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Titel des Beitrags: Treatment of peritoneal carcinomatosis by targeted delivery of the radio-labeled tumor homing peptide bi-DTPA-[F3]2 into the nucleus of tumor cells.

Abstract: BACKGROUND: Alpha-particle emitting isotopes are effective novel tools in cancer therapy, but targeted delivery into tumors is a prerequisite of their application to avoid toxic side effects. Peritoneal carcinomatosis is a widespread dissemination of tumors throughout the peritoneal cavity. As peritoneal carcinomatosis is fatal in most cases, novel therapies are needed. F3 is a tumor homing peptide which is internalized into the nucleus of tumor cells upon binding to nucleolin on the cell surface. Therefore, F3 may be an appropriate carrier for alpha-particle emitting isotopes facilitating selective tumor therapies. PRINCIPAL FINDINGS: A dimer of the vascular tumor homing peptide F3 was chemically coupled to the alpha-emitter (213)Bi ((213)Bi-DTPA-[F3](2)). We found (213)Bi-DTPA-[F3](2) to accumulate in the nucleus of tumor cells in vitro and in intraperitoneally growing tumors in vivo. To study the anti-tumor activity of (213)Bi-DTPA-[F3](2) we treated mice bearing intraperitoneally growing xenograft tumors with (213)Bi-DTPA-[F3](2). In a tumor prevention study between the days 4-14 after inoculation of tumor cells 6x1.85 MBq (50 microCi) of (213)Bi-DTPA-[F3](2) were injected. In a tumor reduction study between the
days 16-26 after inoculation of tumor cells 6x1.85 MBq of (213)Bi-DTPA-[F3][2] were injected. The survival time of the animals was increased from 51 to 93.5 days in the prevention study and from 57 days to 78 days in the tumor reduction study. No toxicity of the treatment was observed. In bio-distribution studies we found (213)Bi-DTPA-[F3][2] to accumulate in tumors but only low activities were found in control organs except for the kidneys, where (213)Bi-DTPA-[F3][2] is found due to renal excretion. CONCLUSIONS/SIGNIFICANCE: In conclusion we report that (213)Bi-DTPA-[F3][2] is a novel tool for the targeted delivery of alpha-emitters into the nucleus of tumor cells that effectively controls peritoneal carcinomatosis in preclinical models and may also be useful in oncology.