

Imaging Ligands Targeting Glypican-3 (GPC3) Receptor Expression in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is the third leading cause of cancer mortality and is increasing in incidence worldwide. Early detection of HCC is important since potentially curative therapies exist in the initial stages of HCC; no curative therapies exist for late-stage HCC. However, the initial detection of HCC remains challenging due to the lack of symptoms during the early stage of the disease. Other methods of screening and detecting HCC, including blood serum tests and conventional imaging methods, remain inadequate due to genetic differences between patients and the high background activity of liver tissues. Thus, there is a need for an accurate imaging agent for the diagnosis, staging, and prognosis of HCC. Glypican-3 (GPC3) is an oncofetal receptor responsible for regulating cell division, growth, and survival. GPC3 is a clinically relevant biomarker for imaging and therapeutics, as its expression is HCC tumor-specific and absent from normal and other pathological liver tissues. The development of novel GPC3-targeting imaging agents has encompassed three classes of biomolecules: peptides, antibodies, and aptamers. These biomolecules serve as constructs for diagnostic imaging (demonstrating potential as positron emission tomography [PET], single-photon emission tomography [SPECT], and optical imaging agents) and HCC treatment delivery. At least 20 unique ligands have been identified in the literature as showing specificity for the GPC3 receptor. Although several ligands are currently under clinical investigation as therapies for HCC, clinical translation of GPC3-targeting ligands as imaging agents is lacking. This review highlights the current landscape of ligands targeting GPC3 and describes their promising possibilities as imaging agents for HCC.