Abstract

Carbohydrate dimers in tumor immunotherapy

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One possible approach to tumor immunotherapy is an activation of killer lymphocytes through specific ligands for their surface receptors. CD69 is a molecule greatly widespread among various cells of haematopoietic origin. Since the physiological ligand for this receptor is still unknown, ligand mimetics are used for modulation of its activity. The mimetics tested in this work are based on monomeric or oligomeric carbohydrated attached through two different chemical groups to the central linker of varying length, giving rise to thiourea and triazole series. The ability to precipitate soluble NKR-P1 and CD69 receptors was evaluated in precipitation assays and the optimal length of the linker for NKR-P1 receptor was found to be decyl. On the other hand, cross-linking of CD69 is not so dependent on the length of the linker.

The aim of this work was to describe *in vitro* effect of the tested compounds on cellular signalization, natural killing of leukemic cell lines and activation-induced apoptosis. Compounds of triazole series containing two disaccharides (GalNAc β1→4 GlcNAc) linked by a linker were found to have the strongest effect on the production of inositolphosphates and the elevation of intracellular calcium ions, as well as on the natural killing. Although compounds belonging to the triazole series showed almost none effect on activation-induced apoptosis, the compounds of thiourea series affected greatly cytotoxicity-induced cell death. The activation abilities of the tested carbohydrate dimers make them suitable for evaluation in experimental *in vivo* animal tumor therapies. (In English)