FKBPL: A NOVEL TARGET FOR OBESITY AND METABOLIC SYNDROME

RCSI researchers have discovered a novel target, FKBPL, which regulates energy expenditure, and have shown that obesity and Type 2 diabetes (T2D) develop when levels of this protein are low in mice and humans. Proof of concept data demonstrates that therapeutic delivery of FKBPL improves T2D and promotes weight loss in mice. The aim is to develop a novel mRNA-FKBPL nanoparticle therapeutic and to pre-select patients who are suitable for treatment based on their serum FKBPL levels.

BACKGROUND

Currently, 59% of adults and 33% of children in Europe are overweight or living with obesity and excess adiposity contributes to 1.2 million deaths in Europe per year.

Recent approval of GLP1 receptor agonists (GLP1-RA) drugs for the treatment of T2D and obesity have revolutionised the treatment paradigm.

However, unmet needs persist. Existing drugs focus on reducing appetite and can cause significant side effects, including gastrointestinal and muscle loss issues. In addition, some patients do not respond to treatment and there no approved biomarkers or companion diagnostics to address this.

VALUE PROPOSITION

We aim to address these unmet needs by developing an FKBPL-mRNA therapeutic for obesity and T2D which will be differentiated to existing drugs by:

1. Utilising a novel target
2. A differentiated mechanism of action
3. Pre-selecting patients suitable for treatment based on their FKBPL profile.

Existing drugs such as GLP1-RAs primarily induce weight loss by reducing appetite, whilst FKBPL acts independently of food intake and promotes energy expenditure, Therefore, GLP1-RA and FKBPL-based therapeutics could have synergistic mechanisms of action and could be well suited as a monotherapy or as a combination drug.

TECHNOLOGY

We have demonstrated that:

- FKBPL deficiency predisposes mice to obesity and metabolic syndrome
- Lower serum FKBPL levels are associated with higher BMI in humans
- Therapeutic FKBPL protects from obesity and glucose tolerance in mice

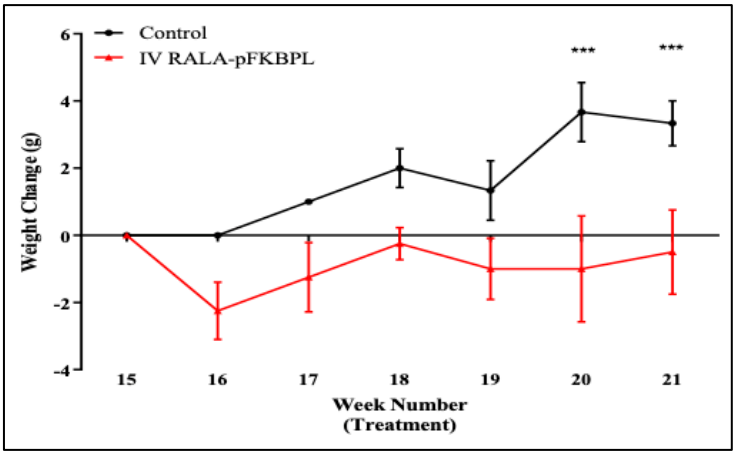

Fig 1. IV delivery of plasmid FKBPL/nanoparticle complex ('RALA-pFKBPL') results in **reduced weight gain** vs control in mice on a high fat diet.

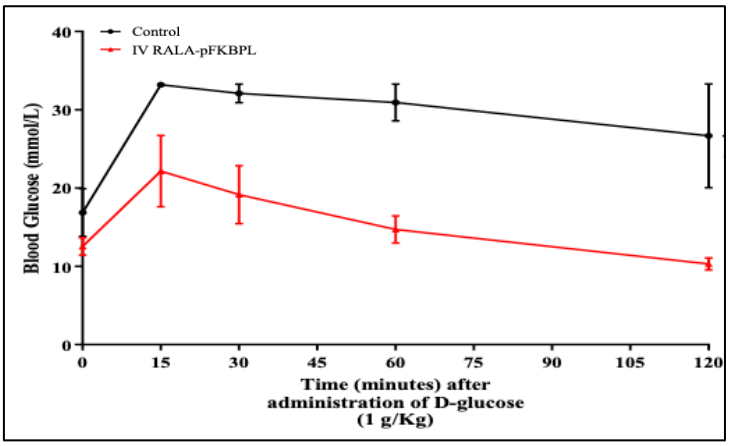

Fig 2. IV delivery of plasmid FKBPL/nanoparticle complex ('RALA-pFKBPL') results in **improved glucose tolerance** vs control in mice on a high fat diet.

FEATURES	BENEFITS
Novel target & mechanism	Unique FKBPL strategy, differentiated to other approaches; promotes energy expenditure instead reducing appetite
Precision medicine	Pre-select patients suitable for treatment based on FKBPL profile, improving response rates

TECHNOLOGY READINESS LEVEL

- *In vivo* POC achieved
- Patents issued

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