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.

Benefits

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.

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 cells 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

Commercial Application

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.

Patent Status

A NOVEL AND EFFICACIOUS THERAPY FOR HUMAN LIVER CANCER

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(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.

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About the Inventors

Vishwajeet Puri, Ph.D. is a Professor in the Department of Biomedical Sciences and the Diabetes Institute. Since 2015 he has been a Heritage Endowed Professor at the Heritage College of Osteopathic Medicine (HCOM), Ohio University. He is an accomplished cell biologist with 17 years of research experience in the area of lipid transport and metabolism and over 9 years of experience in fat metabolism in relation to metabolic disease including obesity, type 2 diabetes and cardiovascular disease. After finishing his PhD in lipid Biochemistry from a prominent institute in India, Institute of Microbial Technology, he performed his postdoctoral studies in lipid Cell Biology and Molecular Biology at Mayo Clinic, Rochester, MN. Following that he was a junior faculty at Umass Medical School, Worcester, MA for 5 years and then moved on to establish an independent research program at Boston University School of Medicine (BUSM), Boston, MA. After 6 years of accomplished research at BUSM, he was recruited at Ohio University to establish a research program in the area of Obesity and Diabetes. He pioneered the identification of FSP27 and Cidea as lipid droplet associated proteins with a significant role in fat metabolism and improved metabolic health in humans. His research has been funded by National Institute of Health, Ohio Heritage Foundation and HCOM.

John J. Kopchick is an internationally recognized leader in the growth hormone field. Since 1987 he has been the Goll-Ohio Eminent Scholar and Distinguished Professor of Molecular Biology in The Edison Biotechnology Institute and the Heritage College of Osteopathic Medicine at Ohio University in Athens, Ohio. He attended Indiana University of Pennsylvania (IUP) and received his B.S. and M.S. degrees in Biology/Chemistry. His Ph.D. in Biomedical Sciences was awarded in 1980 by the University of Texas at The M.D. Anderson Cancer Center in Houston, Texas. He then performed postdoctoral studies in molecular virology at the Roche Institute of Molecular Biology, Nutley, N.J. Following that, he was a group leader in molecular medicine at Merck & Co., Rahway, N.J. Dr. Kopchick and his group were the first to discover and characterize GH receptor antagonists, an accomplishment for which he and Ohio University were awarded several US and European patents. He also was instrumental in founding a company, Sensus, which applied his research to the development of an FDA approved drug called Somavert (Pegvisomant for injection) which is marketed for patients with acromegaly. Dr. Kopchick has published more than 350 scientific articles and serves or has served on the Editorial Boards of Endocrinology, Molecular Endocrinology, GH & IGF-1 Research, Pituitary, and The Journal of Biological Chemistry. He is Past-President of the Growth Hormone Research Society and currently is a member of their Counsel. He has received many awards including the British Endocrine Society Transatlantic Award (2011) and the title of Ohio University Distinguished Professor in 2012. He has advised 30 Ph.D., 14 M.S., 35 Post-doctoral fellows, and over 300 undergraduate students in the molecular aspects of growth, diabetes, and aging.

Vishva M. Sharma received his Ph.D. in Biotechnology/Molecular Biology from the Institute of Microbial Technology, (IMTech), India and is a research Scientist at the Ohio University Heritage College of Osteopathic Medicine in Athens, Ohio. He was instrumental in developing thermotolerant yeast strains with enhanced ethanol productivity. Royalties from the sale of that yeast strain has yielded ~Rs 2.2M to IMTech, India. He has received awards from Lymphoma Research Foundation (US), American Cancer Society and Council of Scientific & Industrial Research, India.

Reeto Basu is a postdoctoral researcher with the Edison Biotechnology Institute (EBI), Ohio University, in the Kopchick lab. Dr. Basu received his Ph.D. in Molecular and Cellular Biology (MCB) from Ohio University in 2016. Prior to that he obtained MS degrees in Neuroscience at Ohio University and in Biochemistry at Bangalore University, India. He also worked as a junior scientist in the industry at AstraZeneca, India, working on tuberculosis drug discovery projects. His current research at EBI includes work on endocrine aspects of human cancers and cancer drug resistance, identification of anti-cancer properties of natural compounds and multiple collaborative drug discovery projects.