NOVEL USE OF A RECOMBINANT ENDOGENOUS PROTEIN FOR THE TREATMENT OF FAT MALABSORPTION AND GASTRIC MOTILITY ISSUES

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INVENTION NOVELTY

The invention is a recombinant form of an endogenous protein that can be used to increase fat absorption and modulate gastric motility.

VALUE PROPOSITION

Malabsorption is the failure of the digestive tract to properly absorb nutrients such as vitamins, protein, and/or fat. Fats, in particular, are a major energy source and their inefficient absorption can lead to weight loss and a lack of energy. Impaired fat absorption can also impact the uptake of the fat-soluble vitamins (A, D, E, K). In addition, excess unabsorbed fats can lead to diarrhea, bloating, flatulence, and abdominal discomfort. Fat malabsorption can be due to various causes including, but not limited to:

- **Damage to the bowel.** The intestinal lining can be damaged by inflammatory disorders such as Celiac, Crohn's, or ulcerative colitis. In the US, Celiac affects ~3M individuals while Crohn's and ulcerative colitis combined affect ~1.4M. Radiation therapy targeted at pelvic cancers (cervical, pancreatic, prostate, uterine, colorectal) can also lead to long-term bowel damage in up to ~50% of patients.
- **Impairment of pancreatic function.** The pancreas secretes enzymes that are critical for breaking down fats in order for them to be absorbed. Disorders such as cystic fibrosis (~30,000 affected individuals in the US), pancreatic cancer (~40,000 new cases each year in the US), or chronic inflammation of the pancreas (pancreatitis) can significantly limit pancreatic function.
- **Impairment of bile production and delivery.** Bile is produced by the liver to aid in the breakdown of fats. The most common cause of reduced bile production is chronic liver disease (cirrhosis) which affects ~500,000 individuals in the US.
- **Rapid gastric emptying/dumping syndrome.** A common side-effect of gastric bypass surgery, this disorder is caused by the stomach emptying too quickly which results in the malabsorption of fats in addition to other nutrients.

Other than dietary modifications, the only method to improve fat absorption is to treat the underlying cause. There are currently no treatments to directly improve fat absorption while the underlying

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OTHER INFORMATION

KEYWORDS

malabsorption, gastric motility issues, fat absorption, rapid gastric emptying/dumping, recombinant protein

CATEGORIZED AS

- **Medical**
  - Disease: Digestive System
  - Disease: Metabolic/Endocrinology

RELATED CASES

2013-082-0

condition is being identified and treated OR to improve absorption if the underlying issue is untreatable. There are also no treatments available to directly address rapid gastric emptying/dumping syndrome.

TECHNOLOGY DESCRIPTION

Scientists at the University of California, San Francisco have recently characterized the novel role of a soluble protein in fat absorption and gastric motility. Mice lacking this protein have a lower percentage of body fat than their wild-type (WT) littermates. Using a fluorescent fatty acid analog, the researchers determined that fatty acid uptake was reduced in both primary adipocytes and enterocytes isolated from mice lacking the soluble protein (knockout (KO)) relative to those from WT mice. Treatment of these cells with a recombinant version of the protein in question increased fatty acid uptake in both KO and WT cells. Intriguingly, this effect was blocked by an antibody that disrupts a key protein-protein interaction.

The physiological relevance of these in vitro findings was confirmed by monitoring serum triglyceride levels after administration of an olive oil bolus to both KO and WT mice. Consistent with the in vitro findings, both serum and liver triglyceride levels were significantly lower for KO animals, an effect that was eliminated by oral administration of the recombinant protein. Furthermore, treatment of WT mice with the recombinant protein also resulted in significantly higher serum triglyceride levels compared to control treated WT mice. This difference persisted for the entire time measured (8 hours).

In a separate line of experiments, the scientists also determined that gastric motility, as measured by transit time through the intestine and the strength of contraction, is increased in KO animals. This change is reversed by treatment with the recombinant protein.

Taken together, these results confirm the role of this soluble protein in fat absorption and in modulating gastric motility. They also demonstrate the potential use of the recombinant version as a treatment to increase fat absorption and reduce gastric motility. Specific receptors in these pathways could also be individually targeted for the desired therapeutic outcome (control of obesity or gastroparesis) to reduce potential side effects.

APPLICATIONS

- Treatment to increase fat absorption in the digestive tract.
- Treatment to reduce gastric motility.

LOOKING FOR PARTNERS

To develop and commercialize this technology as an effective treatment for fat malabsorption and/or modulation of gastric motility.

STAGE OF DEVELOPMENT

Pre-clinical

RELATED MATERIALS

▶ Khalifeh-Soltani A. et al. Mfge8 promotes obesity by mediating the uptake of dietary fats and serum fatty acids. Nat Med. 2014 Jan 19

DATA AVAILABILITY

Under NDA/CDA

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,005,838	06/26/2018	2013-082

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