GUI12: Target discovery in the gut

Searching for the gastric bypass pharmacological mimetic

The mechanisms underlying Roux-en-Y gastric bypass (RYGB) induced weight loss and the immediate postoperative beneficial metabolic effects remain uncertain. However, enteroendocrine cells' (EECs) secretory function has been proposed as a key factor in the marked metabolic benefits from RYGB surgery.

Identifying novel "diabesity" targets using the Gubra's proprietary discovery platform

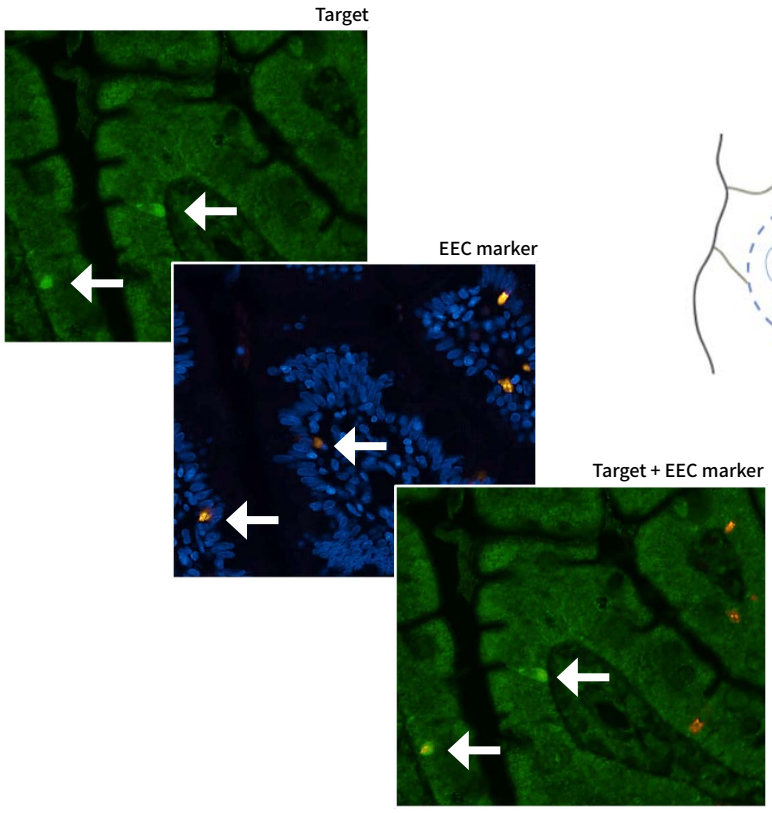
In collaboration with expert university and hospital partners we have unraveled transcriptomic changes in laser capture micro-dissected EECs before, during and after Roux-en-Y gastric bypass surgery – in both rodent and man.

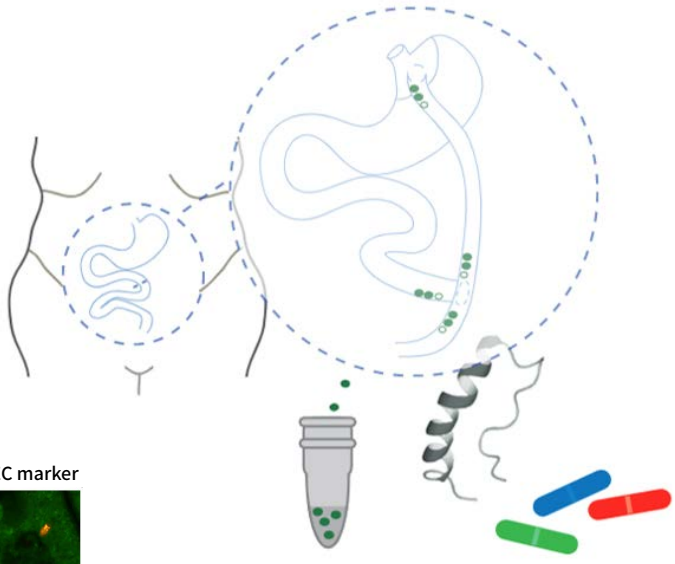
The comprehensive analyses have provided key data for several peer-reviewed scientific papers spanning the full spectrum from early study design to clinical phase 0 testing - and provided the basis for several drug discovery projects.

Our proprietary discovery platform **streaMLine** ***preDict*** enables AI assisted target identification.

Key project features

- Human gut biopsies using pediatric colonoscopy.
- Systematic sampling of gut samples in rat.
- Laser capture microdissection of EECs.
- High-throughput RNA sequencing.
- Preprohormone predictions.
- To date, the RNAseq database includes more than 500 RNAseq analyses of gut samples in man and rat

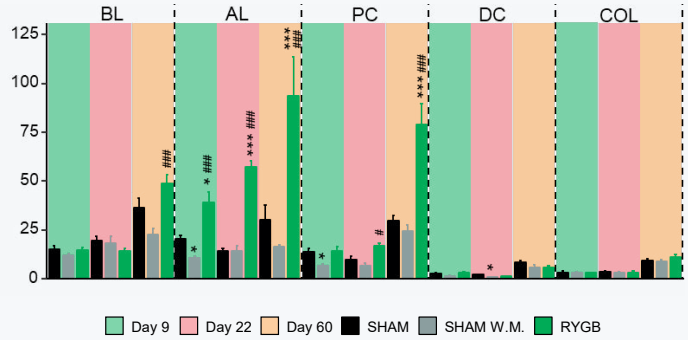




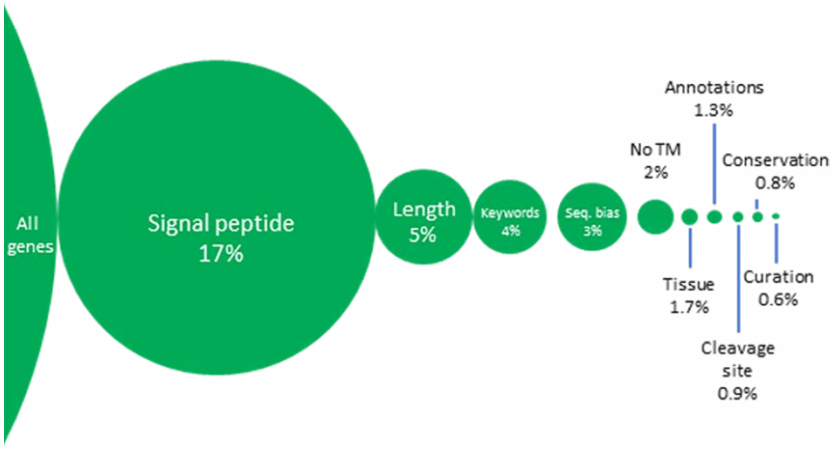
Immunohistochemical staining of target gene (using in-housed developed antibody) co-localise with pan-ECC marker.

RYGB in DIO rats

In depth analyses of the gut secretome at day 9,22 and 60 following RYGB surgery in obese rats led to the discovery of several differentially expressed preprohormones.



BL - Biliopancreatic Limb
AL - Alimentary Limb
PC - Procimal Common channel
DC - Distal Common channel
COL - Colon



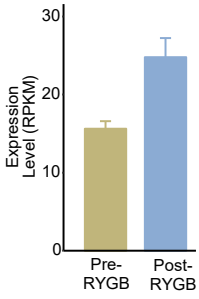
Preprohormone predictions

Bioinformatioc data crunching and **streaMLine** ***preDict*** target identification led to the discovery of several known and novel preprohomes.

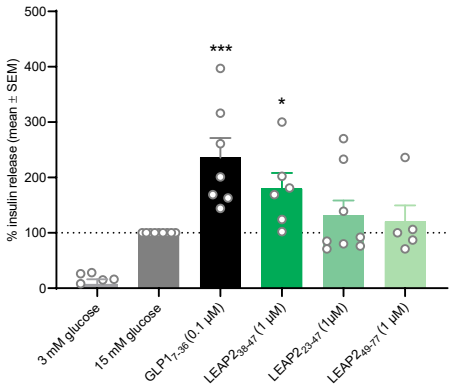
LEAP-2 - a RYGB mimetic?

LEAP-2 was identified as a differentially expressed gene in CHGA positive endocrine cells. A predicted peptide fragment showing glucose stimulated insulin released was selected for clinical phase 0 testing.

LEAP-2 expression



Glucose Stimulated Insulin Release in human islets



Why choose Gubra?

- Proven track record with identification of new disease targets and new peptide drugs. The most advanced are currently in clinical development with pharma partner.
- All projects are led by professional project leaders with strong scientific backgrounds and project management experience.
- All data are generated in-house to ensure high data quality, integrity, speed and flexibility.
- AAALAC accredited in vivo facility