

GUI11: Targeting the body weight set-point

Obesity target discovery - counter regulatory mechanisms in the brain

The fact that human body weight can easily increase - but apparently cannot be easily decreased - indicates that the human body weight set-point is drifting upwards. Targeting that set-point could prove to be an efficient and alternative way for weight reduction and the relapse into increased weight.

The right modelw

Taking onset in the Gubra DIO rat model, a series of pharmacological approaches have been conducted to stress the set-point, including food restriction and refeeding, compound induced orexia/anorexia, lesion studies and bariatric surgery.

More than 73 drugable targets identified

To date, the RNAseq database includes more than 1600 RNAseq analyses of specific LCM isolated areas in the rat brain. More than 73 drugable targets (hormones, kinase, GPCR etc) have been identified, using our proprietary platform **streaMLine *preDict***.

The right method

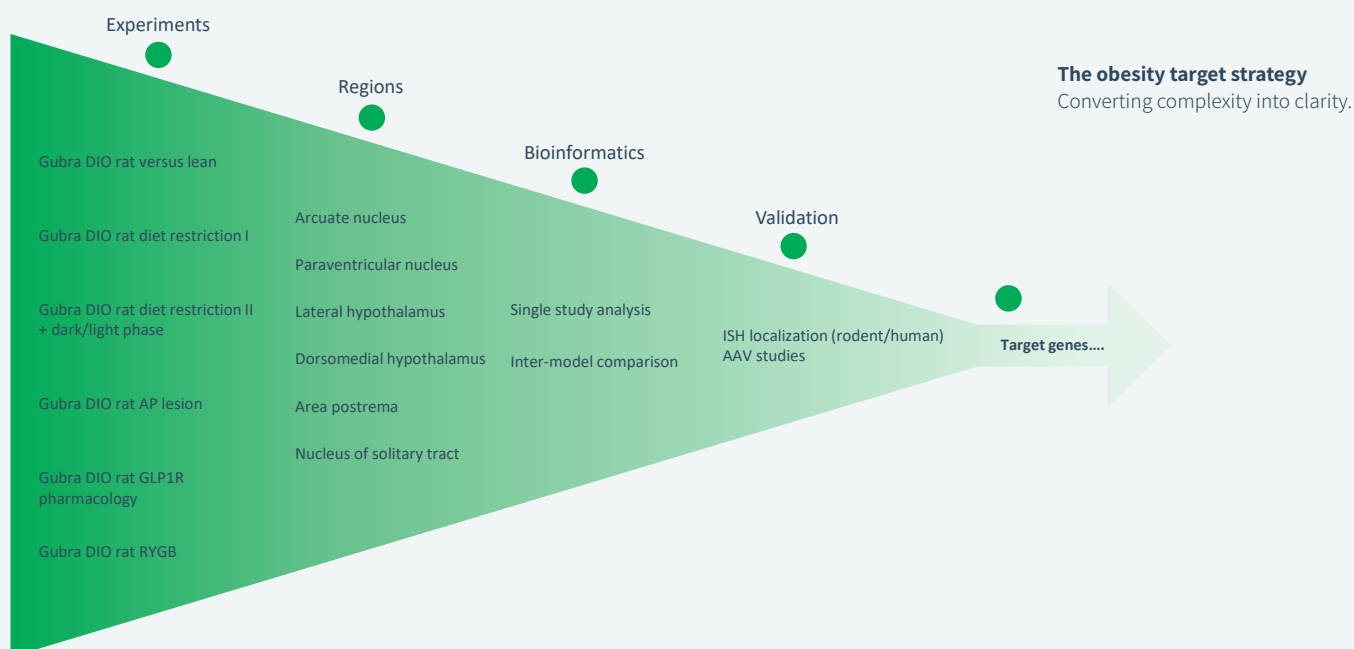
The Gubra target discovery platform is centered around a team of scientists and technicians with years of experience in target discovery in the brain. The platform is based on high-end laser capture microdissection (LCM) coupled with RNA sequencing (high-throughput sequencing) and advanced bioinformatics.

Key project features

- Obesity target list identified across 1700 brain samples in Gubra DIO rats.
- Novel food intake regulating hotspots identify by global cFos patterns.
- Target engagement visualized by 3D imaging.

Target validation

Targets are evaluated in DIO mouse/rat models with in-house synthesized peptide analogs or commercially available target knock-down/overexpression technologies using stereotaxic site directed delivery.

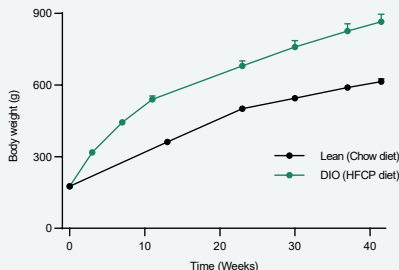
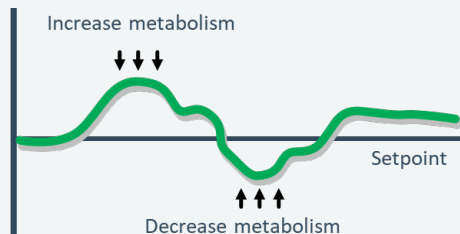


The GUBRA DIO rat model

The GUBRA DIO rat is offered a two-choice diet consisting of standard chow in addition to the Gubra palatable high-fat high-sugar diet made up of chocolate spread, peanut butter and powdered regular rodent chow.



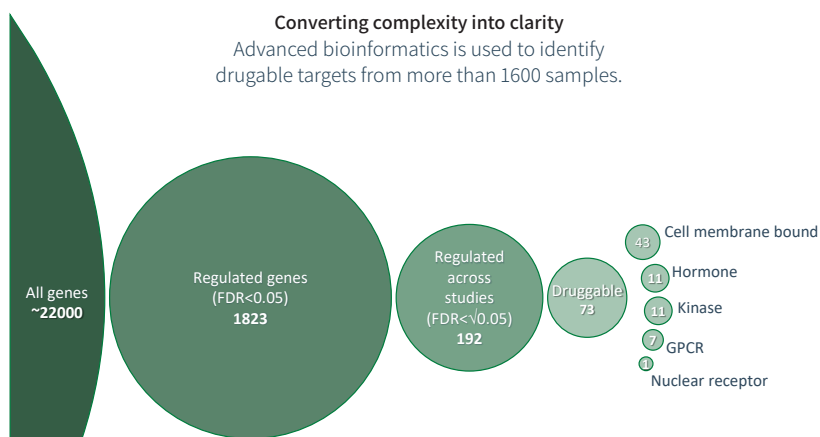
The biological "set point", where our body thrives, is dysregulated upwards in obesity



Body-weight curves in Gubra DIO rats fed the Gubra diet.

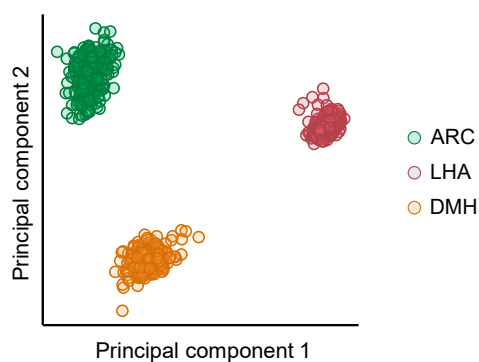
Converting complexity into clarity

Advanced bioinformatics is used to identify druggable targets from more than 1600 samples.



Principal Component Analyses (PCA)

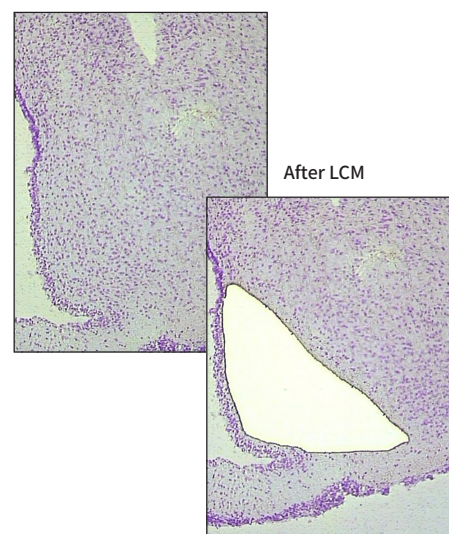
Principal Component Analyses (PCA) of gene regulations in the arcuate (ARC), latera (LHA) and dorsomedial (DMH) hypothalamus



Laser capture microscopy

Laser capture microdissection (LCM) of specific brain areas provides an astonishing insight in specific gene regulations.

The arcuate nucleus before LCM



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

