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CF102 Exerts a Differential Effect in Various Pathological Liver Conditions: Protection from Inflammation Damage and Anti-tumor Activity

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Backgrounds: A_3 adenosine receptor (A_3AR) was found to be highly expressed in a broad spectrum of cancerous and inflammatory tissues. Selective agonists at the A_3AR, such as CF101 and CF102 were found to induce anti-inflammatory and anti-cancer effects. In this study we examined the differential effect of CF102 in pathological conditions of the liver.

Methods: The anti-inflammatory protective effect of CF102 was tested in a model of liver inflammation induced by Concanavalin A (Con. A) and an anti-cancer effect of CF102 was examined by a xenograft model of hepatocellular carcinoma (HCC). The mechanism of action was explored by following the expression levels of key signaling proteins in liver and tumor extracts, utilizing Western blot analysis.

Results: In Con. A-induced liver injury CF102 (100μg/kg) markedly reduced secretion of glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) in comparison to the vehicle-treated group. In addition, CF102 treatment inhibited the Nuclear Factor κB (NF-κB) –Tumor necrosis factor-α (TNF-α) signaling pathway and prevented apoptosis in the liver as was demonstrated by decreased expression levels of Fas receptor (FasR) and the pro-apoptotic proteins Bax and Bad in liver tissues. CF102 was also found to induce up regulation of the apoptotic signaling pathway in the HCC model, resulting in tumor growth inhibition.

Conclusions: CF102 protects the liver against Con. A-induced hepatitis and inhibits HCC tumor growth in experimental models. These results suggest that CF102, through its differential effect, is a potential drug candidate to treat various pathological liver conditions.