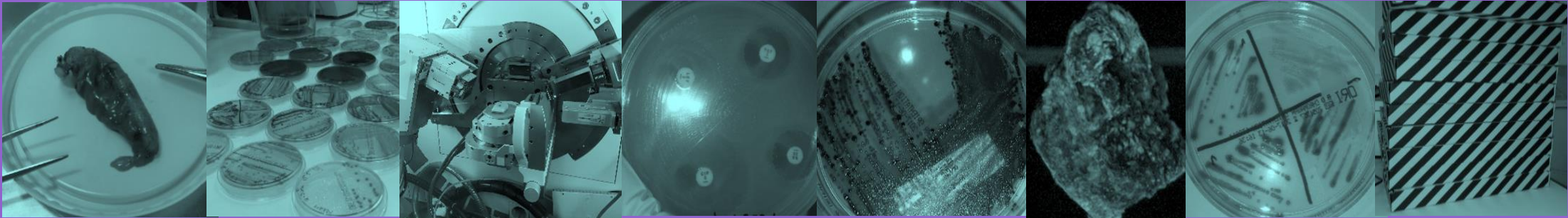


# Acute appendicitis and microbiota:

## Etiology and effects of the antimicrobial treatment



Research director Eveliina Munukka, PhD

6th Microbiome R & D & Business Collaboration Forum, Rotterdam, 21.5.2019

# Acute Appendicitis

- traditionally the standard treatment has been ***appendectomy***
  - the most common cause of emergency abdominal surgery
  - ~ 300, 000 appendectomies per year in United States, ~ 5000 in Finland
  - complicated form always needs surgery
- complicated vs. uncomplicated disease form → in Finland diagnosis is based on CT imaging (OPTICAP)
- obstruction of appendix followed by microbial overgrowth and/or bacterial infection as a primary reason
- treatment by antibiotics ?



# The appendicitis acuta = APPAC

## Original Investigation

### Antibiotic Therapy vs Appendectomy for Treatment of Uncomplicated Acute Appendicitis The APPAC Randomized Clinical Trial

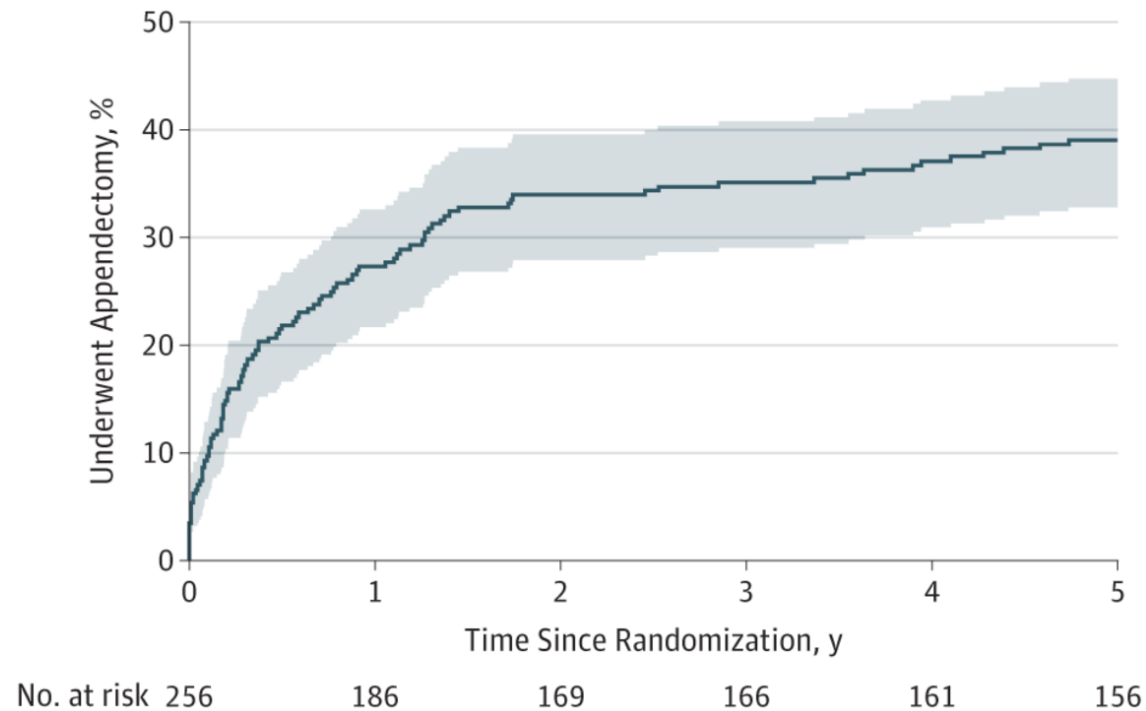
Paulina Salminen, MD, PhD; Hannu Paajanen, MD, PhD; Tero Rautio, MD, PhD; Pia Nordström, MD, PhD; Markku Aarnio, MD, PhD; Tuomo Rantanen, MD, PhD; Risto Tuominen, MPH, PhD; Saija Hurme, MSc; Johanna Virtanen, MD; Jukka-Pekka Mecklin, MD, PhD; Juhani Sand, MD, PhD; Airi Jartti, MD; Irina Rinta-Kiikka, MD, PhD; Juha M. Grönroos, MD, PhD

*JAMA*, 2015; 313: 2340-8.

- non-inferiority trial
- uncomplicated appendicitis patients (n = 530) were randomized either to antibiotics or appendectomy group
- *i.v.* ertapenem (1g/d), 3 d + *p.o.* levofloxacin (500 mg/d) ja metronidazol (3 x 500 mg/d), 7 d
- **73 % of ab patients were successfully treated.**

From: **Five-Year Follow-up of Antibiotic Therapy for Uncomplicated Acute Appendicitis in the APPAC Randomized Clinical Trial**

JAMA. 2018;320(12):1259-1265. doi:10.1001/jama.2018.13201



- the likelihood of late recurrence within 5 years was 39.1%.
- long-term follow-up supports the feasibility of antibiotic treatment alone as an alternative to surgery for **uncomplicated acute appendicitis**.

# APPAC II, APPAC III and MAPPAC

- non-inferiority, randomized, multicenter trials, APPAC III double-blinded

**APPAC II:** Optimization of the AB  
- *i.v. + p.o vs. p.o.*

Ab1: *i.v.* ertapenem + *p.o.*  
levofloxacin and metronidazole

Ab2: *p.o.* moxifloxacin

- open label

**APPAC III:** Spontaneous  
resolution?

– **Ab treatment vs. placebo**

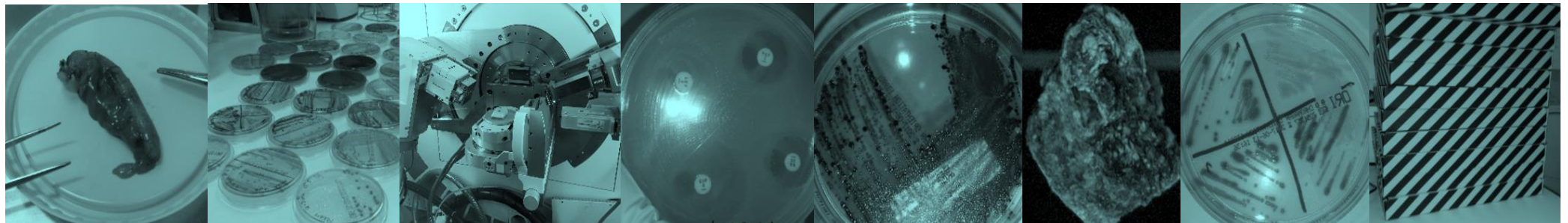
Ab: *i.v.* ertapenem + *p.o.*  
levofloxacin and metronidazole

– double-blinded

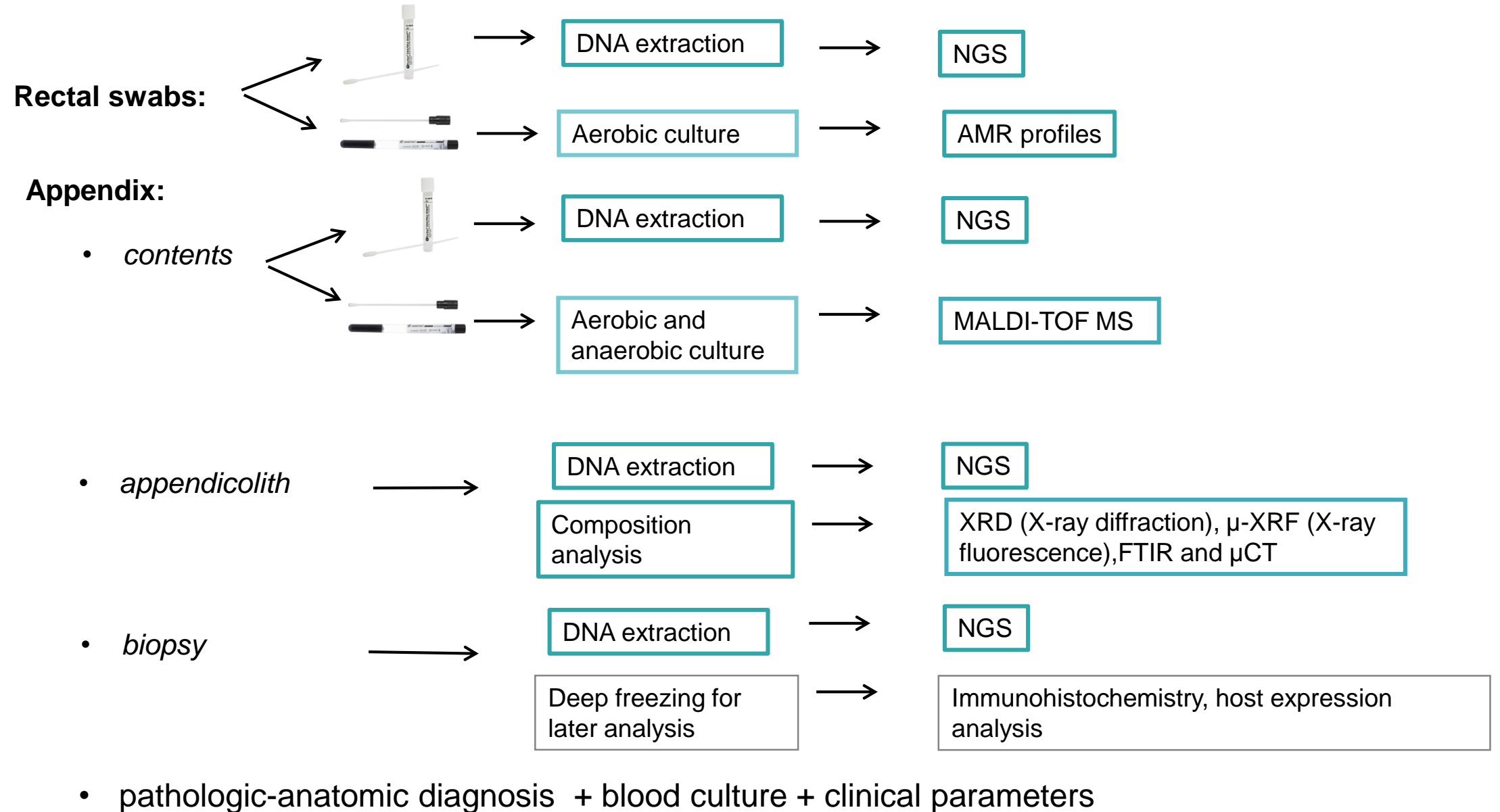
**MAPPAC (Microbiology Appendicitis Acuta)**

# Microbiological etiology of appendicitis

- Whether or how complicated and uncomplicated AA differ microbiologically?
  - appendix microbiome studied by NGS (Illumina MiSeq) and trad. culture combined with MALDI-TOF
  - gut microbiome of AA patient at the same time point *i.e.* novel microbiological markers that can be identified from rectal samples?
  - serum metabolome profiles
- Can microbiological factors explain the recurrence/treatment failure of AA?
- What is appendicolith?



# Sample collection, methods and analysis



# Appendix culture and MALDI-TOF/MS identification



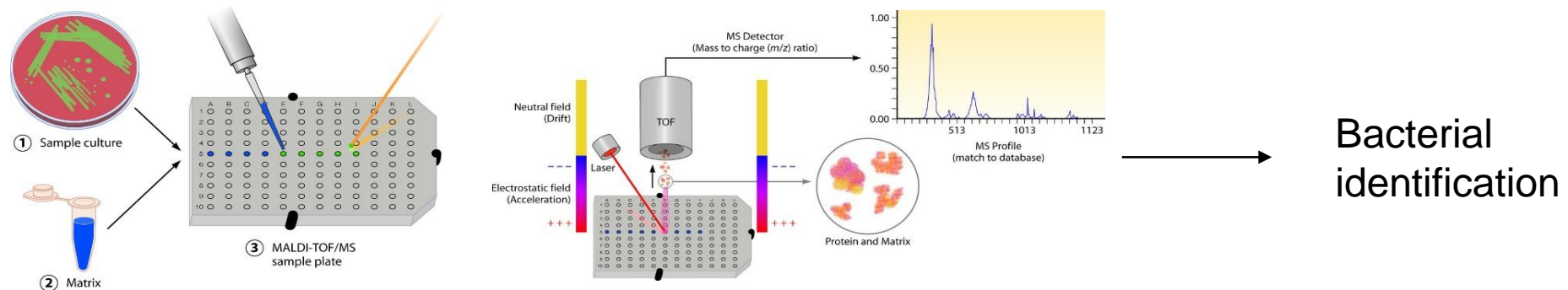
## Aerobic culture:

Chromagar orientation, blood agar, Streptococcal blood agar, Yersinia agar

## Anaerobic culture:

Kanamycin-vankomycin laked blood agar and FAA

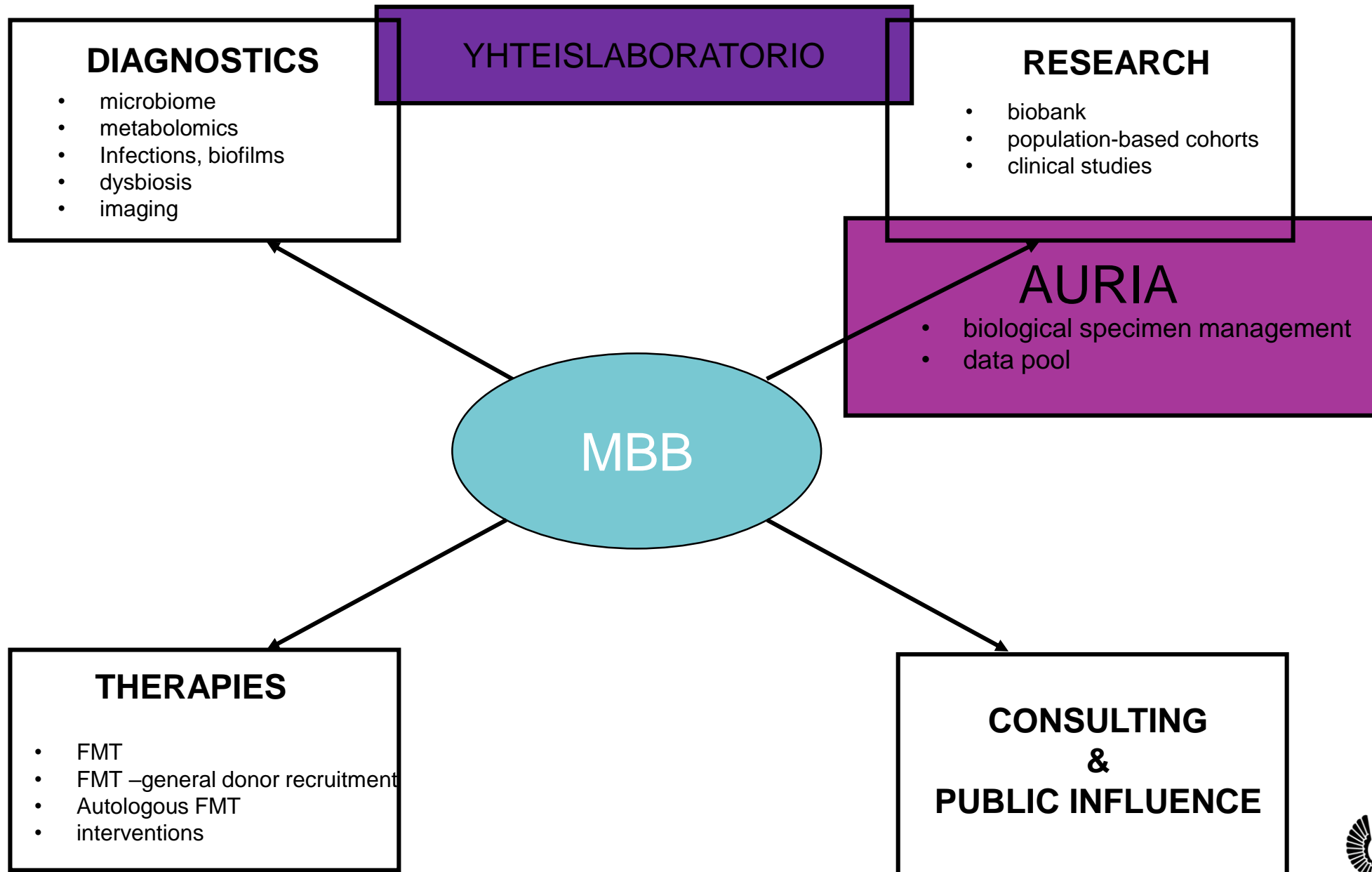
© Sanja Vanhatalo





# Turku Microbiome Biobank

- first microbiome biobank in Finland, launched at August 2018
- joint project: Turku University/Medical faculty, Tyks Clinical Microbiology and Auria Biobank
- facilities in MedisiinaD building in Kupittaa Health Campus
- Collaboration:
  - various departments and clinicians within Tyks (Gastroenterology, Infectious diseases, Gastrosurgery, Hygiene unit, Yhteislaboratorio, TYKSlab etc.)
  - academy fellow, Reetta Satokari, University of Helsinki
  - cohort studies within Turku area: Finnbrain birth cohort (prof. Hasse Karlsson & doc. Linnea Karlsson), Young Finns Study / STRIP Study (prof. Olli Raitakari, doc. Katja Pahkala)
  - academy fellow, docent Leo Lahti (bioinformatics)
  - Turku Centre for Biotechnology: bioinformatics, metabolomics
  - University of Jyväskylä, Dept. Of Health Sciences & Central Finland Central Hospital
  - Finnish Olympic Committee, responsible Dr. Maarit Valtonen,



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### **Auria Biobank**

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