MP01-14 BORON NEUTRON CAPTURE THERAPY OF BLADDER CANCER BY TUMOR VASCULAR ENDOTHELIAL TARGETING IF7 PEPTIDE-BORON DRUG

Shingo Hatakeyama*, Tohru Yoneyama, Mihoko Yoneyama, Hayato Yamamoto, Takahiro Yoneyama, Yasuhiro Hashimoto, Shintaro Ishiyama, Minoru Suzuki, and Chikara Ohyama*,Department of Urology, Hirosaki University Graduate School of Medicine, **Hirosaki, Japan**

Objectives:

Boron neutron capture therapy (BNCT) is based on selective accumulation of B10 carriers in tumors followed by neutron irradiation. As the major limitation of BNCT was drug delivery of BPA. We developed a tumor-targeting BNCT using tumor vasculature endothelium targeting peptide (IF7) conjugated boronophenylalanine (BPA-IF7) to improve the biodistribution of BPA.

Methods:

BPA or BPA-IF7 (7 mg/kg, 1/35 of effective dose) was intravenously administrated to MBT2 tumor-bearing C3H/HeNJc mice. Tumor concentration of B10 was measured by neutron-induced prompt gamma-ray analysis at 5, 20, and 40 min and compared between the BPA and BPA-IF7. The tumors received reactor thermal neutron beam irradiation following the single administration of 7 mg/kg of BPA-IF7. Tumor growth was compared between the irradiated (n=7) and control (n=19) mice for 2 weeks.

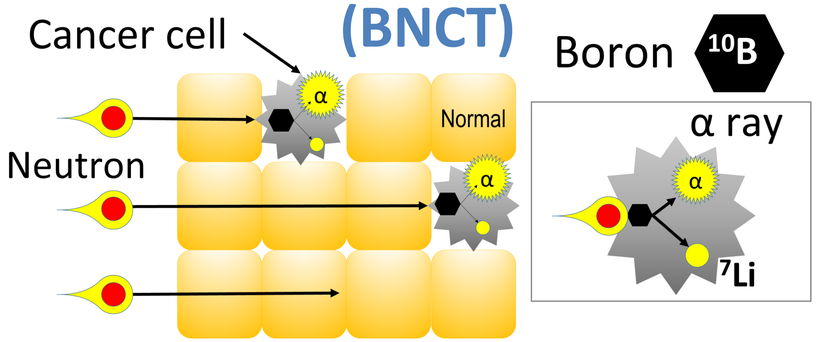
Results:

Tumor concentration of B10 was 5-fold higher in the BPA-IF7 than that in the BPA. The tumor concentration of B10 reached 20 ppm within the 20 min in the BPA-IF7 mice. Tumor size was significantly decreased in the BPA-IF7 mice than that in the control mice (12 vs 1845 mm 3, P=0.040)

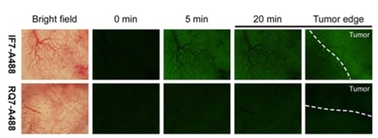
Conclusions:

BPA-IF7 showed faster tumor-specific boron accumulation than conventional BPA and showed antitumor effects at low doses. BPA-IF7 has the potential to improve drug delivery of BPA and antitumor effect for BNCT.

Boron neutron capture therapy (BNCT)

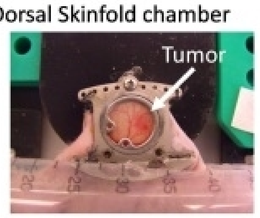


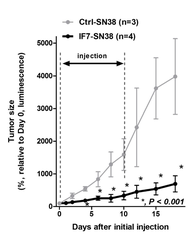
Tumor vasculature endothelial targeting IF7 peptide

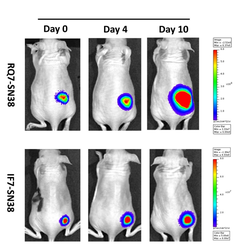


IF7 — SN-38

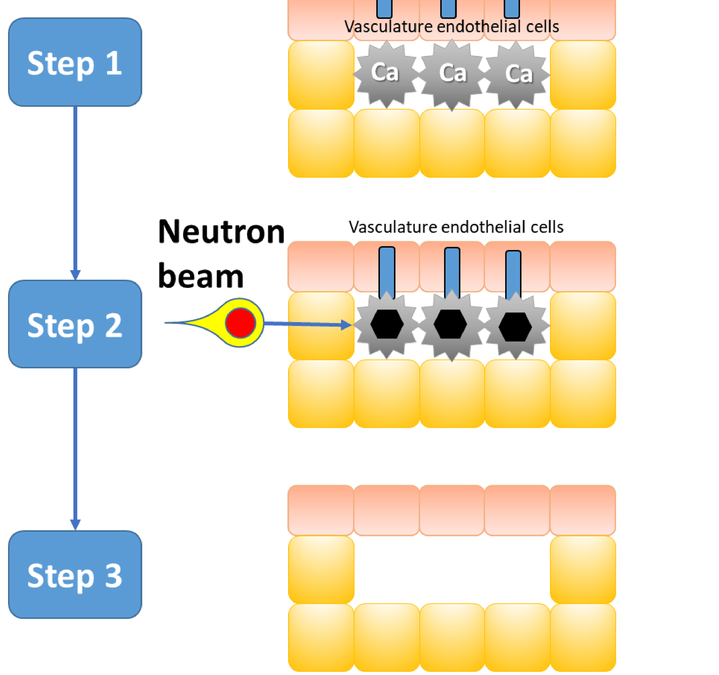
Dorsal Skinfold chamber

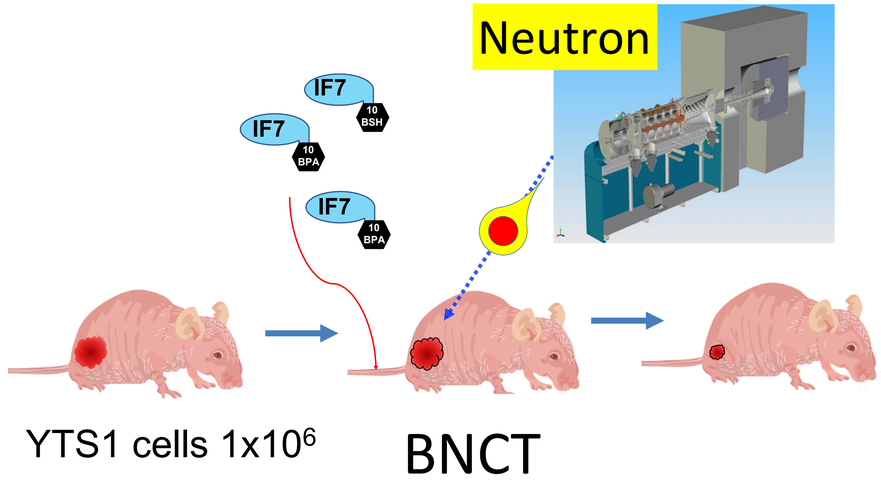


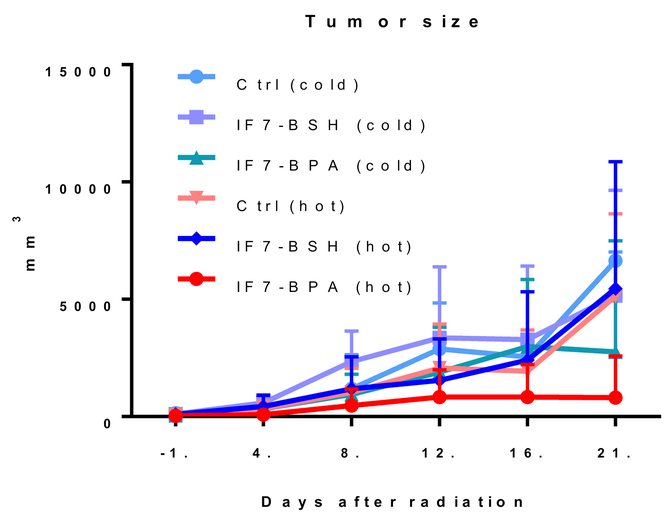




IF7 assisted BNCT therapy







Tumor vessel targeting B-IF7