CONTROL ID: 1736092

SESSION TITLE: Parallel 37: Liver Cancer: Pathogenesis and Treatment

SESSION START TIME: 11:15 AM **SESSION END TIME:** 12:45 PM

SESSION LOCATION: Ballroom AB

SESSION ROLE & SESSION HOST (ALL): Moderator (Tamar Taddei)

SESSION ABSTRACT START TIME: 12:00 PM

SESSION ABSTRACT END TIME: 12:15 PM

Abstract:

TITLE: A novel immunotherapeutic treatment for experimental hepatocellular carcinoma (HCC) using the host-defense derived peptide LTX-315.

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ABSTRACT BODY: Host defense peptides can kill pathogens directly and have immune-modulating properties. Shorter chemically modified peptides derived from host defense peptides, have shown potent anti-neoplastic properties on different types of cancers (1). The aim of the present study was to test whether the 9-mer peptide, LTX-315, could be utilized as a novel immunotherapeutic agent for hepatocellular carcinoma in a rodent model

Two main treatment regimens were utilized: In group A, liver tumors were induced in Male Fisher rats by direct intrahepatic (i.h.) injection of 1 x 106 JM1 cells. After 5 days the animals were treated intratumorally with LTX-315 for three consecutive days. In group B, a vaccination protocol consisting of s.c. injection of LTX-315 and cell lysate of JM1 cells once weekly for 4 consecutive weeks was used. After another 4 weeks animals were inoculated with 1 x 106 JM1 cells s.c.. Control animals in both groups received saline instead of LTX-315.

Tumors in group A were successfully ablated in 6 out of 7 treated animals, whereas all control animals developed a lethal hepatic tumor in the course of 3-4 weeks. Re-challenge with 1 x 106 JM1 cells s.c. one month after treatment did not lead to tumor development, whereas control animals developed large s.c. tumors in the course of 2-3 weeks.
In group B, the 5 animals developed a slow growing tumor with maximal size after 29 days, that subsequently regressed completely in the course of the next 30-40 days. The animals were protected against i.h. and s.c. re-challenge with JM1 cells after another 50 and 100 days respectively, whereas controls had to be sacrificed 3 weeks after inoculation due to large tumor burden
To investigate whether the treatments (A and B) invoked a transferrable anti-tumor response, 6 new animals were subjected to total body irradiation and thereafter immunologically reconstituted by infusion of 3 x 106 splenocytes from the cured animals in either group A or B. This led to complete protection against both intrahepatic and subcutaneous tumor growth, whereas irradiated control animals reconstituted with splenocytes from wild type animals developed large s.c. or intrahepatic tumors.

Conclusion: LTX-315 can induce specific, transferrable long lasting immune response against experimental HCC tumors, both when used intra-lesionally and in a preemptive vaccine together with HCC cell lysate. LTX-315 is being developed for the treatment of solid tumors and is currently in phase 1.

References.1. Therapeutic vaccination against a murine lymphoma by intratumoral injection of a cationic anticancer peptide. Berge et al. Cancer Immunol Immunother (2010) 59:1285–1294.