SINTEF

70 år

1950-2020

MICROBIOTA@SINTEF

Ýrr A. Mørch and Tonje M. B. Heggeset

Blue Legasea Webinar 11.12.2020

SINTEF

Department of Biotechnology og Nanomedicine

Research Director
Trond E. Ellingsen

Biotechnology
Håvard Sletta

Massespectrometry
Sjoerd Hak

Polymer particles and surface chemistry
Heidi Johnsen

Projects and infrastructure

Norwegian and international research groups and industry

78 employees
120 projects

How we work

Competence, methods and technology established through research-led national and international projects

Using expertise

Driving competence

Main goals for SINTEF

Solve challenges for industry and develop technology for a better society

Markets, products, core competence

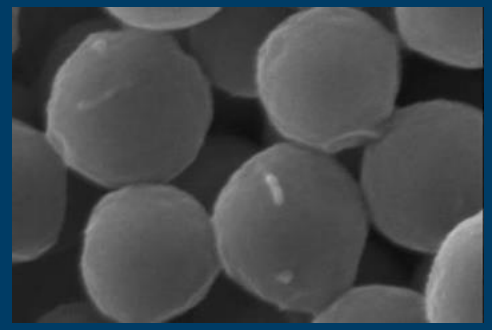
Pharmaceuticals

Aquaculture

Biomass/Biorefining/
Biopolymers/Enzymes

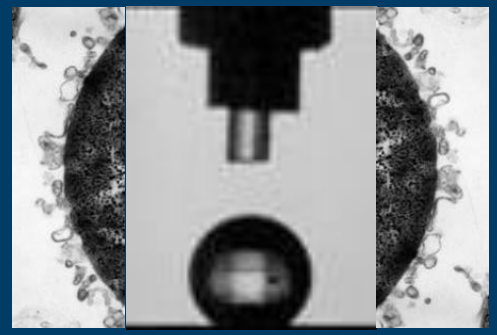
(Bio-)Chemicals

Food and water

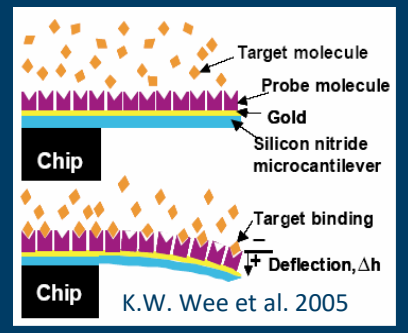


Nanomedicine

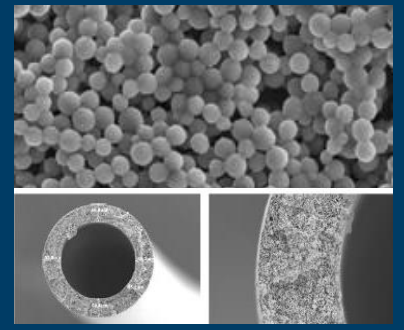
Analytics R&D
Services



Coatings/surfaces



Sensors/tracers



Membranes/particles

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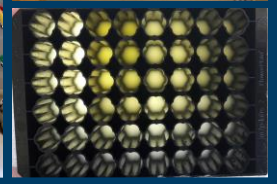
State-of-the-art infrastructure platforms

Microbial fermentation and cell culture

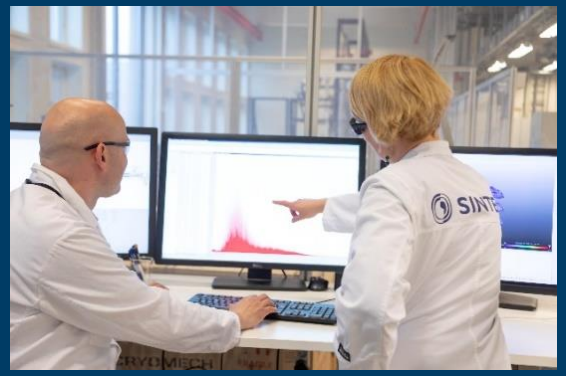


Molecular biology and bioinformatics



Robotic high-throughput screening




Advanced analysis


Particles, membranes and surface modification

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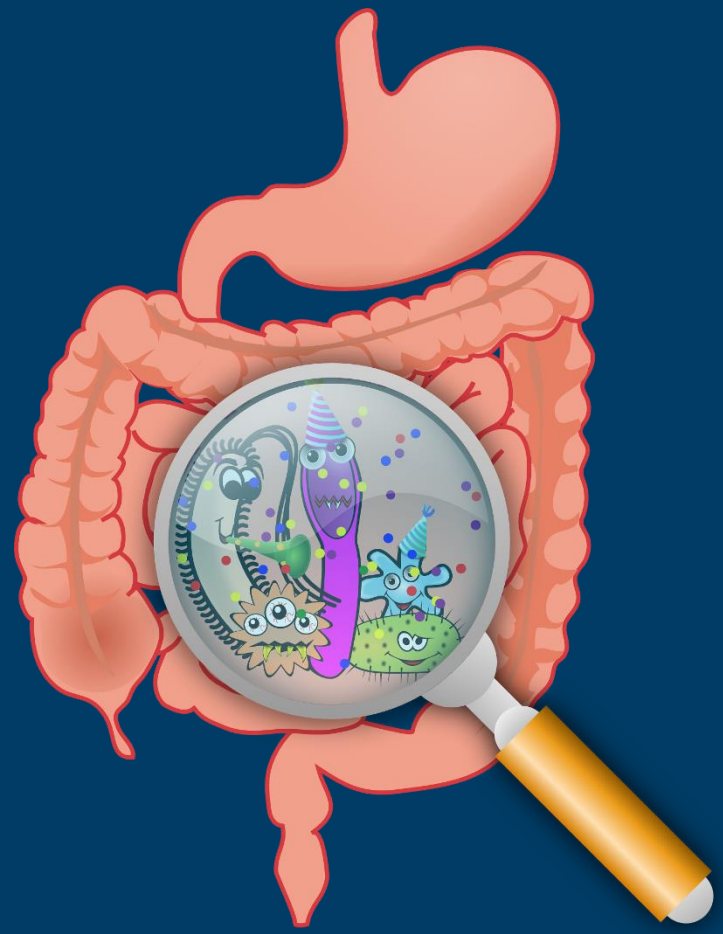
Microbiota@SINTEF

- SINTEF has unique competence and infrastructure in a range of the technology components needed to fill important technology and knowledge gaps within gut microbiota research.
- We are in the process of establishing a complete toolbox within selected areas of gut microbiota research to support national and international research activity.



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Characterisation & Data handling tools

Metabarcode sequencing

Microbial potential

Metatranscriptomics

Microbial function

Mass spectrometry analysis, fingerprinting and imaging

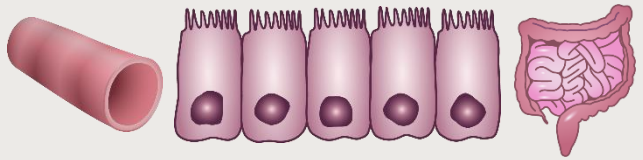
Microbial activity

Multi-omics integration and interpretation

Gut Microbiota in human and animal health

Biological models

Advanced in vitro gut models



Disease models in rodents

Smart delivery systems

Controlled delivery of pro- pre- and synbiotics

Nanoformulation of small molecule drugs ("drug the bug")

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Characterization and data handling tools

Microbial activity

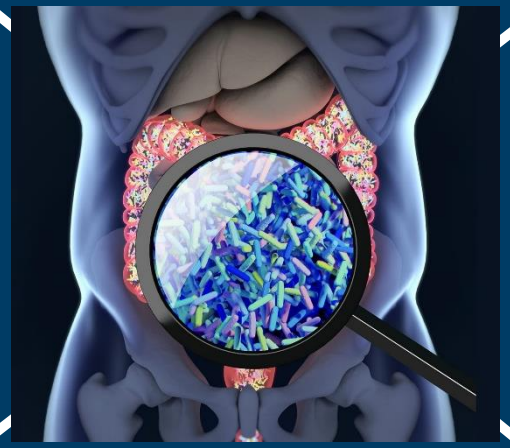
Metabolome

Mass spectrometry analysis
MS imaging

Microbial potential

Metagenome

Metabarcode sequencing
(which organisms)
DNA-sequencing



Metadata

Patient data, model data

Integration, Translation & Interpretation

Network analysis/mapping
Multi-omics integration
Multivariate data analysis
Data handling

Microbial function

Metatranscriptome

RNA-sequencing
RT-qPCR (targeted)

Implementation

- Microbiota characterization in model systems and human samples
- Effect of pharmaceuticals, nutraceuticals, and (pre/pro/syn) biotics on microbiota
- Biodistribution
- Host-bacteria interactions
- Health-microbiota relationships

Infrastructure

- Sequencing (MiSeq, MinION
- QX200 Droplet Digital PCR System
- Robotics platform
- Mass spectrometry platform:
  - LC-MS/MS, GC-MS, GC-MS/MS
  - High resolution MS
  - Ultra-high-resolution MS
  - MALDI-MS
  - MS Imaging
  - Inorganic analysis: ICP-MS
- Data storage

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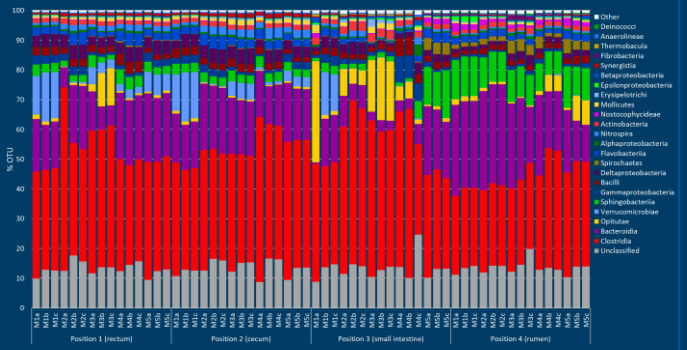
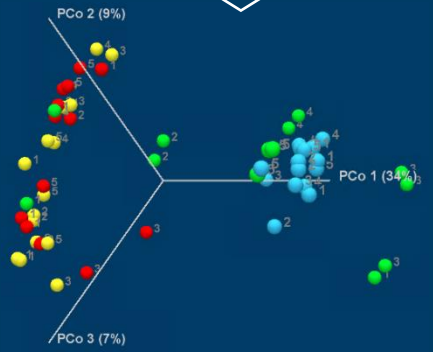
DNA and RNA sequencing

Which microorganisms are in the sample?

Metabarcode (amplicon) sequencing



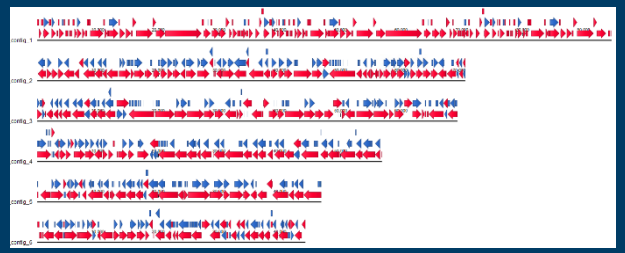
Clustering analysis



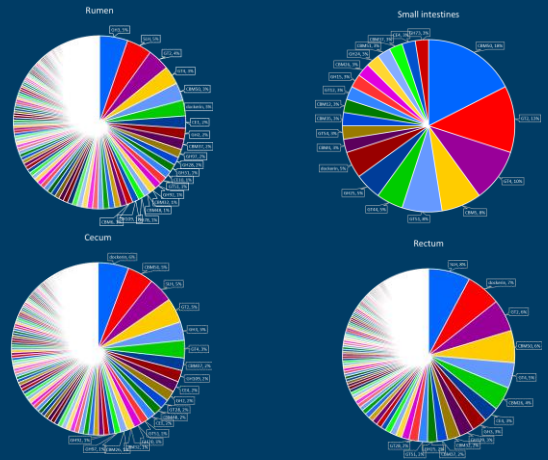
Rumen, Small intestine, Cecum, Rectum

Which genes do they encode?

Shotgun sequencing/Nanopore

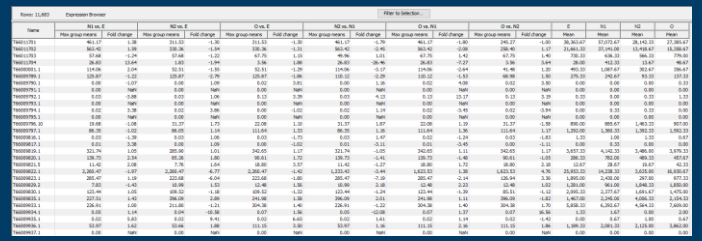


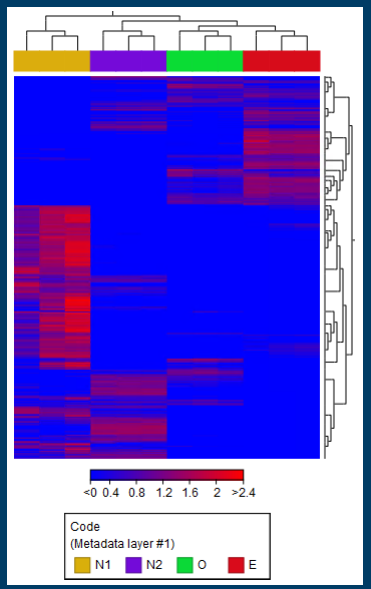
Functional annotation

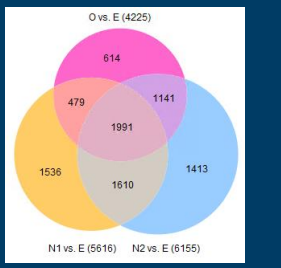


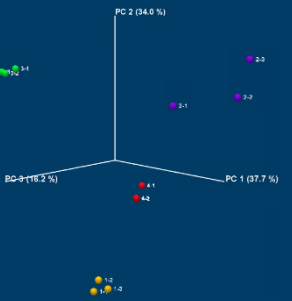
Which genes are active and when?

RNA-Seq









Microbiota from Moose gut (H2020 Metafluidics)

ω-3 FA-producing thraustochytrid (NFR: ThraustoENG)

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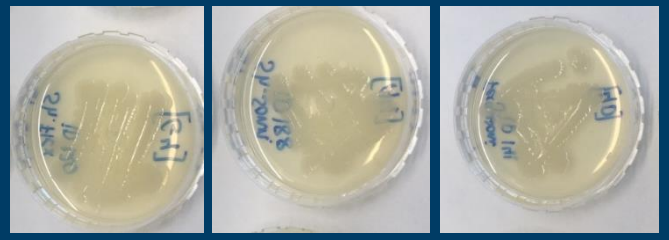
Mass-spectrometry fingerprinting and imaging

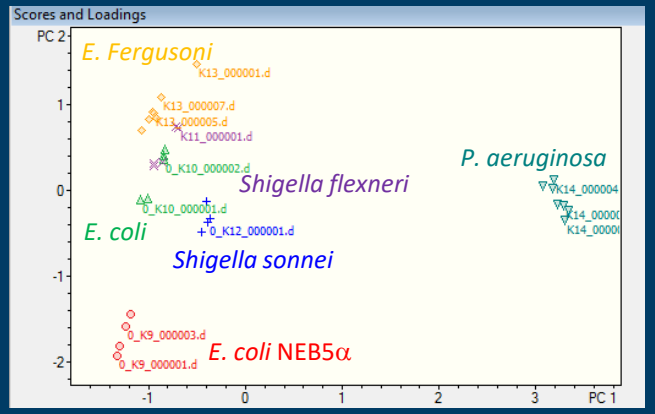
Microbial genotyping

Aim: Fast sub-typing of bacterial strains

- Mass spectrometry typing of bacterial strains
- MALDI- High resolution MS
- Multivariate data analysis



Shigella flexneri *Shigella sonnei* *Escherichia Fergusoni*

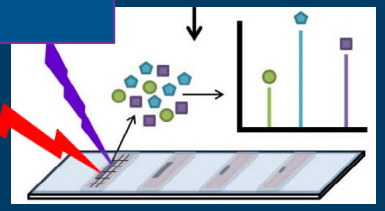


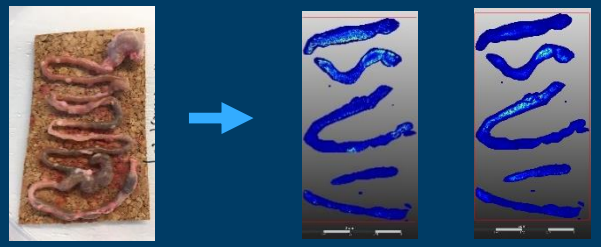
Microbiome profiling

Embedding

Frozen sectioning

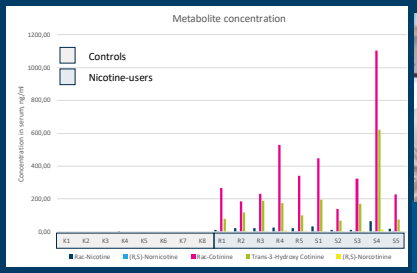
Imaging metabolite analysis

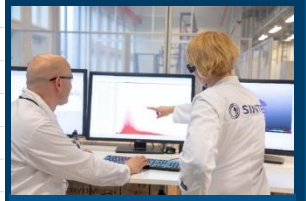




Tentatively identified components include: lipids, fosfatidylcholiner & amino acids

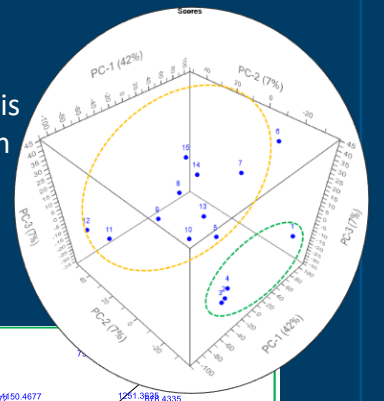
Metabolomics/Lipidomics

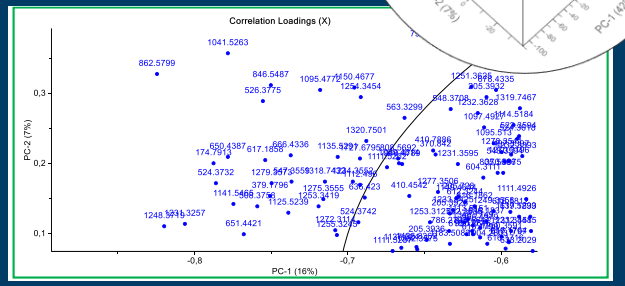




FT-ICR-MS ultra high resolution MS

- Mass spectrometry
- Targeted analysis,
- Non-targeted analysis
- Ultra-High resolution MS
- Multivariate data analysis





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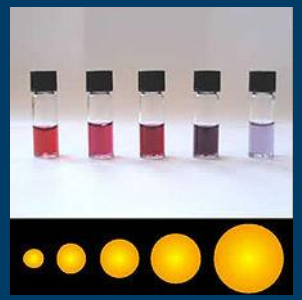
Environmental & Food/Feed analysis

Inorganic analysis

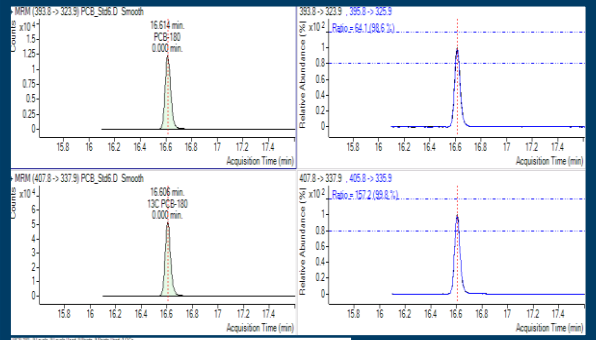
- ICP-MS
- Sample work-up and analysis

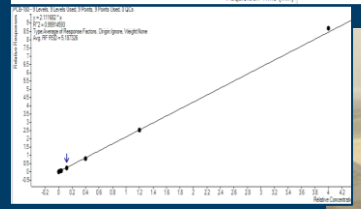
Arsenic, Cadmium, Cupper, Iron
Lead, Mercury,



PAH/PCB/Dioxin…

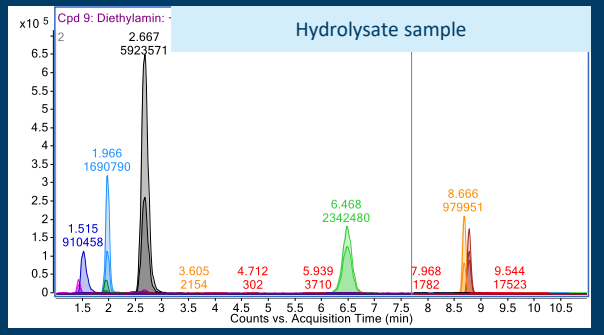
- GC-MS/MS
- Sample work-up and analysis
- Internal standards
- Validation

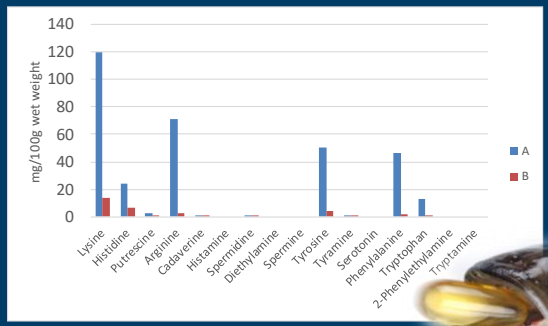




Following Commission Regulations (EU) 589/2014 & (EU) 709/2014

Microplastic, PAH, pesticides, toxins, fatty acids, vitamins, biogenic amines





Performed according to ISO 17025:2017

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Characterisation & Data handling tools

Metabarcode sequencing

Microbial potential

Metatranscriptomics

Microbial function

Mass spectrometry analysis, fingerprinting and imaging

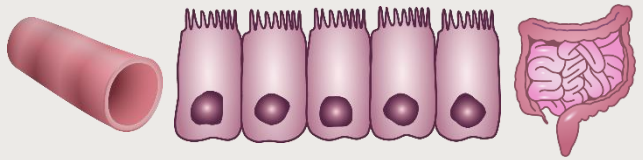
Microbial activity

Multi-omics integration and interpretation

Gut Microbiota in human and animal health

Biological models

Advanced in vitro gut models



Disease models in rodents

Smart delivery systems

Controlled delivery of pro- pre- and synbiotics

Nanoformulation of small molecule drugs ("drug the bug")

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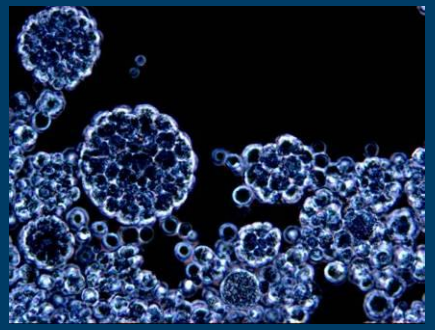
Cultivation and processing

High competence in the cultivation of microorganisms from ml to pilot scale fermentation

Inoculation for pilot scale fermentation



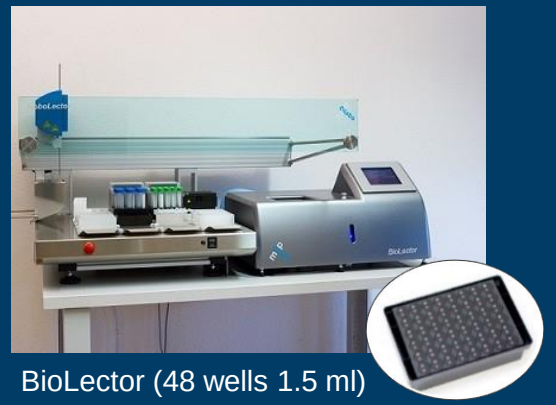
ω-3 FA-producing thraustochytrid

Centrifugation

Cell paste

Example:
Microbial production of lipids and the ω-3 fatty acid DHA to meet feed demands from the fish farming industry (supply from fish oil is not sufficient)
How can we increase the productivity?

Other relevant example:
- bioactive oligosaccharides from algae



BioLector (48 wells 1.5 ml)

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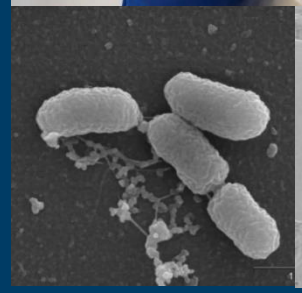
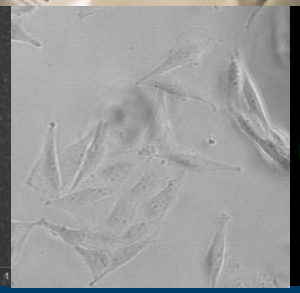
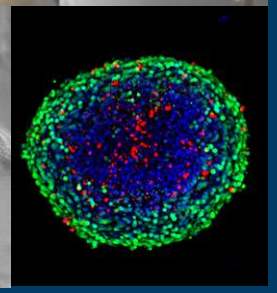
Biological models – in vitro



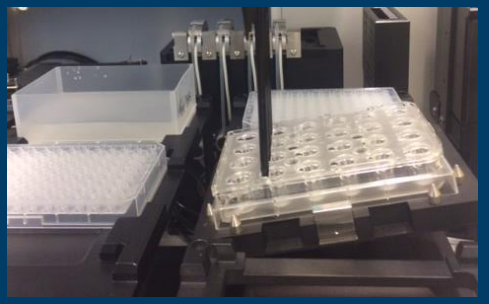




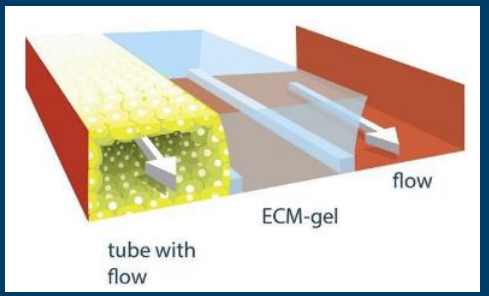
- **More than 70 mammalian cell lines available**
  In vitro efficacy and toxicity
- **Biosafety II approved**
  Assays with a range of multi-resistant microbial strains implemented (G-, G +, fungi)
- **2D and 3D in vitro assays**
  High throughput screening using 3D cell culture models for improved in vivo relevance
- **Fully automated *in vitro* model systems**
  Barrier assays: colon, lung. Image based readouts
- **Infrastructure for anaerobic cultivation**

To be implemented for gut microbiota research

- OrganoPlate® system from MIMETAS (gut-on-a-chip)
- Effect of phamaceuticals and nutraceuticals on gut microbiota

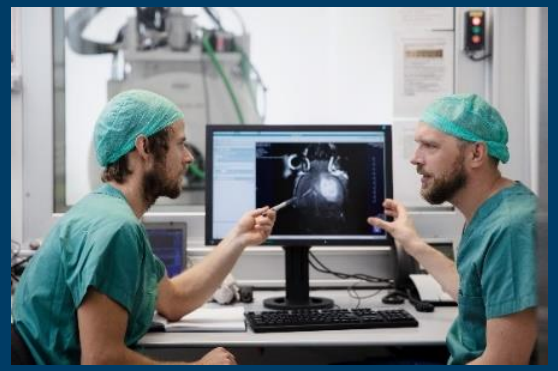


Liquid handling robot sampling from the basolateral side during fully automated CaCO-2/HT29 transwell assays.



Cross-section of OrganoPlate® 3-lane https://mimetas.com/page/organoready-caco-2

Biological models – in vivo



- **Treatment and effect**
  Efficacy, pharmacokinetics and biodistribution of pharmaceuticals and nutraceuticals in mouse models of diseases
- **Safety**
  In vivo safety evaluation of substances in mice and rats
- **Administration methods**
  Intravenous and local injections, surgical techniques, oral
- **Imaging systems**
  Whole animal imaging, ultrasound, animal PET/MRI, MS imaging, multiphoton and confocal microscopes
- **Microbiota analysis in rodents**

- **To be implemented for gut microbiota research**
  Inflammatory bowel disease and colorectal cancer models

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Characterisation & Data handling tools

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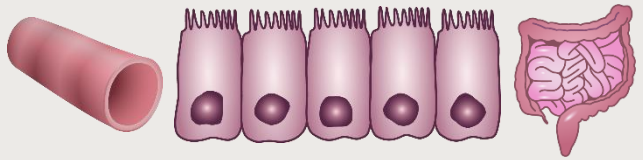

Disease models in rodents

Smart delivery systems

Controlled delivery of pro- pre- and synbiotics

Nanoformulation of small molecule drugs ("drug the bug")

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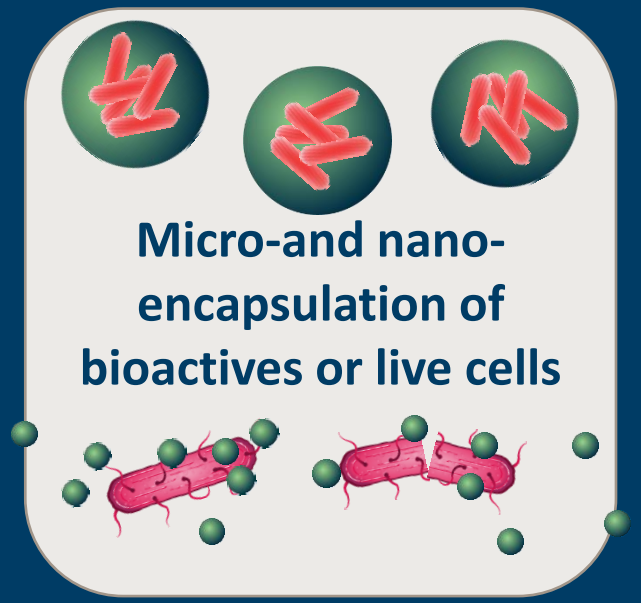
Smart delivery

Protect from degradation

Targeted delivery

Increased shelf life

Solubilization



Lower toxicity

Controlled release

Increased bioavailability

Combination of several compounds

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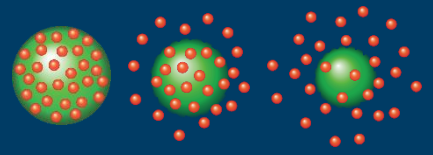
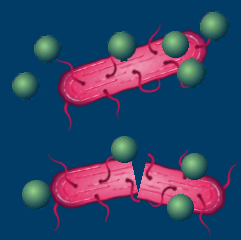
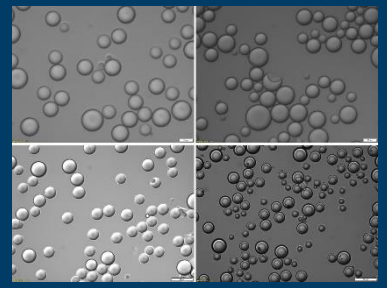
Competence and expertise on smart delivery



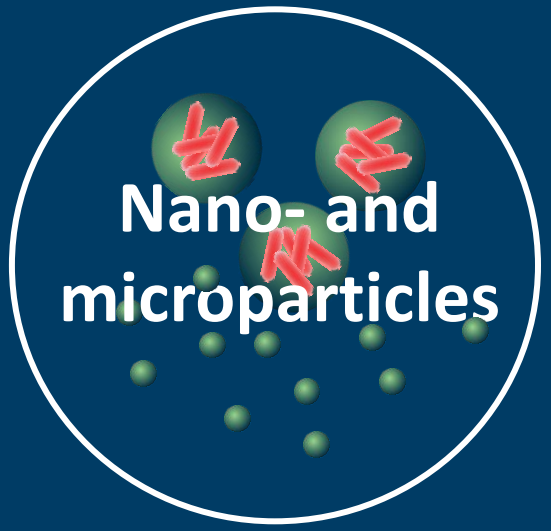
Programmable release profiles and release studies

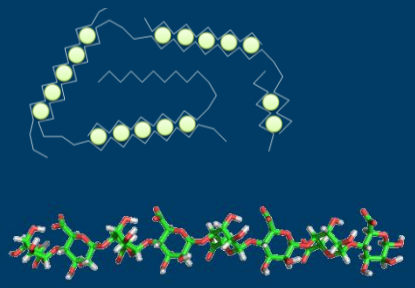
Various encapsulation techniques



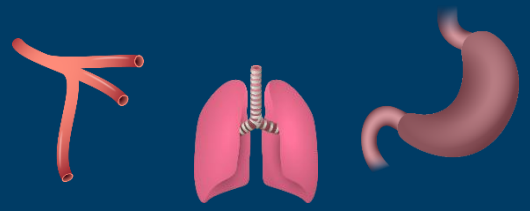


Antibiotics, vaccines, anti-cancer, anti-inflammatory and anti-fungal drugs, human and bacterial cells, nutraceuticals, vitamins, ω-3/fish oil, odours





Degradable natural and synthetic materials tailor-made for smart delivery



Various administration routes

Advanced characterisation

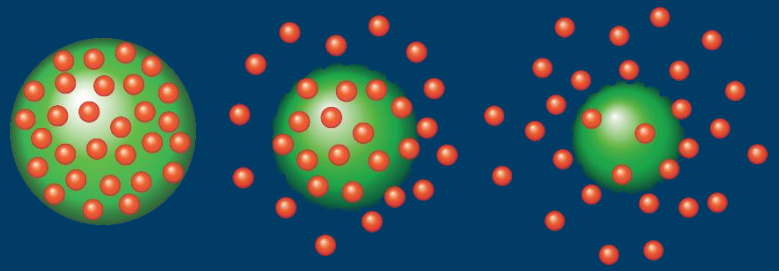
SINTEF

Smart delivery for targeting gut microbiota

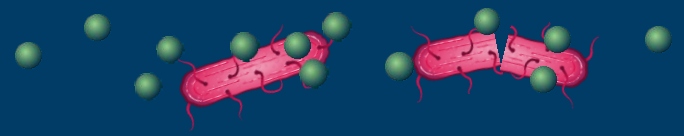
For human and animal health and welfare

Nano/microformulation of bioactives

Controlled release



"Drug the bug"



Controlled delivery of pro-, pre- and synbiotics

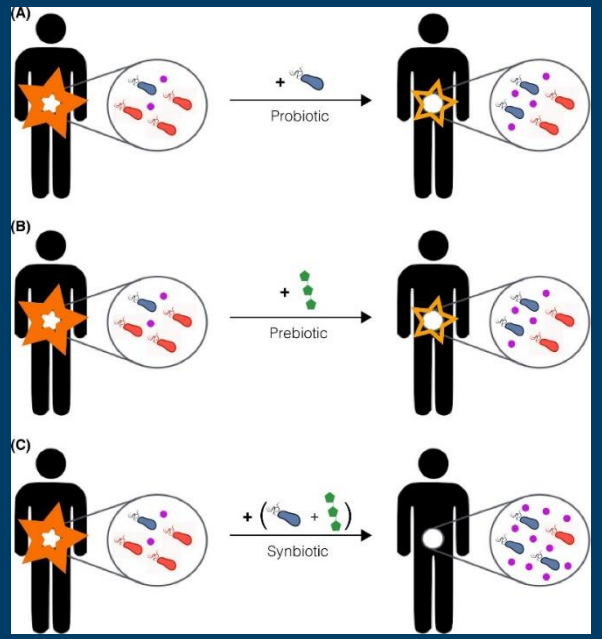


Image: Gurry, Microbial Technology, 2017, 10, 1070-1073

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Closing remarks

- Gut microbiota is a new strategic research area at SINTEF
- Through internal funding we are currently developing novel methods and building competence to support gut microbiota research
- We are looking for industrial and academic collaborations where we can contribute with our state-of-the art infrastructure and broad competence in ongoing or new projects

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70 years

1950-2020

Technology for a better society