A Novel and Efficacious Therapy for Human Liver Cancer [ID: 18001]

Published date: Oct. 23, 2018

Technology description

Overview

Human liver cancer is one of the most pharmacologically challenging cancer types with almost 700,000 (40,710 in the US) new diagnoses and 600,000 (28,920 in US) deaths worldwide, annually. Current approved treatments are limited to surgery (liver transplant, laparoscopy), radiation (brachytherapy), and a single small molecule (sorafenib). Surgery and radiation are limited to early diagnoses, leaving sorafenib as the only treatment option for advanced and metastatic cases of liver cancer. Sorafenib has a high effective dose (>1500mg/daily) and multiple undesirable side effects (cardiovascular complications, internal bleeding). Even with treatment, there is still a high degree of disease recurrence (>50%). Therefore, the field of human liver cancer has a standing order for new, effective drug candidates.

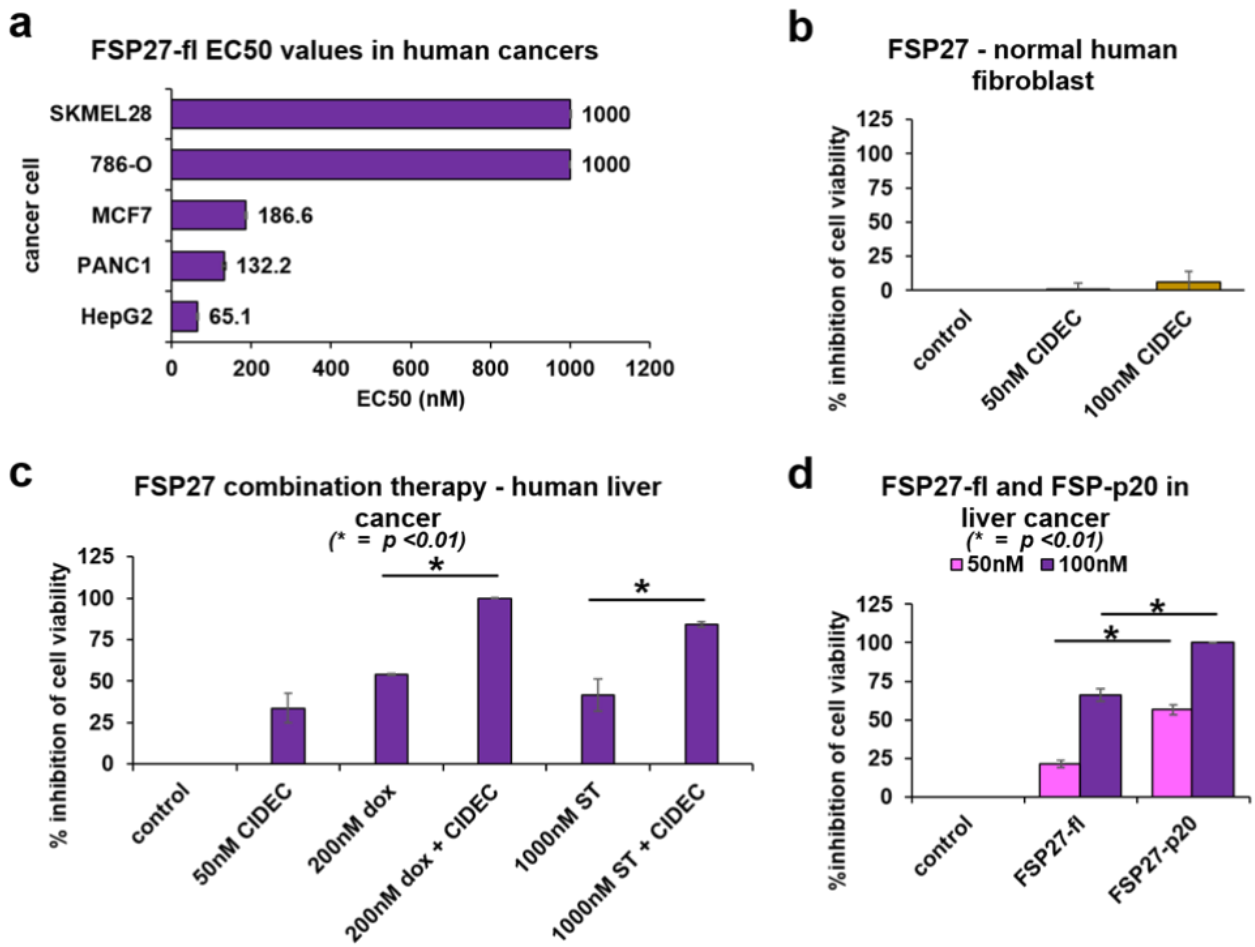
Extracellular administration of recombinant human full length (fl) FSP27 (FSP27-fl) on human cancer cells demonstrated the following:

EC50 of FSP27-fl against human cancers show marked specificity for HepG2 liver cancer cells (65nM)

FSP27-fl has low toxicity against non-cancerous human fibroblast cells, showing specificity for cancer calls over normal cells

FSP27-fl markedly augments the effects of sorafenib and doxorubicin in liver cancer when used as an adjuvant therapy, even at sub-EC50 doses

A unique, 20-amino acid peptide fragment of full-length human FSP27 (FSP27-p20), identified by fragment analyses study, shows increased potency and efficacy over FSP27-fl against human liver cancer



(a) EC50 (effective concentration for 50% reduction in cell viability) of full length human FSP27 against several human cancer cell lines (Liver, Pancreatic Breast, Renal and Melanoma). (b) FSP27-fl has very low toxicity against non-cancerous human fibroblast cells showing specificity for cancer cells over normal cells. (c) FSP27-fl augments sorafenib and doxorubicin effects significantly even at sub-EC50 doses when used as an adjuvant therapy in liver cancer cells. (d) A unique 20-amino acid peptide of human FSP27 (FSP27-p20), shows increased potency over full length FSP27, against human liver cancer.
Printable Overview

Application area

Recombinant FSP27 can be formulated as a singular therapeutic to treat human liver cancer, either as full length or a peptide fragment. In addition, FSP27 can be delivered as an adjuvant therapy to improve the efficacy and decrease the toxicity of existing liver cancer treatments.

Advantages

Fat Specific Protein (FSP27), also known as cell death-inducing DFFA-like effector c (CIDEC in humans and Cidec in mice) is a 238-amino acid protein and a member of the cell death-inducing DNA fragmentation factor-like effector family (CIDE) - a group of genes that play an important intracellular role in apoptosis. FSP27 is principally known to promote lipid droplet formation in adipocytes,

following insulin action. We have identified a hitherto unknown and novel role of FSP27 as a highly effective therapy specifically targeting liver cancer.

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