Dokumenttyp: journal article

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Titel des Beitrags: Tumor imaging and targeting potential of an Hsp70-derived 14-mer peptide.

Abstract: We have previously used a unique mouse monoclonal antibody cmHsp70.1 to demonstrate the selective presence of a membrane-bound form of Hsp70 (memHsp70) on a variety of leukemia cells and on single cell suspensions derived from solid tumors of different entities, but not on non-transformed cells or cells from corresponding ‘healthy’ tissue. This antibody can be used to image tumors in vivo and target them for antibody-dependent cellular cytotoxicity. Tumor-specific expression of memHsp70 therefore has the potential to be exploited for theranostic purposes. Given the advantages of peptides as imaging and targeting agents, this study assessed whether a 14-mer tumor penetrating peptide (TPP; TKDNNLLGRFELSG), the sequence of which is derived from the oligomerization domain of Hsp70 which is expressed on the cell surface of tumor cells, can also be used for targeting membrane Hsp70 positive (memHsp70+) tumor cells, in vitro. The specificity of carboxy-fluorescein (CF-) labeled TPP (TPP) to Hsp70 was proven in an Hsp70 knockout mammary tumor cell system. TPP specifically binds to different memHsp70+ mouse and human tumor cell lines and is rapidly taken up via endosomes. Two to four-fold higher levels of CF-labeled TPP were detected in MCF7 (82% memHsp70+) and MDA-MB-231 (75% memHsp70+)
cells compared to T47D cells (29% memHsp70+) that exhibit lower Hsp70 membrane positivity.
After 90 min incubation, TPP co-localized with mitochondrial membranes in memHsp70+ tumors. Although there was no evidence that any given vesicle population was specifically localized, fluorophore-labeled cmHsp70.1 antibody and TPP preferentially accumulated in the proximity of the adherent surface of cultured cells. These findings suggest a potential association between membrane Hsp70 expression and cytoskeletal elements that are involved in adherence, the establishment of intercellular synapses and/or membrane reorganization. This study demonstrates the specific binding and rapid internalization of TPP by tumor cells with a memHsp70+ phenotype. TPP might therefore have potential for targeting and imaging the large proportion of tumors (~50%) that express memHsp70.

Zeitschriften: PLoS ONE

Jahr: 2014
Band: 9
Heft / Issue: 8
Seiten: e105344
Sprache: eng

TUM Einrichtung:
Klinik und Poliklinik für RadioOnkologie und Strahlentherapie; II. Medizinische Klinik und Poliklinik

Occurences:
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > II. Medizinische Klinik und Poliklinik (Gastroenterologie) > 2014
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > Klinik und Poliklinik für RadioOnkologie und Strahlentherapie > 2014

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