M1 internship project for qBio master - IDIL Summer School 2025

Dissecting the mechanisms by which intestinal AIEC promote macrophage-induced inflammation during Crohn's disease

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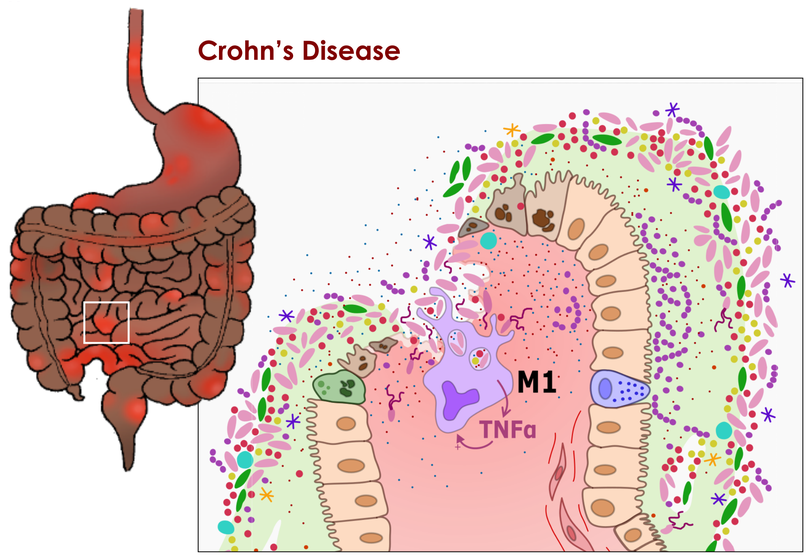
Host Lab: Laboratory of Pathogens and Host Immunity (LPHI)

SCIENTIFIC CONTEXT

Crohn's Disease (CD), a raising inflammatory pathology with no curative treatment

Crohn's disease (CD) is one of the 2 major forms of **inflammatory bowel diseases**. It is a **highly invalidating pathology**, characterized by recurrent and very **painful inflammatory episodes**, associated with numerous extraintestinal complications and an **increased risk of colon cancer**. The inflammatory burden is fed by an aberrant production of TNFa, elicited by the prevalence of pathogenic species due to intestinal dysbiosis.



No curative treatment exists yet for CD, only palliative treatment with **anti-TNFa antibodies**.

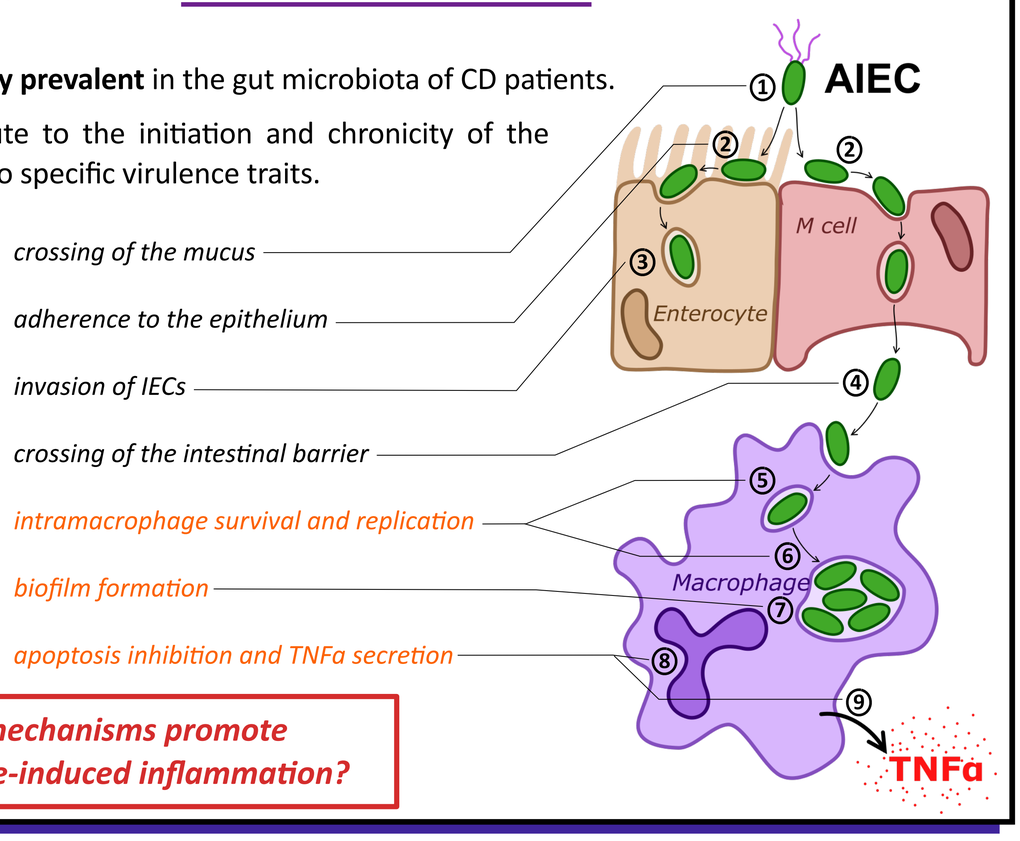
The **constantly raising incidence** of the disease urges for the development of **novel anti-CD therapeutics**.

Pathogenic gut microbiota: a promising drug target in CD

Adherent Invasive E. coli (AIEC), a major pathogenic agent in Crohn's Disease (CD)

AIEC are **highly prevalent** in the gut microbiota of CD patients.

They contribute to the initiation and chronicity of the disease, due to specific virulence traits.



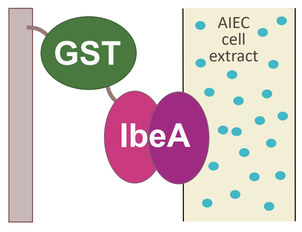
Which mechanisms promote macrophage-induced inflammation?

PROPOSED METHODOLOGIES

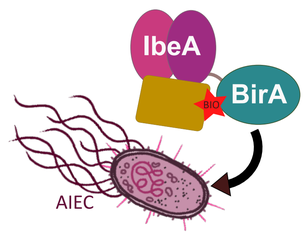
In vitro approaches - Interactomics and 3D-modelling

1. Identify IbeA's binding partners

Experimental approaches

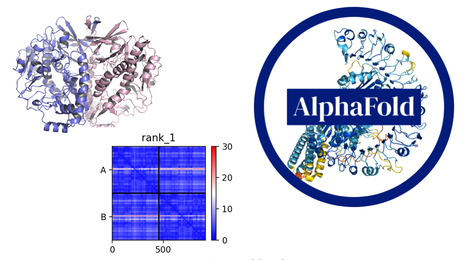


GST pull-down



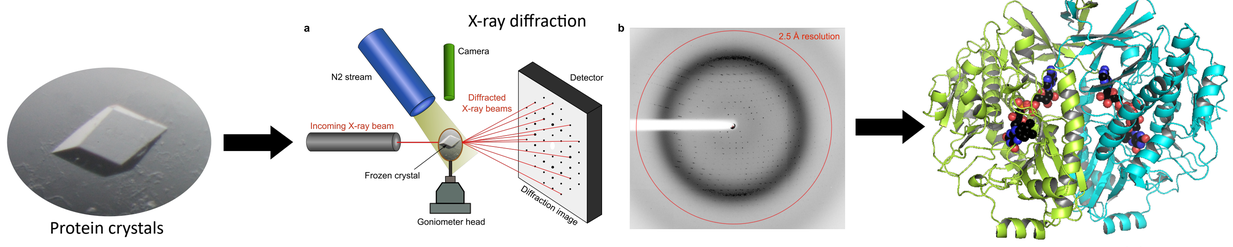
TurboID

In silico approaches



Virtual pull-down

2. Elucidate IbeA's structure-function relationship



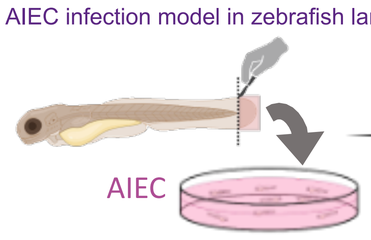
3D-structure determination - IbeA alone + complexes

Aim: define IbeA's precise **biological function** and the **redox mechanisms** it controls

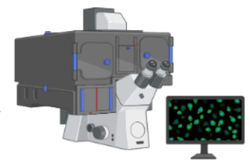
In vivo approaches - zebrafish, imaging & transcriptomics

1. Role of IbeA/partners in intramacrophage survival & inflammatory burst

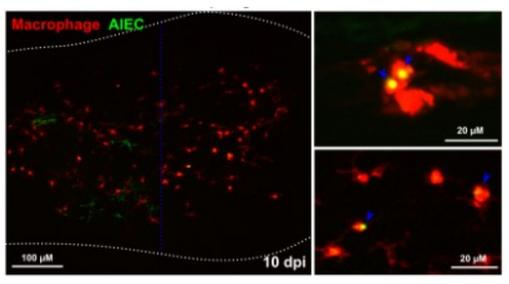
AIEC infection model in zebrafish larvae



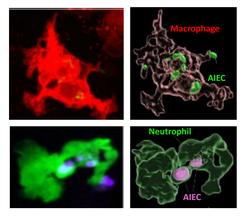
Tail fin amputation + balneation



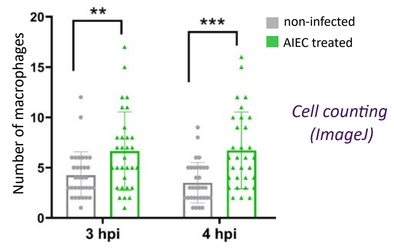
Imaging with confocal microscopy (MRI)



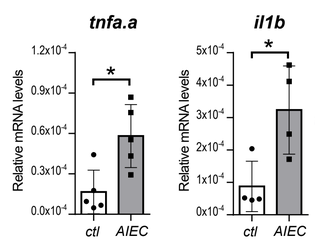
3D-reconstruction (IMARIS)



Quantification of immune cell recruitment and activation

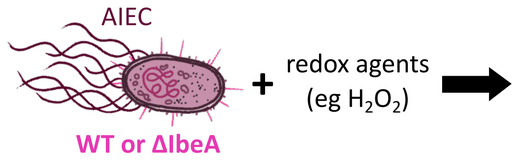


Cell counting (ImageJ)



Targeted transcriptomics by RT-qPCR

2. Role of IbeA/partners in resistance to oxidative stress



WT or ΔIbeA

Growth assay

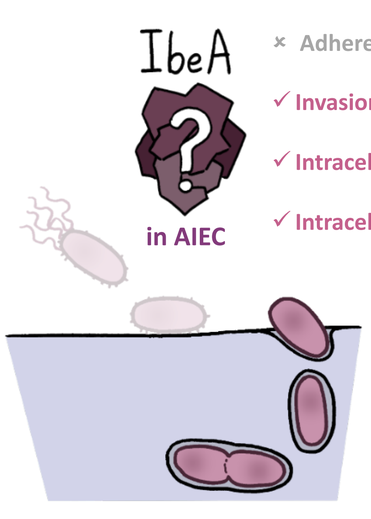
Does IbeA contribute to **macrophage-induced inflammation** and/or to **redox control within macrophages**?

OBJECTIVES & PRELIMINARY RESULTS

Identify novel AIEC virulence factors for drug targeting

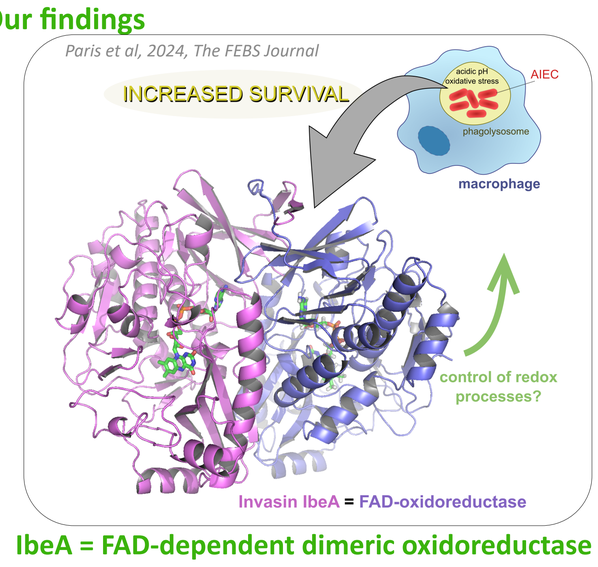
O1. Identify VFs important for intramacrophage survival

O2. Unravel the biological processes they control to induce inflammation



Among AIEC's VFs, **IbeA** recently described as required for **invasion, survival & replication inside macrophages**.

Our findings



IbeA = FAD-dependent dimeric oxidoreductase

Involved in resistance to oxidative stress? Through which mechanims/pathways?

MORE ABOUT THE PROJECT & TEAM

The team: Mechanisms of Normal & Pathological Inflammation

https://lphi.umontpellier.fr/research-teams/mechanisms-of-normal-and-pathological-inflammation/

Recent publications

Demou M & Yatime L (2025) **bioRxiv** 2025.07.25.666771; doi:10.1101/2025.07.25.666771

Hernandez L et al (2025) **bioRxiv** 2025.06.10.658860. doi:10.1101/2025.06.10.658860

Paris T et al (2024) **FEBS J** 291, 177-203. doi:10.1111/febs.16969

Leiba J et al (2023) **Biology** 12, 153. doi:10.3390/biology12020153

Kowalewski J et al (2021) **PLoS ONE** 16, e0254533. doi:10.1371/journal.pone.0254533

Videos about what we do in our team

https://www.youtube.com/watch?v=azDtPVfmYkA

https://www.youtube.com/watch?v=M_8CuYbYpU0

https://www.youtube.com/watch?v=SMBUqwfKQZU

Fundings