

# Inflammatory Bowel Diseases Research Group. 2007.....

**Disease mechanisms from  
clinical material**

**Translate findings to  
clinical use**

- 1. The group up to now***
- 2. The CAG***



# Patient and society

COUNTRY: Spain    DISEASE: Ulcerative Colitis    FORMAT: Painting  
TITLE: Paquita Tiene Colitis (Paquita Has Colitis)  
ARTIST: Jesús Sánchez Fajardo

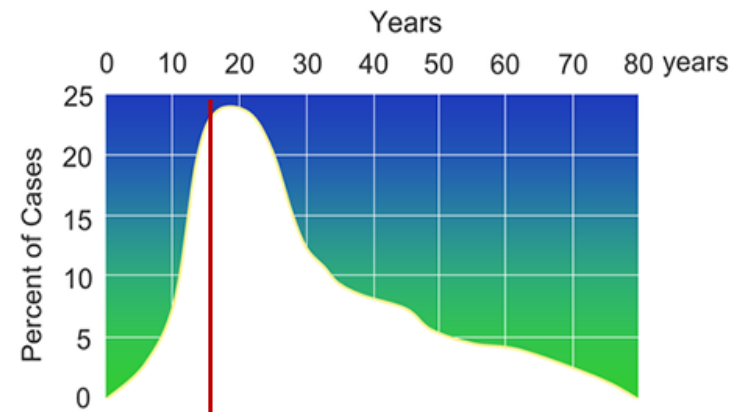


**CDC:**  
**AN EXPENSIVE DISEASE**  
**WITHOUT A CURE**

**IBD incidence: 69/100.000-yr**  
**IBD prevalence: 767/100.000**

- Young adults/children
- Decisive years of life
- Decades of disease
- Unpredictable course
- Great personal burden
- Great societal burden

## Age of Onset of IBD





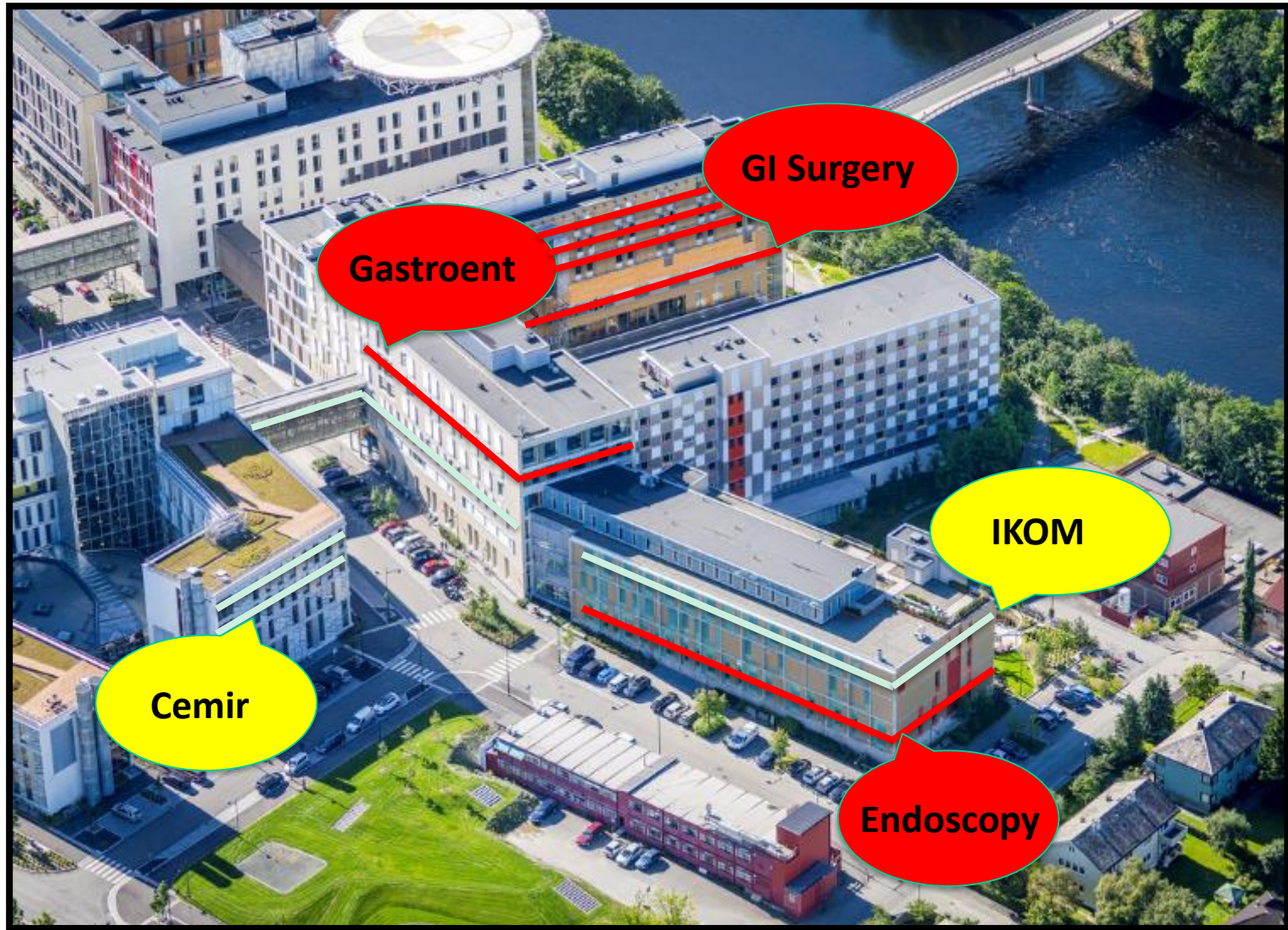
Primary hospital for 315.000

Secondary/tertiary hospital for 750.000

(China – 149 cities of > 1.000.000)

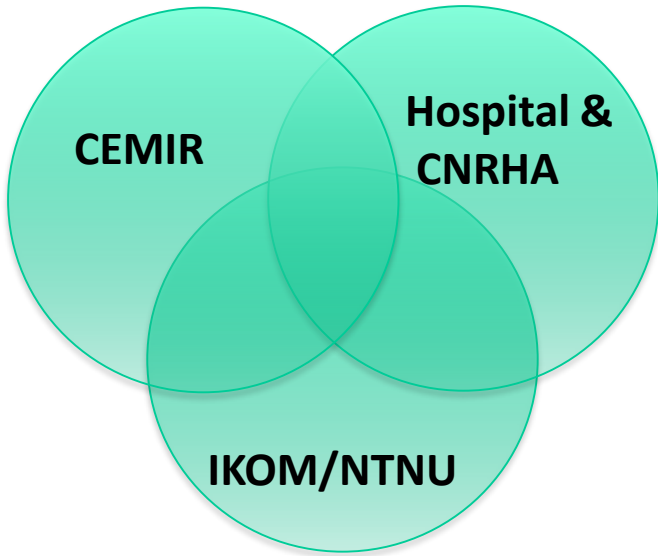
2018: 5863 IBD publications (PubMed)

# St Olav/NTNU integrated research-clinical areas



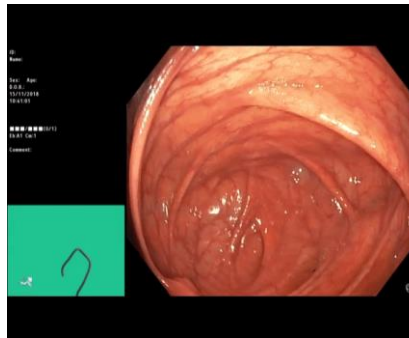
# IBD research from bed to bench – and back to bed

## Organization



## Basic skills

Gastroenterology  
Pathology  
Molecular biology  
Cell biology



## Core group

One prof. I/consultant  
One consultant/assoc prof. II  
One assoc prof. I  
Two researchers  
One postdoc/consultant  
One postdoc  
Three PhD-students  
One research medical student  
Two science master students  
50% research nurse



# IBD biobank(s)

## In-house IBD biobank (>800)

- Biopsies (FFPE/N<sub>2</sub>)
- RNA/DNA
- Serum
- Plasma
- PBMC
- Feces\*

• Clinical info incl. follow-up

Patient-derived organoids

## Population bio-bank IBD (1700)

- DNA
- Serum
- Clinical info
- Background info
- 30-yr follow-up



### IBD-biobanken:

#### *Styrke:*

- Stort og bredt materiale, oppfølging

#### *Svakhet:*

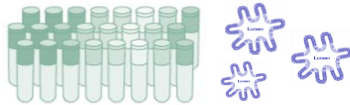
- Tverrsnittsamling, heterogen historie

# Materials and methods

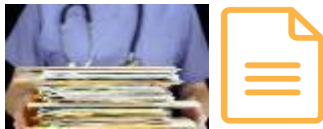
IBD patients – clinical and molecular stratification



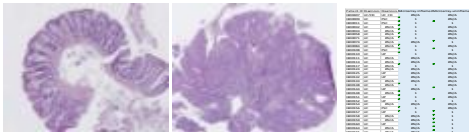
IBDSelect biobank  
(biopsies, blood, feces, organoids)



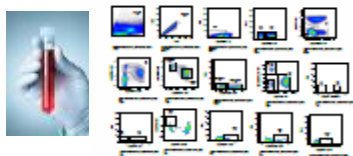
Medical records - patient data and clinical outcomes



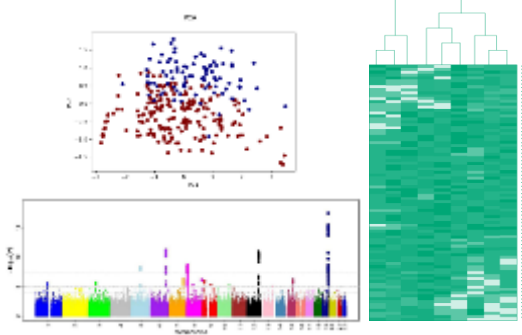
Histological indexing



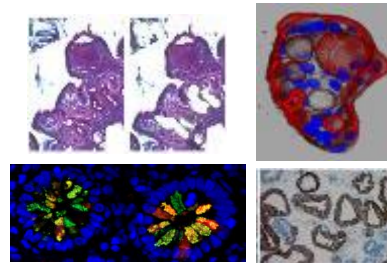
Immunophenotyping in blood



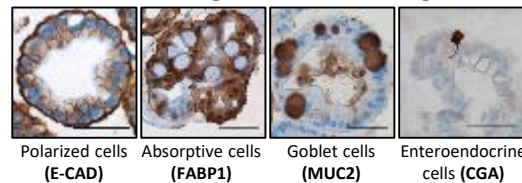
Multomics  
(genotyping, -omics profiling)



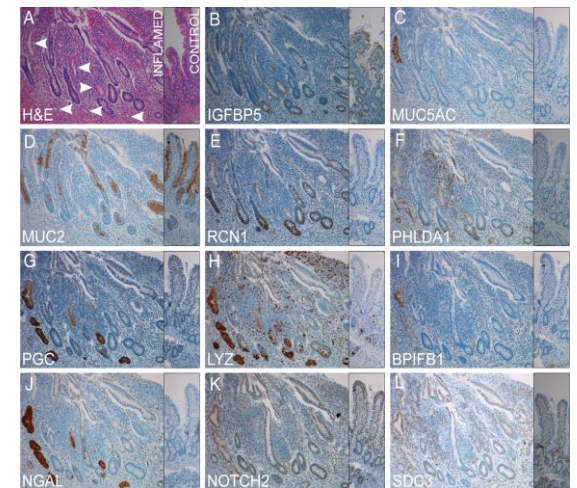
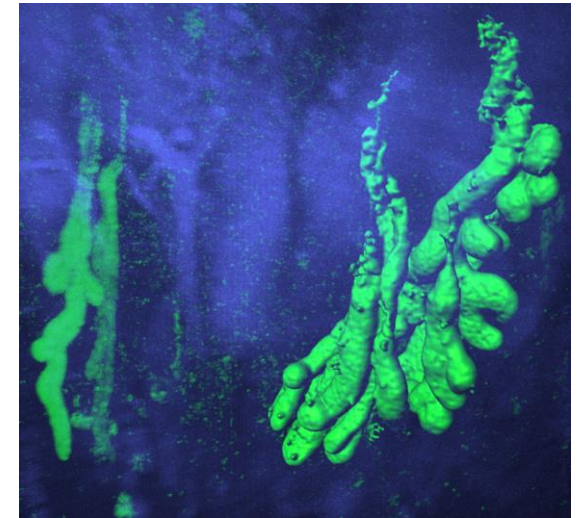
Digital molecular pathology



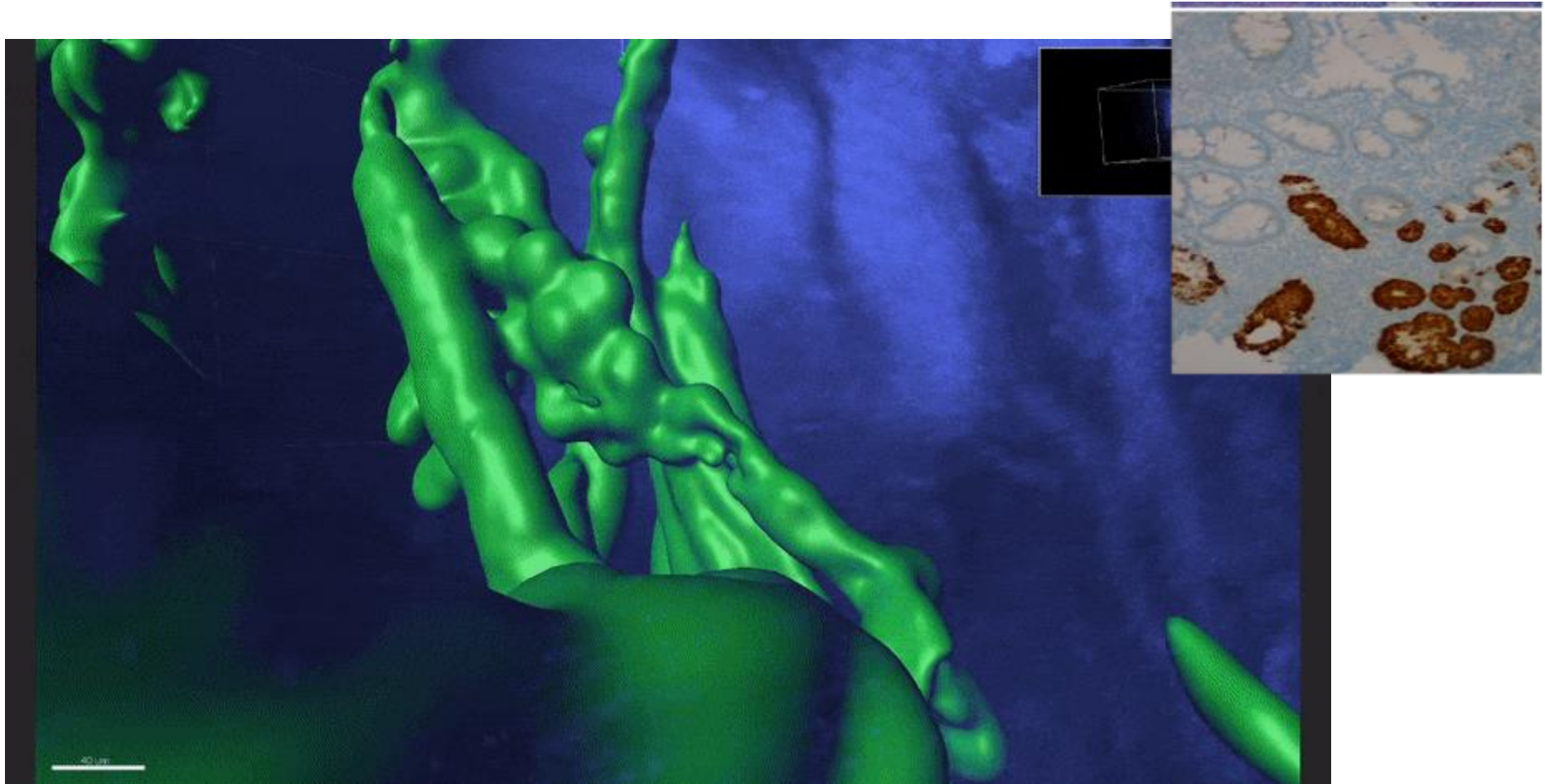
IBD patient-derived colonoid culturing and modelling



Main focus – epithelial factors in IBD pathobiology



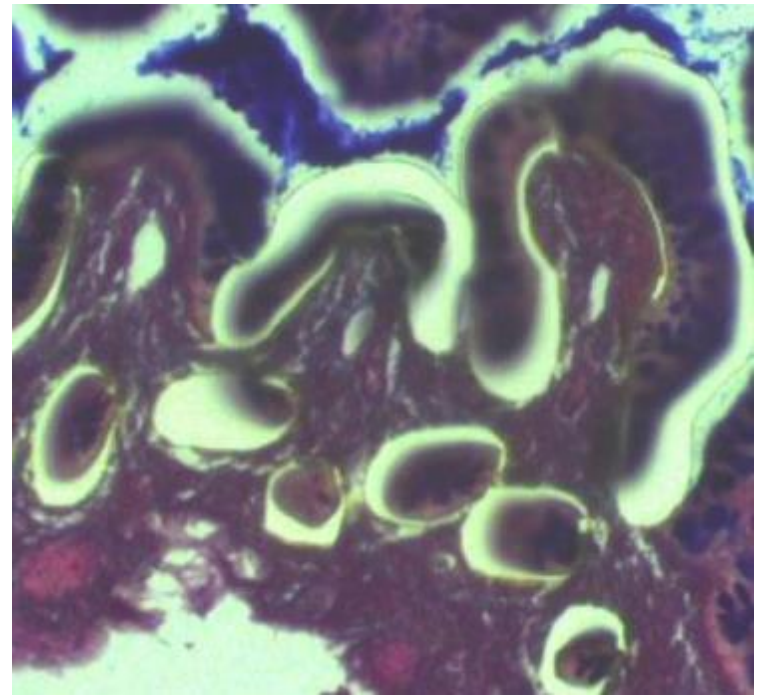
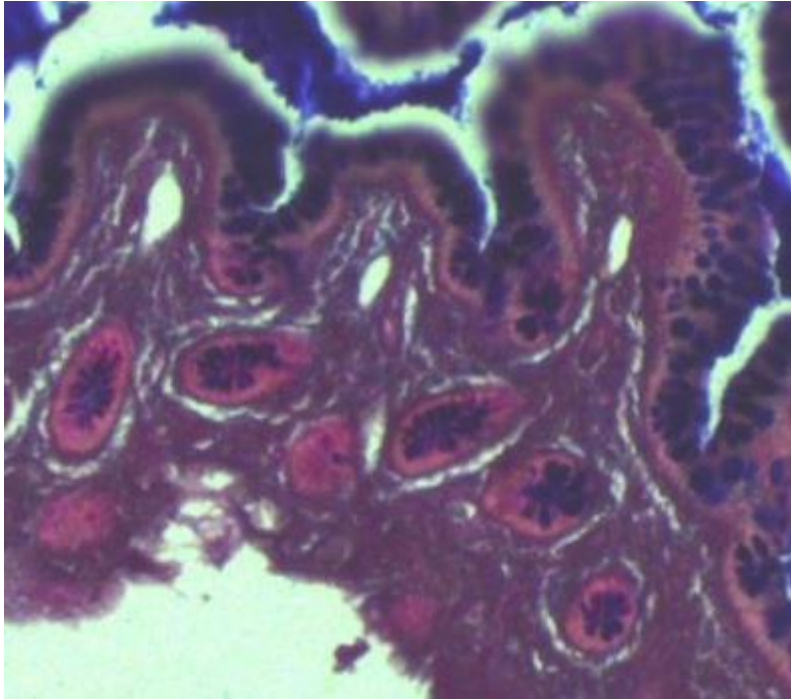
# Advanced imaging of disease samples (Core facility – CMIC)



**c-DISCO prep - mucosal repair in small intestinal CD (UACL)**



## GE patterns in epithelium alone (Core facility - GCF)



**Microdissected epithelial layer UC - transcriptome**

# IBD Research Group - collaboration



# A CAG (Clinical Academic Group)

## The main goals of the CAG:

- increase both scope and quality of knowledge development with **transfer value and improvement effect for the health services**
- build strong groups that can compete internationally
- organize a **cross disciplinary team to address a defined health challenge in the region**
- contribute to the use of research-based knowledge in training, practice and teaching
- identify and remove obstacles for professional cooperation between the sectors
- provide the basis for health service innovation and business development.

# Søknaden om CAG - organisasjon

## CAG Governance Team

CAG leader: Prof., senior consultant MD Arne K. Sandvik, MH Faculty, Dept. of Clinical and Molecular Medicine (IKOM), NTNU

CAG co-leader: Senior consultant MD, assoc. prof. II Ann Elisabeth Østvik, Clinic of Medicine, Dept. of Gastroenterology and Hepatology, St. Olav's University Hospital

**St. Olav's University Hospital**  
Clinic of Medicine  
Dept. of Gastroenterology and Hepatology *Ann Elisabeth Østvik (MD, PhD)*  
Children's Clinic  
Dept. of Medicine  
*Anders Lindgren (MD)*  
Clinic of Laboratory Medicine  
Dept. of Pathology  
*Elin S. Røyset (MD, p.t. PhD candidate in IBD)*

**NTNU**  
MH Faculty  
Dept. of Clinical and Molecular Medicine  
*Arne K. Sandvik (MD, PhD) (CEMIR, GCF)*  
*Torunn Bruland (MSc, PhD)*  
*Atle vB. Granlund (MSc, PhD) (CEMIR)*  
*Ingunn Bakke (MSc, MD, PhD)*  
IE Faculty  
Dept. of Mathematical Sciences  
*Mette Langaas (MSc, PhD)*

**Nord-Trøndelag Hospital Trust**  
**Levanger Hospital**  
Clinic of Medicine and Rehabilitation Dept. of Medicine  
*Øystein Brenna (MD, PhD)*

**Møre og Romsdal Hospital Trust**  
**Molde Hospital**  
Clinic of Medicine, Dept. of Medicine  
*Espen Skarsvåg (MD)*  
Clinic of Diagnostics, Dept. of Pathology  
*Karla Tomic (MD)*

**UiT The Arctic University of Norway/ University Hospital of North Norway**

**Oslo University/ Oslo University Hospital**

**HUNT Research Center**

**NTNU IE Faculty**

**Clinic of Surgery, St. Olav's University Hospital**

**Clinic of Medicine, St. Olav's University Hospital**

**Yale University (US)**

**Singapore Immunology Network**

**Linköping University/ Linköping University Hospital**

**Lund University/ Skåne University Hospital, Lund;**

# CAG IBD – Precision Medicine in Inflammatory Bowel Disease

**De to første Clinical Academic  
Groups i Midt-Norge er tildelt**



# Precision medicine in IBD – idea and approach

## Basic idea

IBD **pathobiological traits can inform** on prognosis and response to treatment for the individual. How can we identify these factors?

## Approach

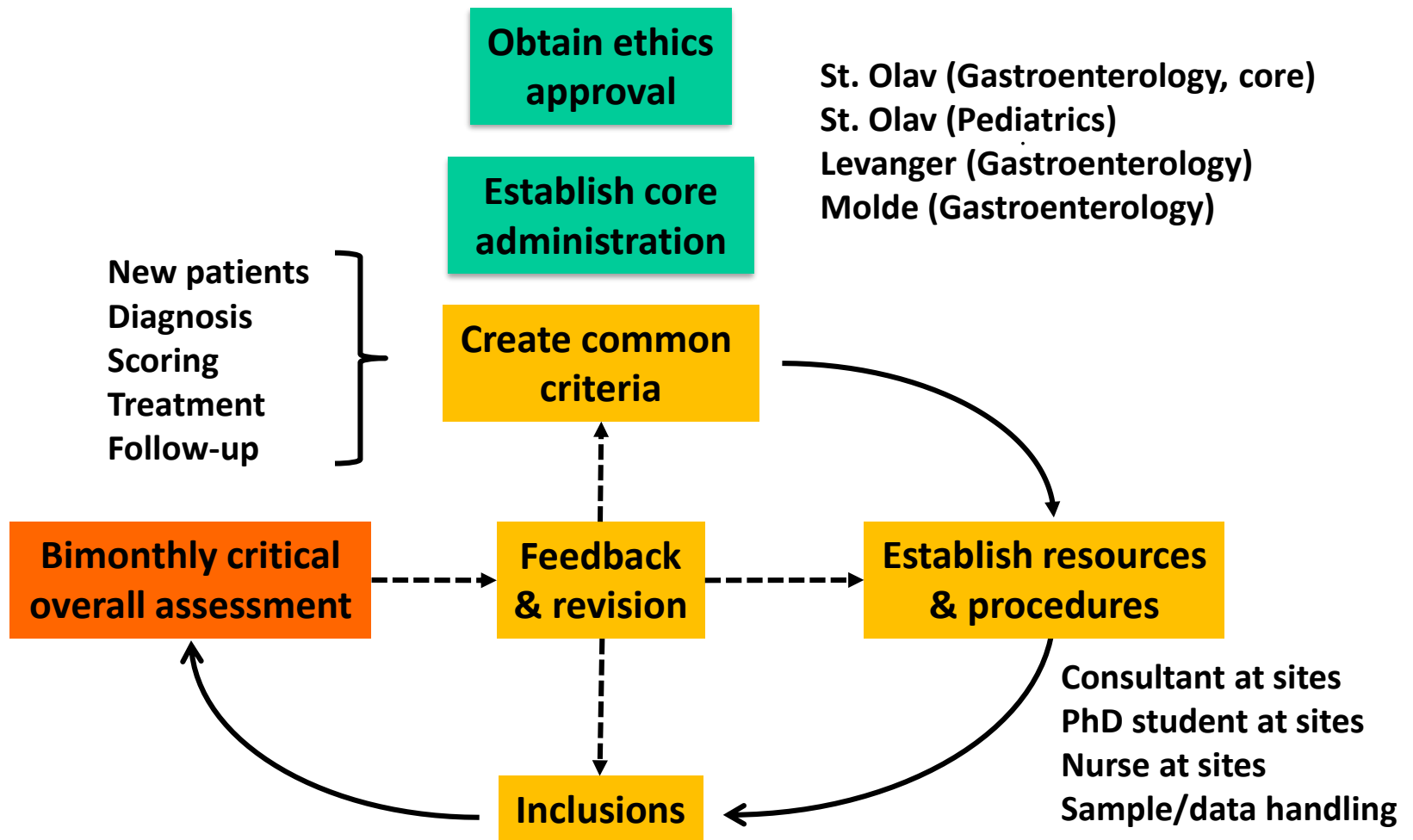
Create a large, informative patient cohort **through standardized clinical procedures** (diagnostic, therapeutic and follow-up) combined with a **detailed characterization** (clinical and research lab)

## Result

Clinical information and research data generate **candidate predictors** for prognosis/treatment responses to be evaluated prospectively.

Understanding disease mechanisms generates **novel treatment targets** for IBD.

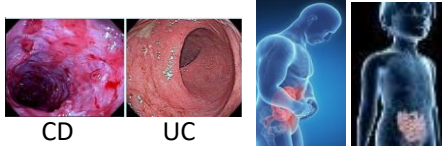
# Precision medicine in IBD – clinical implementation



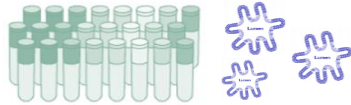
**Amendments are needed for pediatric patients**

# Precision medicine in IBD – translational elements

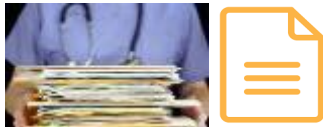
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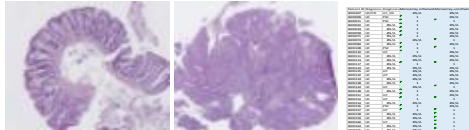
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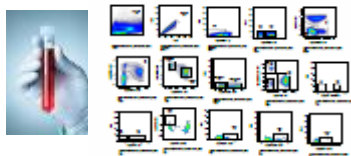
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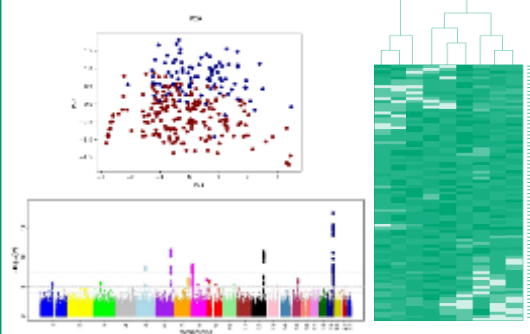
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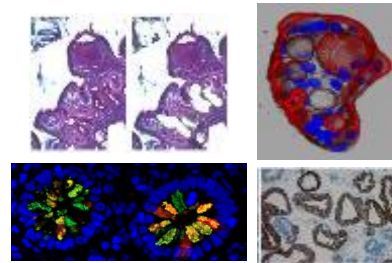
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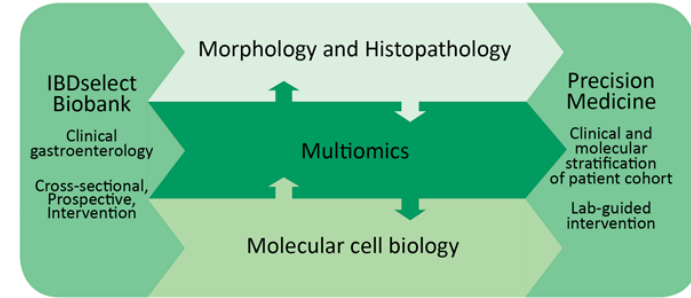
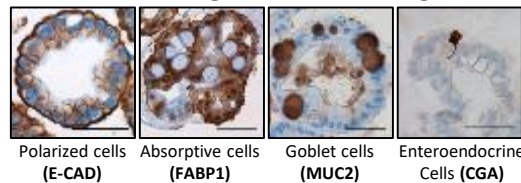
Multiomics  
(genotyping, -omics profiling)



Digital molecular pathology



IBD patient-derived colonoid culturing and modelling



Numerous relevant methods are available in the NTNU IBD lab

Experienced scientists in the group, NTNU core facilities and partners nationally/internationally are able to establish new methods as needed.

Critically; several large datasets need to be merged.

**Bioinformatics/biostatistics!**



# Precision medicine in IBD – project outcomes

## **Direct clinical value**

The major success criteria are to find and implement tools aiding in diagnosis, choice of treatment and assessment of prognosis. Example: fecal NGAL

## **Added clinical value**

A systematic approach to diagnosis and treatment decisions beyond the research cohort, saving resources and simplifying transfer of patients between hospitals or departments

## **Staff training**

Attending meetings and conferences with presentations by involved staff (doctors, nurses) will develop skills as well as scientific insight in IBD. Trained and insightful IBD nurses will ease the routine workload for gastroenterologists

## **Lasting scientific value**

The cohort will be among the most systematic and thoroughly characterized in the world, a lasting resource for research and create opportunities for collaboration

# IBD research – the coming years



Whitepaper March 2019

*“With **well-designed longitudinal studies** that use **multi-omics analyses** interpreted in the context of **clinical metadata**, tremendous insight into disease **mechanisms, course and outcome** can be gained. Coupling such insights with **experimental models that involve patient-derived cells** and other informative *in vitro* and *in vivo* approaches shows **great promise ahead....**”*