TREATMENT FOR CANCER-ASSOCIATED CACHEXIA (CAC)

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CANCER-ASSOCIATED CACHEXIA

• Cachexia is characterized by anorexia and body wasting.
• Cachexia affects 1.3M cancer patients each year in the US alone.
• 80% of cancer patients suffer from cachexia and 30% die directly from cachexia.
NO FDA-APPROVED DRUGS TO TREAT CACHEXIA

PHASE 2
• Curcumin, dietary supplement
• PF-06946860 (Pfizer), a GDF15 inhibitor

PHASE 3
• Megestrol acetate (progesterone analog)
  –found to induce severe blood clotting problems
OUR METHOD ACTIVATES AGRP NEURONS IN THE HYPOTHALAMUS

CACHEXIA IS ASSOCIATED WITH INHIBITION OF AGRP NEURONS

WE HAVE A PATENT ON THIS NOVEL TREATMENT WITH BATES COLLEGE ON BOBCAT339 AND DERIVATIVES
MECHANISM OF ACTION: DEGRADES TET3 PROTEIN

Lv et al, PNAS, 2023

Decreases steady-state TET3 protein level without affecting its mRNA in cultured neurons

Destabilizes TET3 protein in cultured neurons

Decreases TET3 protein in AgRP neurons without affecting its mRNA in mice

Activates AgRP neurons in mice

AgRP neurons in green, TET3 protein in red
OUR METHOD MITIGATES ANOREXIA IN A MOUSE MODEL

Activity-Based Anorexia mouse model

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Mitigates psychological problems associated with anorexia

Decreases anxiety/depressive behaviors

No Liver Toxicity

No Kidney Toxicity
OUR METHOD ACTIVATES AGRP NEURONS IN A TUMOR MODEL
LEWIS LUNG CARCINOMA (LLC)

- Lung cancer accounts for ~1/5 of all cancer deaths.
- Cachexia is a major contributor to morbidity and mortality in lung cancer.
- LLC is a mouse lung cancer cell line that is highly representative of human lung cancer.
- LLC has been used extensively to study lung cancer biology and treatments.
- LLC is a well-established model for cancer-induced cachexia.
$30K Accelerator Funding
- Huang Lab PoC efficacy study in LLC

PK and MedChem of BC
- In vitro PK
- In vivo PK
- Optimization of dosage
- Optimization of compound

Efficacy and Safety
- CRO run efficacy and preliminary toxicology studies

Proposal for full Blavatnik Award in 2023-24

PLATFORM DEVELOPMENT PLAN
TEAM:

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