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CYANOBESITY

Cyanobacteria as a source of bioactive compounds with effects on obesity and obesity-related co-morbidities

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Margreth Thornsteinsdóttir

ERA-MBT 2nd Transnational Joint Call: Biodiscovery

21st Novmber 2017

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December 2013 - November 2017

THE CONSORTIUM

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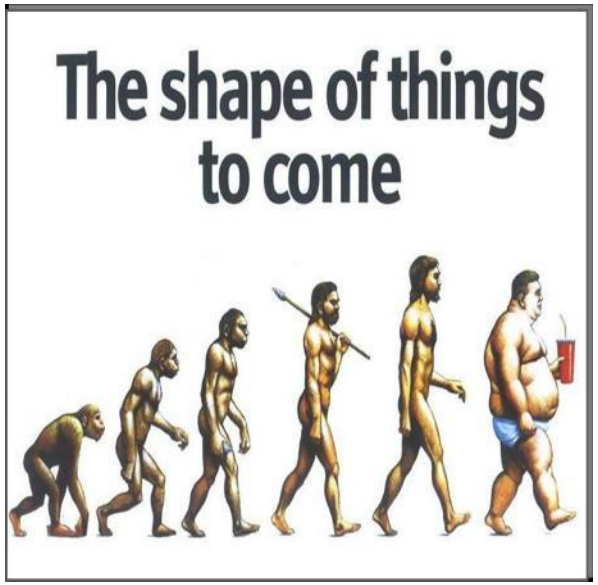
Project period: May 2017 to April 2020

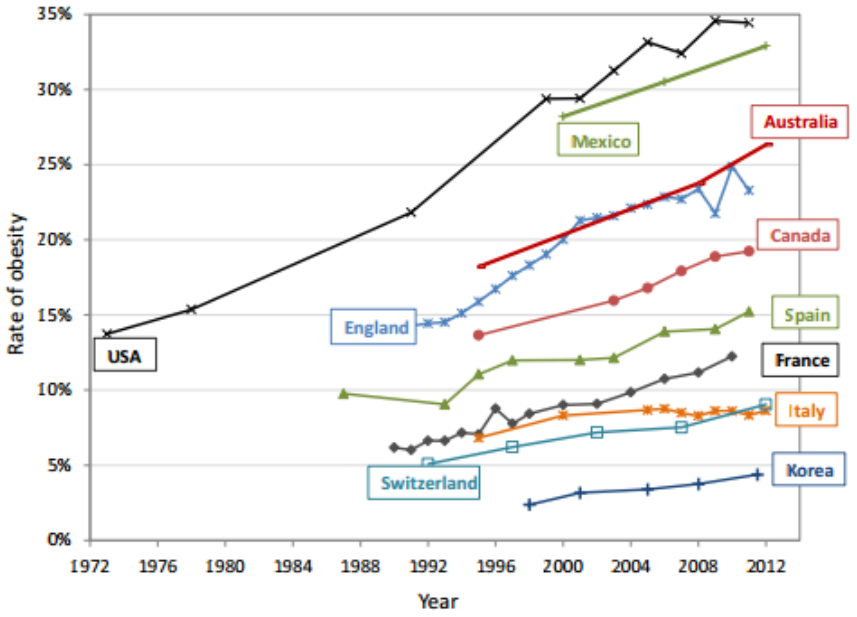
Why antiobesogens?

Obesity is a worldwide epidemic, > 500 millions are obese (WHO, 2013)

Obesity = caused by a positive energy balance
= accumulation of fat in different body regions

Many serious health problems including metabolic syndrome, heart disease, diabetes type II, atherosclerosis, or cancer

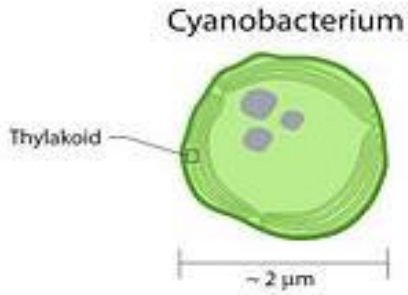


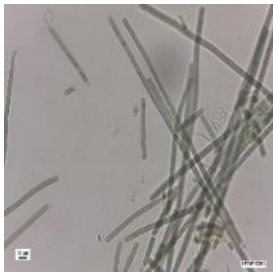


World obesity rates (from Obesity Update, OECD 2014).

Why cyanobacteria?

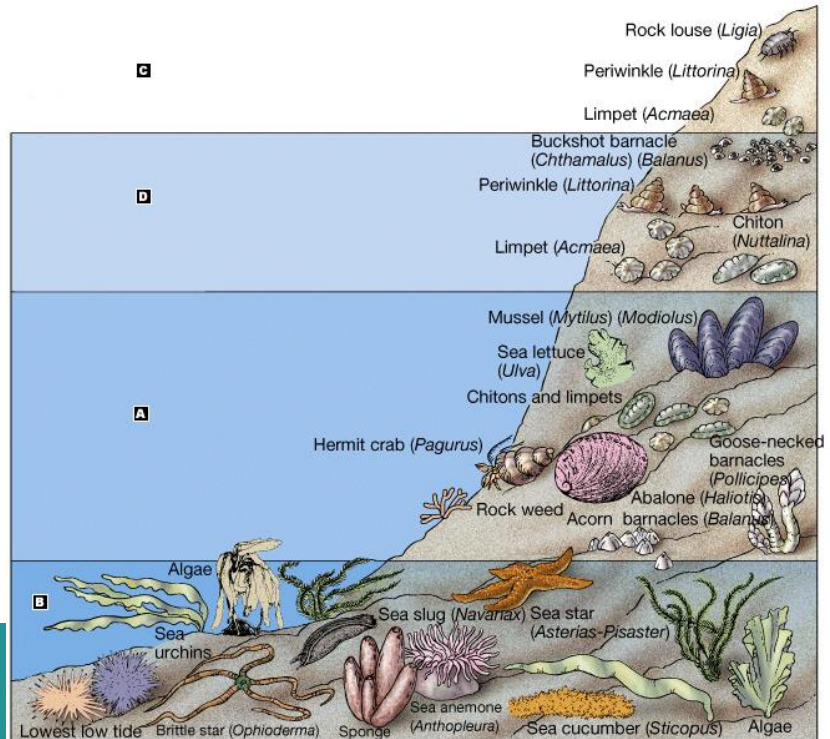
Photosynthetic prokaryotes
3.3 – 3.5 billion years old





High adaptability
Wide occurence

Chemical richness
Bioactive compounds



Why cyanobacteria?

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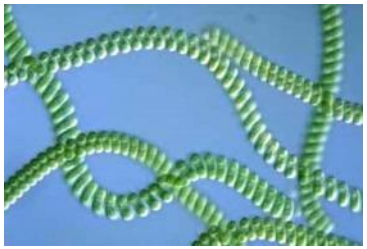
Anti-cancer

FDA approved drug

+ 17 compounds in the marine drug pipeline, in various stage of clinical trials (I, II, III)

http://marinepharmacology.midwestern.edu/clinPipeline.htm

Anti-obesity



- Spirulina (*Arthrospira* sp)
- reduction of blood TG and cholesterol level
- confirmed in humans

CYANOBESITY project

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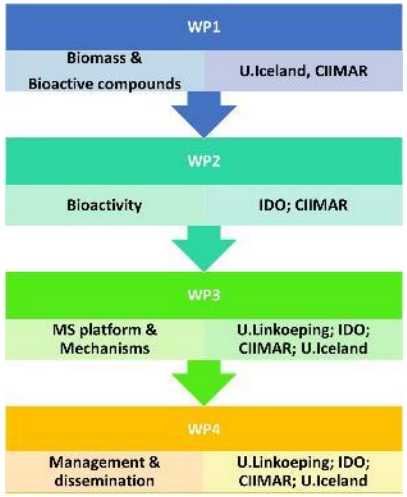
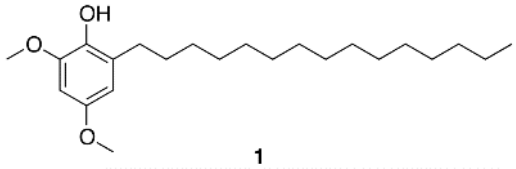
culture collection

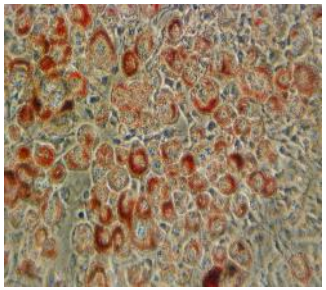
- CIIMAR, Portugal





structural elucidations, dereplication & untargeted screening

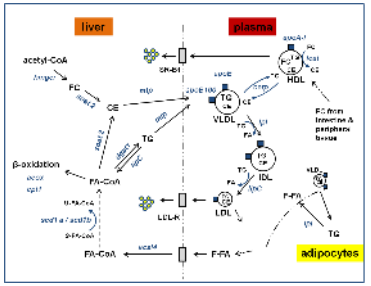
- U. Iceland / ArticMass, Iceland



→ novel nutraceuticals

Bioactivities: Obesity, diabetes, fatty liver disease

- Helmholtz Center, Germany
- CIIMAR, Portugal



mechanism of action, target identification

- U. Linkoeping, Sweden

Bioassay-guided isolation

UNIVERSITY OF ICELAND
FACULTY OF PHARMACEUTICAL SCIENCES

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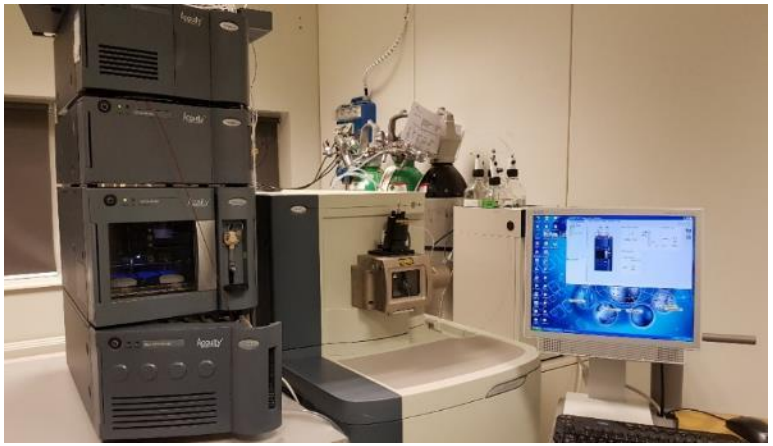
Objectives

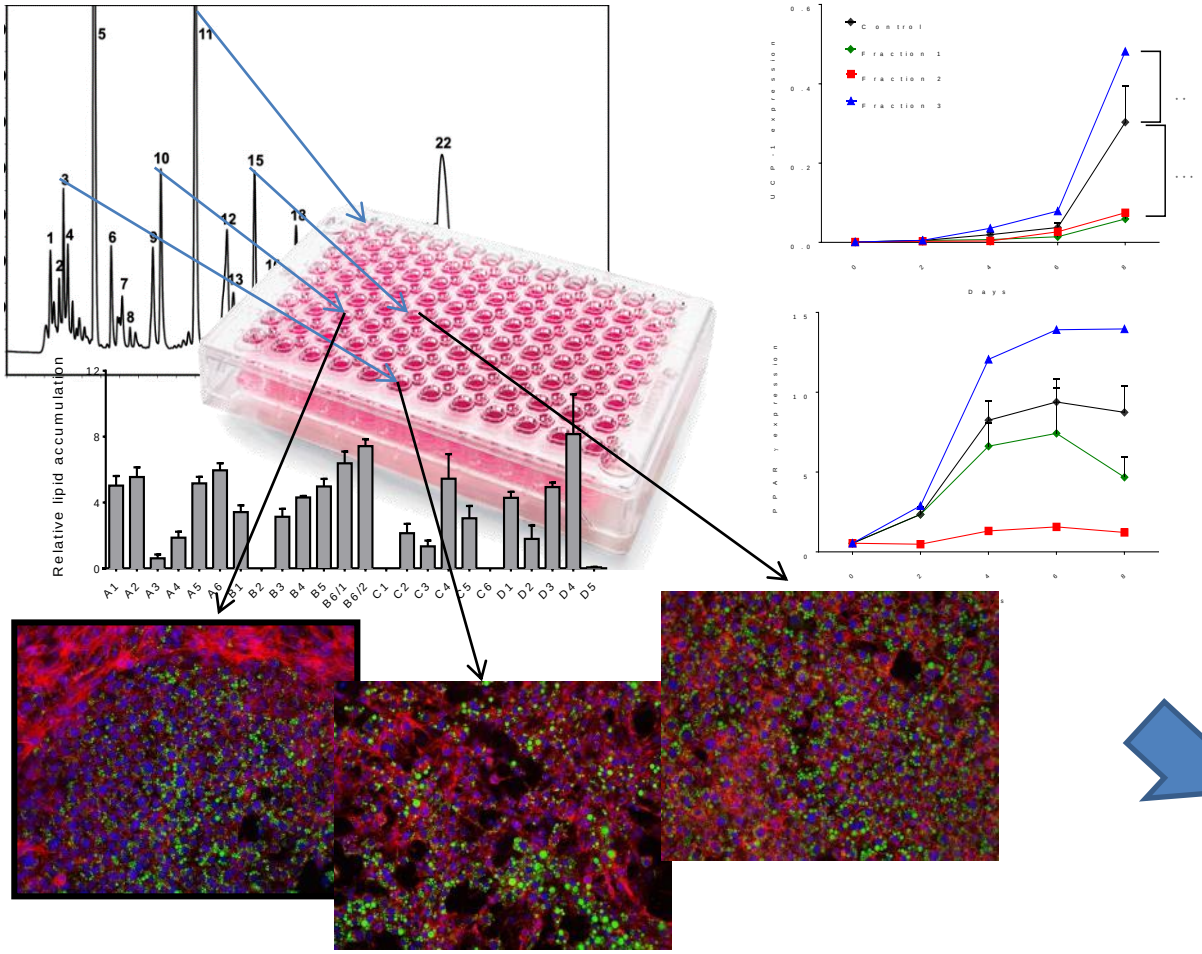
- **Develop and optimize a UPLC-QTOF method** for identification and from cyanobacterial structural evaluation of bioactive compounds strains
- **Structural elucidation** of compounds with previous known anti-obesity activity utilizing UPLC-QTOF and NMR
- **Untargeted screening** of metabolites with UPLC-QTOF will be initiated

Infrastructure/Equipments

- UPLC-MS/MS
- UPLC-Q-TOF
- GC-FID
- NMR
- SIMGA for multivariate data analysis (PCA, PLS, OPLS)

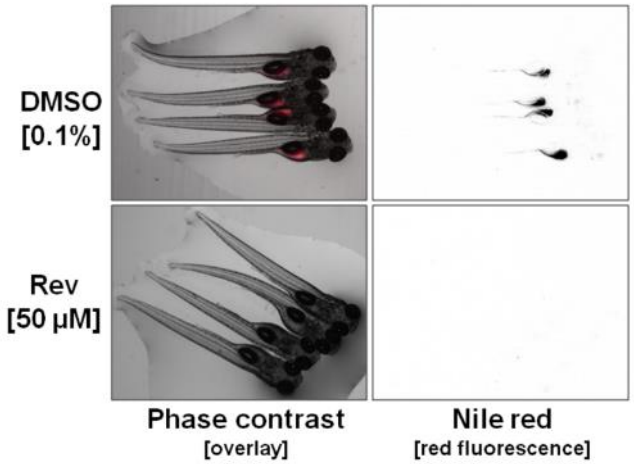


Phenotypic screening

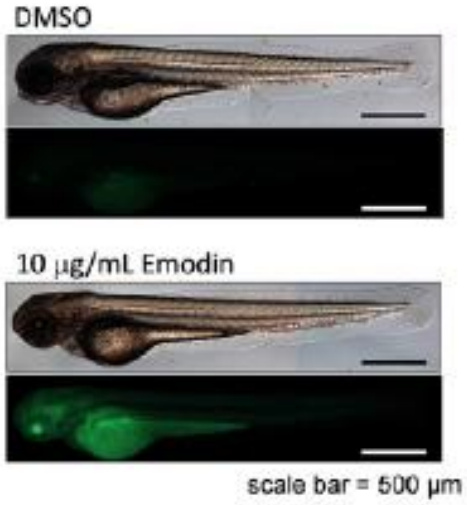


Focus on white and brown adipocyte differentiation

Phenotypic screening



Anti-obesity screen

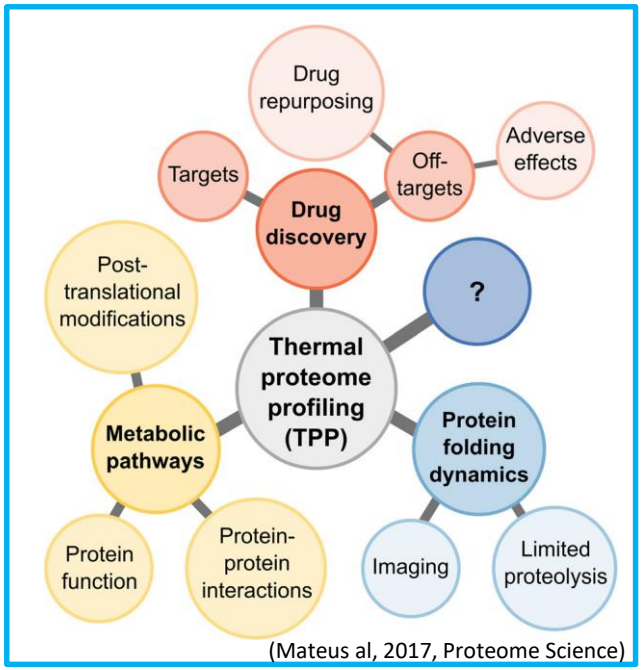


Anti-diabetes screen:
ACS Chem. Biol. 2013, 8, 1803−1814

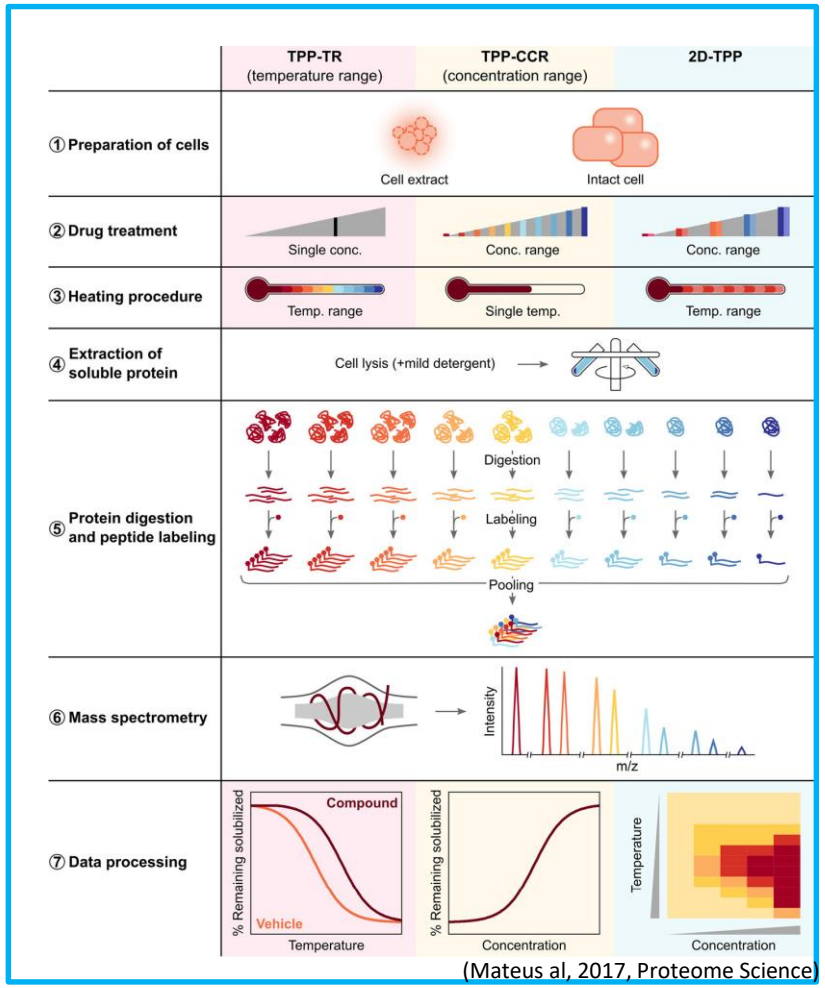
Whole small animal models

- High physiological relevance
- Early incorporation of toxicity evaluation

Thermal proteome profiling to characterize novel compounds mode of actions



(Mateus al, 2017, Proteome Science)



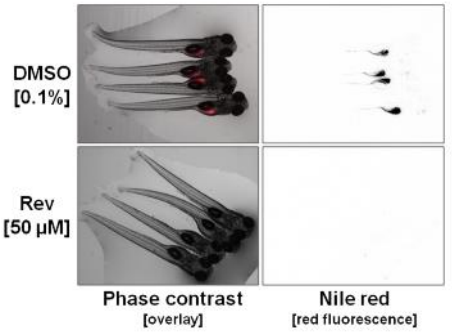
(Mateus al, 2017, Proteome Science)

(Huber *et al*, 2015, Nature)

Progress

- **Cyanobacterial strain selections**
- **Production of 1st biomass and of extracts/fractions; distribution to partners**

- **Setting up of methodologies in the labs:**
  - **UPLC-QTOF**
    Dereplication and complexity of fractions
  - **Bioactivity assays**
    1st screens
  - **Thermal profiling**
    MOA of 1st compound



- **10 cyanobacterial strains with promising activity out of 28 strains**

Potential impacts

Research:

- Novel compounds with activities for obesity and related disorders
- Mechanism of action and molecular targets

Innovation:

- Molecular tools for target identification
- Miniaturization

Societal-related:

- Nutraceuticals for obesity or related disorders

Future directions

- **Discovery of novel organisms** for the production of new bioactive compounds
- **Cultivability** of organisms
- Alteration of **culture conditions** to induce stress (medium, co-culture, …) and therewith production of other compounds

- **Physiologically relevant screening assays** (zebrafish model or other small animal models)
- **Diversity of bio-activities** (much interest funnelled into anticancer)
- Omics for **molecular mechanism**

- **Follow up grants**, e.g. proof of concept ERC

Thank you for your attention…

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FORMAS
ETT FORSKNINGSRÅD FÖR HÅLLBAR UTVECKLING
A SWEDISH RESEARCH COUNCIL FOR SUSTAINABLE DEVELOPMENT

A candy from microalgae to combat obesity?

Um rebuçado de microalgas para combater a obesidade?

Investigadores em Portugal coordenam um projecto internacional de 1,3 milhões de euros que vai estudar as cianobactérias como fonte de compostos bioactivos para actuar na obesidade, diabetes e fígado gordo

Saúde
Andreia Cunha Freitas

Publico, 31/03/2017

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