

**Investigation and development of selective Glypican-3 (GPC3)-targeting receptors for tumor burden monitoring in hepatocellular carcinoma patients.**

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Hepatocellular carcinoma (HCC) is the sixth most common cancer, the second leading cause of cancer-related death and it represents the 85-90% of all primary liver cancers.<sup>1</sup> HCC is often diagnosed at late stages when it becomes symptomatic and no potentially curative treatments are available, leading to death within few months.<sup>1</sup> The high incidence of HCC and its high mortality led to the necessity of finding better diagnostic markers and therapy targets to overcome this disease.<sup>1</sup> Glypican 3 (GPC3) is a heparan sulfate proteoglycan located on the cell surface by a GPI anchor.<sup>2,3</sup> GPC3 protein is expressed in normal tissues during development, whereas in most adult tissues is suppressed.<sup>2,3</sup> GPC3 is highly expressed in HCC, where is involved in cell proliferation by increasing Wnt signaling.<sup>4</sup> Of note, GPC3 expression is specific of HCC malignant lesions, while its expression is low or absent in pre-malignant lesions or normal liver tissues.<sup>5,6</sup> By taking advantage of the specific and high expression of GPC3 in HCC, the present project aims at investigating the use of nanostructures linked with selective Glypican-3 (GPC3)-targeting receptors for diagnostic/theranostic purposes in HCC-affected patients.

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