Dokumenttyp: journal article

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Titel des Beitrags: Immunotherapeutic targeting of membrane Hsp70-expressing tumors using recombinant human granzyme B.

Abstract: We have previously reported that human recombinant granzyme B (grB) mediates apoptosis in membrane heat shock protein 70 (Hsp70)-positive tumor cells in a perforin-independent manner. Optical imaging of uptake kinetics revealed co-localization of grB with recycling endosomes (Rab9/11) as early as 5 min after internalization, with late endosomes (Rab7) after 30 min, and the lysosomal compartment (LAMP1/2) after 60 to 120 min. Active caspase-3-mediated apoptosis was induced in mouse CT26 monolayer cells and 3D tumor spheroids, but not in normal mouse endothelial cells. Granzyme B selectively reduced the proportion of membrane Hsp70-positive cells in CT26 tumor spheroids. Consecutive i.v. injections of recombinant human grB into mice bearing membrane Hsp70-positive CT26 tumors resulted in significant tumor suppression, and a detailed inspection of normal mouse organs revealed that the administration of anti-tumoral concentrations of grB elicited no clinicopathological changes. These findings support the future clinical evaluation of human grB as a potential adjuvant therapeutic agent, especially for treating immunosuppressed patients that bear membrane Hsp70-positive tumors.

Zeitschriftentitel / Abkürzung: PLoS ONE

Jahr: 2012