Reduction of obesity and related diseases by targeted nutritional treatment

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Background

With 2.3 billion overweight and 700 million obese adults worldwide in 2015 (WHO), obesity and consequently diabetes type II are among the biggest global health problems. Even though dietary and lifestyle changes may eventually reduce obesity for some individuals, new safe and more efficacious drugs are required for successful weight reduction and treatment of type 2 diabetes in a large proportion of obese individuals. It has been shown that various G-protein coupled receptors (GPCRs) expressed in various tissues such as liver, muscle, pancreatic islets, immune cells and the central nervous system are involved. GPCRs are important targets for food components. The members of this large family of membrane proteins are involved in virtually every physiological process. This study will focus on the interaction between food ligands and GPCRs.

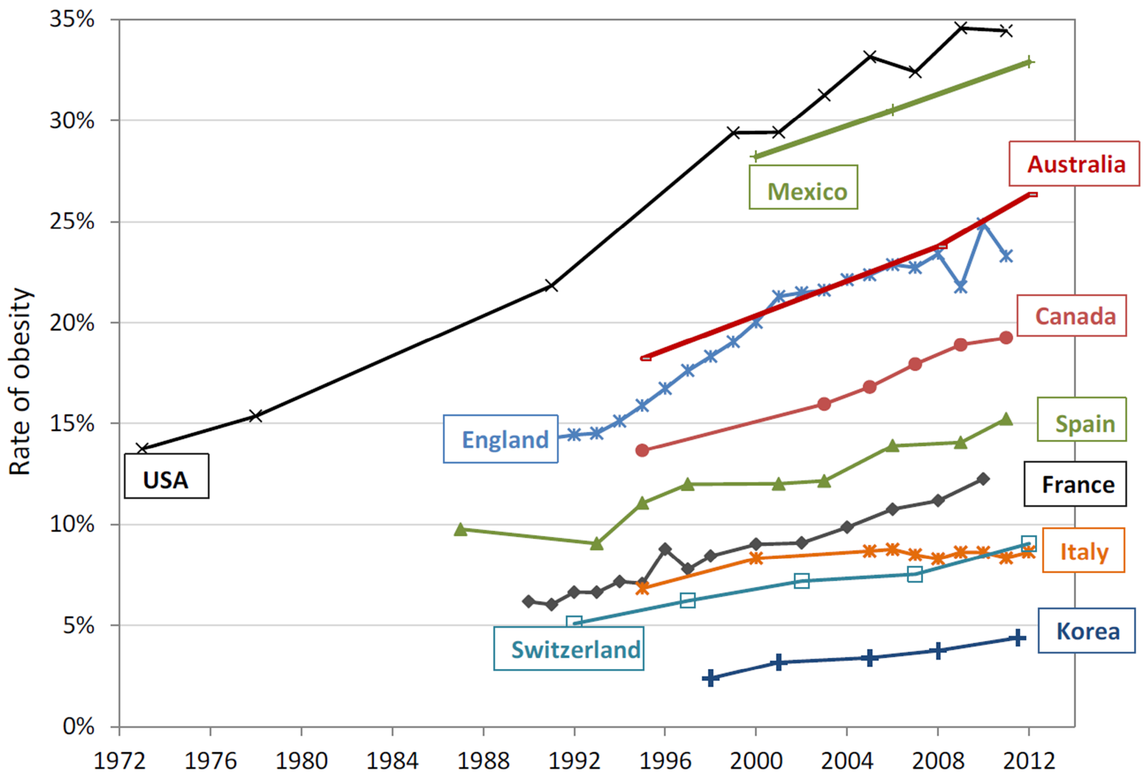


Figure 1. Obesity rates by country. Measured in Australia, England, Korea, Mexico and the United States; self-reported in other countries. *Source*: OECD analysis of health survey data.

Aim and strategy

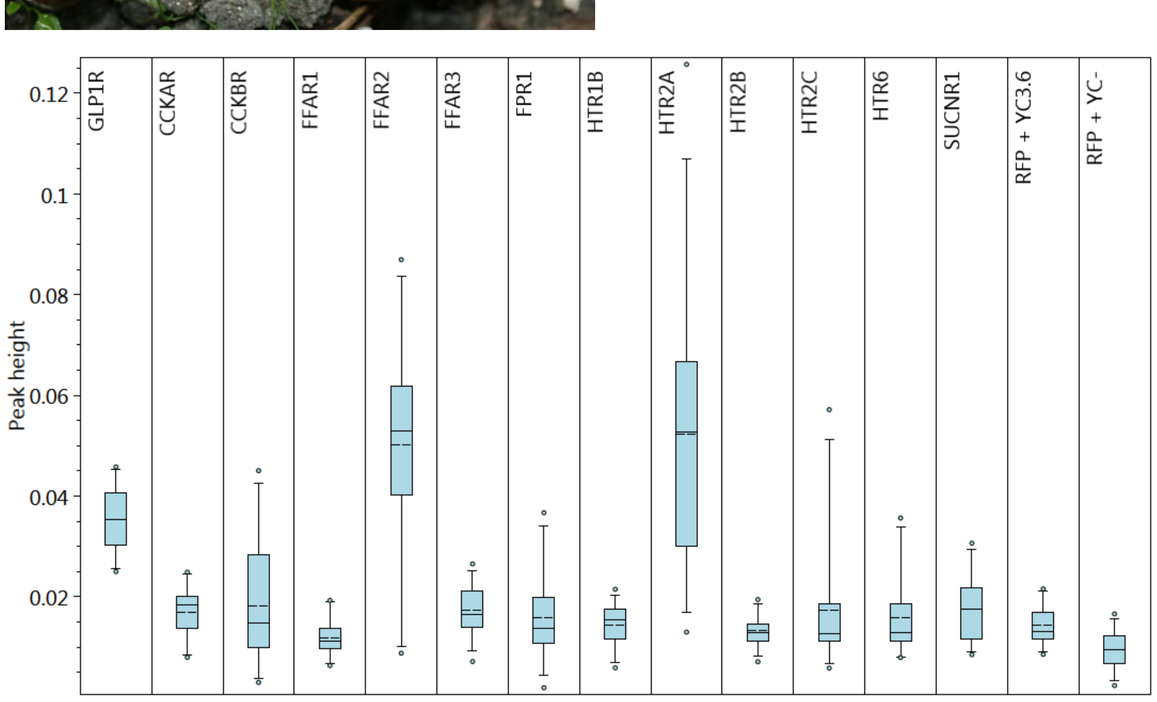
In this project, we will establish the influence of complex receptor and receptor/ligand interactions on the development of obesity and correlated T2DM. Next to this, we aim to identify food related compounds that can prevent or intervene in these chronic diseases. To accomplish this, we propose an integrated approach using state of the art technologies to test different food related compounds on a receptor level (receptor (complex)/ligand interaction), cellular level (*in vitro* experiments using relevant cell lines) and on organismal level (*in vivo* assays).

Method

- Identify food related compounds and receptors involved in obesity and related diseases
- Screen food & plant extracts or compounds for receptor binding, energy metabolism and immune responses in various assays
- Confirm results in *in vivo* assay with high-fat diet (HFD) fed mice

Results

Figure 2. *left:* Picture of *Agraricus blazei* mushroom. *Source*: www.medicalmushrooms.net. *Bottom:* Example of preliminary receptor analysis with *A. blazei* extract using receptors known to be involved in obesity and related diseases. *A. blazei* extract show specific responses to various receptors.



Status and future experiments

A selection of 26 receptors based on literature and expression data was made. Initial receptor binding experiments using mushroom (*Agraricus blazei*) extracts show specific receptor responses to serotonin (HTR2A, HTR2C) and fatty acid receptor (FFAR2) and to a lesser extend to the glucagon-like peptide 1 receptor (GLP1R) and cholecystokinin receptor (CCKBR) (Figure 2). More compounds and extracts will be analyzed for receptor binding this year. Furthermore, compounds and extracts will also be tested in cell assays for metabolic activity and immune responses.

References

Roelse et al., Calcium Imaging of GPCR Activation Using Arrays of Reverse Transfected HEK293 Cells in a Microfluidic System. Sensors Feb 2018

Henquet M.G.L. *et al.*, Metabolomics meets functional assays: coupling LC–MS and microfluidic cell-based receptor-ligand analyses. Metabolomics Jun 2016.

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