells were stimulated with anti-CD3/CD28 antibodies. Moreover, Se-Le-30 decreased the expression of activation markers CD69 and CD25, as well as immune checkpoints TIM-3 and PD-1 on T cells stimulated with anti-CD3 antibody. After stimulation with anti-CD3/CD28 antibodies, an increase in the expression of the above-mentioned markers was observed. Regardless of the type of T cells stimulation Se-Le-30 upregulated production of IL- 6, IL- 10, and TNF- α , while it reduces the production of IL-2 and IL-4 by T cells stimulated only with anti-CD3 antibody. The effect of Se-Le-30 on the production of cytokines and the expression of CD25, TIM-3 and PD-1 was less significant in the culture of isolated T lymphocytes compared to the culture of PBMCs. It was also observed that Se-Le-30 caused decreased phosphorylation of ZAP70, SLP76 and LAT, and increased phosphorylation of Lck in both anti-CD3 and anti-CD3/CD28 antibody-stimulated cultures.

Conclusions: Se-Le-30 has the features of a T-cell immunomodulator, and the direction of its action depending on the stimulation model used is unique in relation to current literature data. The selective effect on T lymphocytes proliferation, cytokines production and expression of surface markers in cultures of isolated T lymphocytes indicate that Se-Le-30 may act directly on T lymphocytes, however, this effect is enhanced in PBMCs culture. This may suggest the influence of this polysaccharide also on other immunocompetent cells present in PBMCs, i.e. monocytes. Further *in vitro* and *in vivo* studies seem to be necessary to fully explain the mechanism of action of Se-Le-30 and to use this compound in therapy in the future.