FGF21: A Novel Regulator of Cachexia

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Cachexia is the loss of weight, muscle atrophy, fatigue, weakness and loss of appetite, which is nutritionally irreversible. It is commonly seen in patients with AIDS, COPD, CHF, TB, and most remarkably, 80% of cancer patients, of which is the cause of death in 20%. FGF21 is a hormone abundant in the liver, pancreas, and white adipose tissue with broad metabolic actions surrounding an adaptive starvation response. FGF21 has been well characterized with exception to its role in muscle catabolism, the key factor of cachexia. With our research we sought to characterize the association between cachexia and FGF21.

AIMS:
1. Characterize atrophy markers in muscle cells supplemented with FGF21;
2. Determine if FGF21 KO mice have a diminished rate of muscle wasting and depressed expression of cachexia markers when fed a low protein highly ketogenic diet;
3. Ascertain whether FGF21 KOmice injected with lewis lung carcinoma (LLC) cells show a diminished cancer-induced lean mass loss.

METHODS: Cell culture experiments were performed on skeletal muscle cells supplemented with varying concentrations of FGF21. Samples were analyzed via RT-PCR for muscle atrophy markers. The animal model studies compared wildtype to FGF21 KO mice, each with 3 varying diet subgroups (low fat diet, high protein ketogenic diet, low protein ketogenic diet). Animals were on the diet for 2 weeks with regular blood glucose, total body mass, lean mass, and fat mass measurements. Muscle atrophy markers were measured in various tissues post sacrifice. The tumor model study was done via LLC injections into the right hind of the mice. Tumor progression was followed for 20 days. The same measurements were taken as those of the diet cohort.

RESULTS: Cell culture experiments showed marked increase in muscle atrophy markers. Additionally, we observed a significant increase in FGF21 expression in mice fed a low protein ketogenic diet. Unfortunately, in the wildtype to FGF21 KO study, significant differences were not seen in any parameter.

CONCLUSION: Initial experiments characterizing FGF21 as an inducer of cancer related cachexia showed promise however further work needs to be done to characterize this relationship in FGF21 KO mice to better understand the true nature of this growth factor.

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