



CF102 an A₃ adenosine receptor agonist induces *in vivo* apoptosis of Hepatocellular carcinoma

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The A₃ adenosine receptor (A₃AR) is highly expressed in solid tumors and has been suggested as a potent target for cancer treatment. In this study we first show that both human and rat Hepatocellular Carcinoma (HCC) cells highly express the A₃AR and that CF102, a highly selective agonist to the receptor induces apoptosis of HCC *in vivo*.

Increased A₃AR expression levels were detected in tumor tissues and in peripheral blood mononuclear cells (PBMCs) derived from patients with HCC. Similar data was observed in N1S1 HCC tumor bearing rats, demonstrating that A₃AR expression levels in the PBMCs reflect receptor status in the remote tumor. The high expression level of the receptor was directly correlated to over expression of NF-κB, known to act as a transcription factor of A₃AR.

To explore whether A₃AR may be utilized as a specific target to combat HCC, CF102 was administered orally thrice daily to N1S1 tumor bearing rats. CF102 induced marked dose response inhibition of tumor growth via de-regulation of the NF-κB and the Wnt signal transduction pathways, resulting in apoptosis of tumor cells.

Taken together, A₃AR is highly expressed in tumors and PBMCs of HCC patients and tumor bearing rats. CF102 targets the A₃AR, to induce apoptosis and tumor growth inhibition. The NF-κB signal transduction pathway is involved in receptor expression and functionality. These data suggest A₃AR as a novel biomarker target therapy to be developed for the treatment of HCC.