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Vasoactive intestinal peptide 10-28 enhances natural killer cell cytotoxicity

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Abstract

Objective: Vasoactive intestinal peptide (VIP) and its synthetic analog VIP_{14-28} enhance NK cytotoxicity. This prompted us to study interaction of the naturally occurring peptide and orphan ligand VIP_{10-28} with NK.

Results: VIP_{10-28} stimulation (10^{-8}-10^{-10} M, 30 min.) increased NK-92 cytotoxicity against K562 max. from 52% +/-2.6% SEM (control) to 68% +/-2.6% SEM (E:T 1:1), similar to long-term IL-2 stimulated NK from different donors (4/6), max. from 38% +/-4.2 SEM (control) to 51% +/-0.9% SEM (E:T 1:1). VIP_{10-28} did not seem to induce degranulation, since granzyme B levels remained unchanged in NK-92. However, stimulation with 10^{-8}-10^{-10} M VIP_{10-28} for 5- 60 min. significantly induced tyrosine phosphorylation with ERK identified as one of the stimulated kinases. We used Informational Spectrum Method (ISM) to predict VIP_{10-28} NK receptor interactions. ISM results suggested potential binding of VIP_{10-28} to LFA-1α (F = 0.03, peptide residues 16-24) and with lower affinity to CD44 or MAC-1, but unlikely to NKG2D, -C, -A, NKp30, -44, -46, CD56, CD94, KIR2DL4, NKR-P1, CD45 or VIP receptors VPAC-1/ VPAC-2.

Conclusion: The neuroendocrine peptide VIP_{10-28} induces increased NK cytotoxicity potentially through LFA-1 signaling pathways involving tyrosine kinase activation of ERK kinases.