Weill Cornell Medicine

Synthetic Peptide Inhibitors of FABP5 for Treatment of Diet-Associated Cancer and Metabolic Disease

Lead Inventors:

John Blenis, Ph.D.
Anna-Maria and Stephen Keller Professor in Cancer Research
Associate Director of Basic Science, The Sandra and Edward Meyer Cancer Center
Professor of Pharmacology, Weill Cornell Medicine

Business Development Contact:
Jeffrey James
Associate Director, Business Development and Licensing
(646) 962-4194
jaj268@cornell.edu

Synthetic Peptide Inhibitors of FABP5 for Treatment of Diet-Associated Cancer and Metabolic Disease

Background & Unmet Need

- mTORC1 signaling is central to linking nutrient availability and cell growth, and is implicated in the pathogenesis of obesity, metabolic disorders, and cancer, amongst other diseases
- Current inhibitors of mTORC1 demonstrate high levels of toxicity, a small therapeutic window, as well as the high rates of resistance in many tumor cells
- High fat diets, which contain high levels of omega-6 polyunsaturated fatty acids (ω6-PUFAs), have been associated with various health complications
- FABP5, a fatty acid sensor, directly activates mTORC1 signaling in response to omega-6-linolenic acid (ω6-LA), the most common form of ω6-PUFAs
- **Unmet Need:** Novel therapeutic approaches that can mitigate the health impacts of excessive dietary ω6-PUFA intake while avoiding the complications associated with direct mTORC1 inhibition

Technology Overview

- **The Technology:** A novel therapeutic approach targeting FABP5's activation of mTORC1 for treating triple-negative breast cancer (TNBC) and metabolic disorders.
- The inventors have engineered synthetic peptides targeting key epitopes of FABP5 that competitively inhibit its interaction with mTORC1
- **The Discovery:** FABP5 is significantly upregulated in TNBC, with elevated protein levels in both patient-derived xenografts and serum from TNBC patients
- FABP5 contains a conserved N-terminal motif that mediates direct interaction with mTORC1
- **PoC Data:** siRNA-mediated knockdown of FABP5 blocked ω6 LA-induced mTORC1 activation and reduced cancer cell proliferation.
- FABP5-targeting peptides selectively inhibited ω6-LA-stimulated growth in aggressive TNBC cells (HCC1806), while sparing normal breast cells

Inventors:
John Blenis
Nikolaos Koundouros
Zhongchi Lee

Patents:
Provisional Filed

Publications:
Koundouros et al. *Science.* 2025

Biz Dev Contact:
Jeffrey James
(646) 962-4194
jaj268@cornell.edu

Cornell Reference:
D-11084

Weill Cornell Medicine

Synthetic Peptide Inhibitors of FABP5 for Treatment of Diet-Associated Cancer and Metabolic Disease

Technology Applications

- Personalized therapeutic strategy for TNBC and other cancer types with high FABP5 expression
- Preventative treatment for the delaying of “unhealthy” ageing symptoms brought about by hyperactivation of mTORC1
- Treatment of metabolic diseases, such as diabetes, that are caused by mTORC1 hyperactivation
- Abrogate side effects of high fat diet

Technology Advantages

- Allows for context-specific inhibition of mTORC1 signaling, potentially reducing side effects
- Allows for combination with existing standard-of-care treatments in TNBC
- Reduces the need for strict dietary interventions in treating certain metabolic diseases, improving patient compliance

Supporting Data / Figures

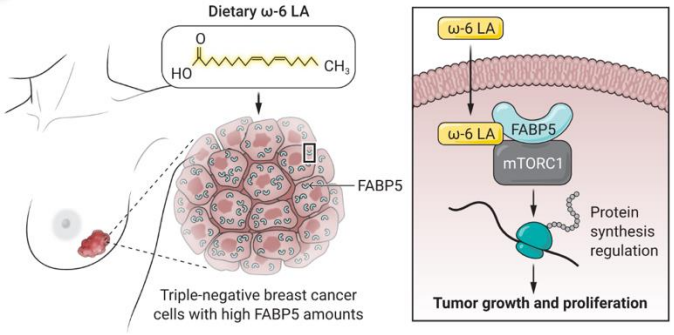


Figure 1: FABP5 is highly expressed in TNBC, and ω6-LA promotes TNBC tumor growth.

Inventors:
John Blenis
Nikolaos Koundouros
Zhongchi Lee

Patents:
Provisional Filed

Publications:
Koundouros et al. *Science.* 2025

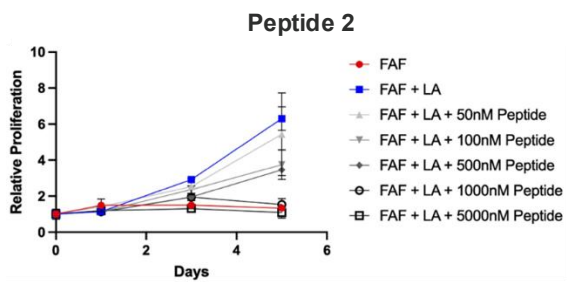
Biz Dev Contact:
Jeffrey James
(646) 962-4194
jaj268@cornell.edu

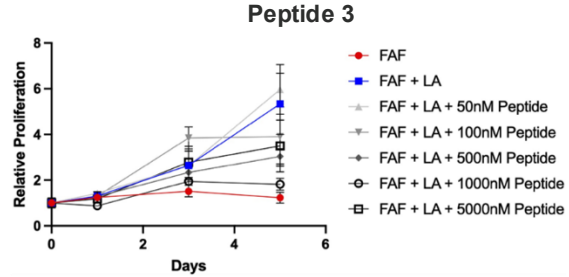
Cornell Reference:
D-11084

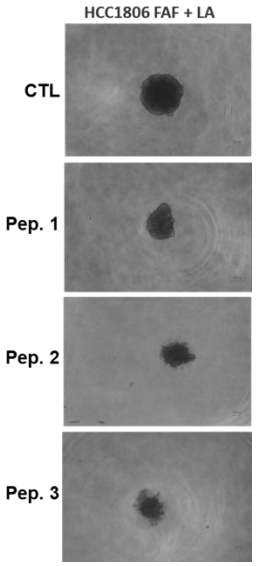
Weill Cornell Medicine

Synthetic Peptide Inhibitors of FABP5 for Treatment of Diet-Associated Cancer and Metabolic Disease

Supporting Data / Figures







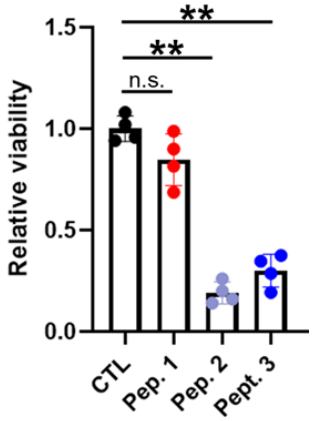


Figure 2: Treatment with FABP5-targeting peptides demonstrated dose-dependent suppression of ω6-LA-induced cell growth across concentrations from 50nM to 5000nM in two-dimensional cell culture models. Peptides 2 and 3 also significantly reduce cancer cell viability in three-dimensional tumor spheroids.

Inventors:
John Blenis
Nikolaos Koundouros
Zhongchi Lee

Patents:
Provisional Filed

Publications:
Koundouros et al. *Science.* 2025

Biz Dev Contact:
Jeffrey James
(646) 962-4194
jaj268@cornell.edu

Cornell Reference:
D-11084

Weill Cornell Medicine

Synthetic Peptide Inhibitors of FABP5 for Treatment of Diet-Associated Cancer and Metabolic Disease

Supporting Data / Figures

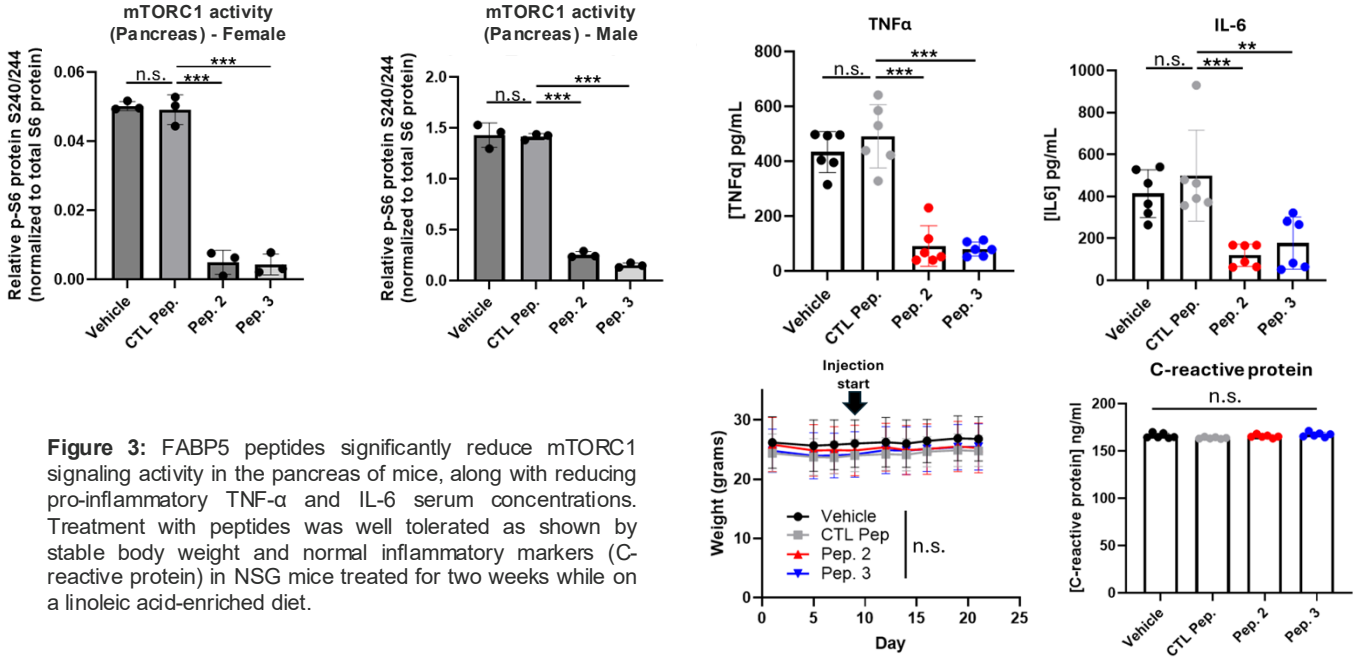


Figure 3: FABP5 peptides significantly reduce mTORC1 signaling activity in the pancreas of mice, along with reducing pro-inflammatory TNF-α and IL-6 serum concentrations. Treatment with peptides was well tolerated as shown by stable body weight and normal inflammatory markers (C-reactive protein) in NSG mice treated for two weeks while on a linoleic acid-enriched diet.

Inventors:
John Blenis
Nikolaos Koundouros
Zhongchi Lee

Patents:
Provisional Filed

Publications:
Koundouros et al. *Science.* 2025

Biz Dev Contact:
Jeffrey James
(646) 962-4194
jaj268@cornell.edu

Cornell Reference:
D-11084

Weill Cornell Medicine

Weill Cornell Medicine