Leptin Induces Proliferation and Notch Expression In Pancreatic Cancer

Felice Watson
Ruben R. Gonzalez-Perez, Ph.D., Morehouse School of Medicine

Coordinating Center: Charles R. Drew University of Medicine and Science

ABSTRACT

Pancreatic adenocarcinoma (PA) is an aggressive cancer. It develops in a way that causes almost no detectable symptoms, which leads to a rapid progression and a short survival rate. Researchers have discovered a link between pancreatic cancer (and other cancer types) and obesity. High levels of leptin, an appetite hormone secreted by adipocytes, have been found in obese people. Studies have shown that the absence of leptin in the body or severe leptin resistance can lead to uncontrolled eating and weight gain, hence, its connection to obesity. Consequently, our lab is analyzing the relationship between obesity and leptin and what effects they have on pancreatic cancer progression.

We hypothesize that in PA cells, leptin induces proliferation, tumorigenesis, and increased levels of Notch and related molecules. These effects are reversed by our leptin antagonist linked to iron nanoparticles, IONP-LPrA2 (iron oxidized nanoparticles leptin peptide receptor antagonist). We’re mainly focused on 4 cell lines: Panc-1, MiaPaCa-2, and BxPc3 (derived from primary tumors) and AsPc-1 (from a metastatic tumor). Of the primary tumors, Panc-1 and MiaPaCa-2 are more aggressive and BxPc-3 is less aggressive.

We expect results validating that leptin will induce proliferation (in Panc-1 and AsPc-1 cells by MTT assay), expression of Notch and other molecules (in BxPc3 and MiaPaCa-2 cells by flow cytometry and Western Blot), and tumorsphere formation (in Panc-1). Leptin may also induce Notch expression in Panc-1 tumorspheres.

In conclusion, this project will demonstrate the involvement of leptin in PA progression. Leptin's effects will be abrogated by the inhibitor of leptin signaling, IONP-LPrA2.

Key words: Obesity, Leptin, Pancreatic Cancer, PA cell lines

ACKNOWLEDGEMENTS

The STEP-UP HS program is supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health, Grant Number: 5R25DK078384-09.