Keywords

Boron neutron capture therapy (BNCT)

high CA19-9 pancreatic cancer

boron agent

precision BNCT

glucose-conjugated drug

chemoradiation therapy

Abstract

Multidisciplinary therapy centered on radical surgery for resectable pancreatic cancer is expected to prolong prognosis, but relies on CA19-9 biomarker levels to determine treatment strategy. Boron neutron capture therapy (BNCT) is a chemoradiotherapy using tumor hyperaccumulator boron drugs and neutron irradiation. The purpose of this study is to investigate novel boron drug agents for BNCT for pancreatic cancer. Bioinformatics was used to evaluate the uptake of current boron amino acid (BPA) drugs for BNCT into pancreatic cancer. The expression of the amino acid transporter LAT1, a BPA uptake transporter, was low in pancreatic cancer and even lower in high CA19-9 pancreatic cancer. In contrast, the glucose transporter was high in high CA19-9

pancreatic cancers and inversely correlated with LAT1 expression. Considering the low EPR effect in pancreatic cancer, we synthesized a small molecule Glucose-BSH, which is boron BSH bound to glucose, and confirmed its specific uptake in pancreatic cancer. uptake of Glucose-BSH was confirmed in an environment compatible with the tumor microenvironment. The therapeutic efficacy and safety of Glucose-BSH by therapeutic neutron irradiation were confirmed with BNCT. We report Glucose-BSH boron drug discovery study of a Precision Medicine BNCT with application to high CA19-9 pancreatic cancer.