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Impaired cytolytic function of natural killer (NK) cells obtained from patients with head and neck cancer can be partially restored by the triggering of toll-like receptor 3 (TLR3) expressed on NK cells

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Background: Human natural killer (NK) cells play a critical role in innate immunity through their capacity to lyse malignant cells without prior antigen-specific priming. TLRs are expressed on inflammatory cells, including NK cells, and provide protection against infections benefiting the host. NK-cell function is impaired in patients with cancer. TLR3 is expressed on NK cells, but little is known about its role in NK-cell mediated activity in cancers. The aims of the study were: a) to analyze the frequency, phenotype and function of peripheral blood NK cells in patients with head and neck cancers (HNC) and b) to evaluate effects of TLR3 triggering on NK cell phenotype and function in these patients.

Materials and Methods: RT-PCR was used to evaluate the expression of TLR3 in NK cells TLR3 expression in NK cells was studied by RT-PCR. Multiparameter flow cytometry was used to evaluate the frequency of NK cells and expression of NK-cell activating receptors (NKp30, NKp46, NKG2D), CD69, interferon gamma, granzyme B, perforin, on NK cells isolated from the PBMC of normal controls (NC, n=10) and HNC (n=14). Lytic activity of NK cells stimulated or not with poly I:C, a ligand of TLR3, (50µg/mL) -/+ a constant dose of IL-2 (50 IU/mL) for 24h was tested in 51Cr-release assays against K562 targets. NF-kappaB translocation to nuclei and formation of conjugates with K562 cells after triggering of TLR3 was studied by confocal microscopy following immunostaining for a p65 subunit.

Results: Expression of CD69, activating receptors, granzyme B and perforin measured as mean fluorescence intensity (MFI) was significantly lower in NK cells of HNC patients vs NC ($p < 0.05$ for all) and correlated with the decreased function of NK cells (1170 vs. 1890 lytic units). TLR3 triggering on NK cell in HNC induced translocation of NF-kappaB, significantly increased lytic activity function and up-regulated expression of CD69 as well as IFN-gamma. However, it had no effect on the expression of activating receptors.

Conclusion: TLR3 expressed on NK cells is involved in the regulation of NK cell activity, and the impaired function of NK cells in HNC can be partially restored via TLR3 signaling using poly I:C.

Biography

Miroslaw J. Szczepanski, MD PhD graduated from Poznan University of Medical Sciences in Poznan, Poland in 2001 and completed his PhD in head and neck cancer immunology in 2010. He was a postdoctoral fellow at the University of Pittsburgh Cancer Institute from 2006-2009. After finishing his training in Pittsburgh he came back to Poland to complete his residency in Otolaryngology at the Department of Otolaryngology in Poznan. He has published 22 papers in reputed journal and has served as a reviewer for two scientific journals. His research interests are focused on cancer stem cells and on the role of toll-like receptors in head and neck cancer. He is also a principal investigator of two Polish Ministry of Sciences and Higher Education and Foundation for Polish Sciences grants on head and neck cancers.