adapter led to a significantly reduced adenoviral liver load and hepatotoxicity in mice. For investigations on antitumoral immune responses and therapeutic efficacy we used an orthotopic animal model in both immunocompetent C57 Bl/6 and immunodeficient nude mice. In these models, only CARsc-pShia-complexing of viruses allowed for significant transduction. Interestingly, improved transduction led to improved local tumor regression and prolonged survival in immunocompetent mice but not in T-cell deficient nude mice. Consistently, large infiltrations of CD45-pos. cells in virus-affected, lytic areas were only detectable in mice which received retargeted OAV. Most important we could show that retargeted OAV induced a mutation-specific CD8 T cell response against the tumor-associated mutation of Gsta2.

Conclusions: In conclusion, our results show that adapter-mediated retargeting of OAV represents a promising strategy to raise immune responses against clinically relevant tumor entities with reduced hepatotoxicity.

P89 HEAT SHOCK FACTOR 1 (HSF1) IS DOWNREGULATED IN RADIOFREQUENCY ABLATED MICE WITH SECONDARY LIVER CANCER PRTREATED WITH NANOLIPOSOMAL shRNA-HSF1

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Background and Aims: Heat shock factor 1 (HSF1), is the master regulator of genes encoding molecular chaperones and is involved in cellular processes such as stress response, cell differentiation and carcinogenesis. Recent studies identified a HSF1-regulated transcriptional program specific to high malignancy and distinct from the classical HSF1-induced heat shock response. We investigated HSF1 during tumour formation and the effect of shRNA-HSF1-nanoliposomes as a possible adjuvant thermosensing therapy in combination with radiofrequency ablation (RFA) in metastatic liver cancer.

Methods: Colon carcinoma CT26 cells were used to assess shRNA-HSF1-nanoliposomal uptake, toxicity/efficiency by employing immunofluorescence, Q-PCR and protein analysis. Sub-lethal heat experiments were performed by using different time points/temperatures. An orthotopic murine model of CRC-liver metastasis was used to analyse HSF1 expression during tumour formation. RFA in small animals was optimized to investigate the HSF1-induced signalling pathway in the treatment of liver metastasis.

Results: shRNA-HSF1-nanoliposomes were taken up by 99% of cells without inducing cytotoxicity. Sub-lethal heat treatment of 45 and 50 degrees C induced p-ERK, p-AKT and HSF1-related proteins and this coincided with a nuclear to cytosolic shift of HSF1, HSP70/90, AKT and ERK. Apoptosis was only significantly induced after 10 days post-heat treatment. In vivo, tumours highly expressed HSF1, HSP70/90, AURKB and p-ERK and p-AKT. Six and 10 days after RFA, tumour tissue showed an upregulation of HSF1, HSP70/90 suggesting tumour recurrence.

Conclusions: This study demonstrates that HSF1 is highly expressed in CRC liver metastasis. We are currently investigating the effect of pre-treatment with shRNA-HSF1-nanoliposomes followed by RFA in reducing tumour recurrence.