

MEETING ABSTRACTS

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Inhibition of KSHV-associated lymphoma engraftment in SCID mouse by morpholino oligomers

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Kaposi's sarcoma-associated herpesvirus (KSHV), also known as human herpesvirus 8, is associated with several malignant disorders, including Kaposi's sarcoma, primary effusion lymphoma (PEL), and multicentric Castlemann's disease. We have explored peptide-conjugated antisense phosphorodiamidate morpholino oligonucleotides (PPMOs) against KSHV and found effective PPMOs in inhibition of KSHV gene expression in cell culture. PPMOs are single-stranded DNA analogues that have a modified backbone and penetrate cells readily. In this study, we further tested the PPMOs in a SCID mouse model to assess their effect on engraftment and growth of PEL cells. PEL cells were engrafted into SCID mice via intraperitoneal route. PPMO was administered at the same time and repeated every other day for 10 doses. The mice were observed and scored for ascites development. The tumor cell burden was assessed by flow cytometry. Administration of anti-vIL-6 PPMO protected the mice from lymphoma development, while those mice receiving a control PPMO developed ascites and had high ratio of PEL cells in peritoneal lavage. The results demonstrate that PPMO against key KSHV genes can potently reduce KSHV replication and growth of PEL cells in SCID mice. Further exploration of PPMOs in the animal model is warranted.

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