GS1-3 Development of Boron Delivery System for Neutron Capture Therapy

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Boron neutron capture therapy (BNCT) is a binary cancer treatment based on the nuclear reaction of two essentially nontoxic species, ^{10}B and thermal neutrons. The neutron capture reaction by ^{10}B produces an α-particle and a lithium-7 ion bearing approximately 2.4 MeV, and these high linear energy transfer particles afford precise cell killing. Therefore, the marked accumulation and selective delivery of boron into tumor tissues are the most important requirement to achieve an effective BNCT of cancers. We focused on a liposomal boron delivery system. Accumulation of boron in the liposomal bilayer is highly potent, because drugs can be encapsulated into the vacant inner cell of a liposome. Furthermore, functionalization of liposomes is possible by combination of lipid contents. Therefore, boron and drug may be simultaneously delivered to tumor tissues for both BNCT and chemotherapy. We report synthesis of *closo*-dodecaborate containing boron lipids. Our design of the boron lipids is based on biomimetic composition of phosphatidylcholines. Mercaptoundecahydrododecaborate ($B_{12}H_{11}SH^{2-}$, BSH) was chosen as an alternative hydrophilic function of boron lipids. BSH is a water-soluble divalent anion cluster and significantly lowered toxicity, and has thus been utilized for clinical treatment of BNCT. We prepared the boronated liposomes from diacylphosphatidylcholines and boron lipids and examined their BNCT effect using tumor bearing mice. Suppression of tumor growth was observed in the mice injected with the boronated liposomes two weeks after neutron irradiation.