MYENTERIC PLEXITIS AND POST-OPERATIVE RECURRENCE IN CROHN’S DISEASE

The role of enteric glial cells and ICAM-1


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DOP Session 3: Translational science in IBD
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Conflicts of interest

• None
Background

• >50% of patients with Crohn’s disease require surgery within 20 years of diagnosis.
• Post-operative recurrence is frequent.

7 risk factors identified:
  o Smoking, prior intestinal surgery, absence of prophylactic treatment
  o Penetrating disease, perianal location
  o Granulomas in resection specimen
  o **Myenteric plexitis in the proximal resection margin**

Definition: ≥1 immune cell in contact with or within ganglion cells or nerve bundles
Background

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Involved mechanisms?
Objectives

(1) To analyse plexitis by immunohistochemistry

(2) To determine which cells of the enteric nervous system interact with T cells

(3) To identify the molecules responsible for these interactions
Methods

In vitro

Full-thickness slices of the proximal resection margin

- 9 controls (cancer)
- 20 Crohn’s disease

Immunohistochemistry to identify:
- Enteric glial cells (S100β)
- Neurons (Hu)
- T cells (CD3, CD4, CD8)

Counting of T cells in contact with ganglia of the myenteric plexus

Immunocytochemistry

- S100β
- CD4
- CD8
- CFSE

T cell activation
- 5 days
- Anti-CD3/anti-CD28

CFSE labelling of T cells

Pre-treatment of EGC
- 24h
- LPS or IL1β/TNFα

Co-culture (2h)

In situ

9 controls (cancer)
20 Crohn’s disease

Immunochemistry to identify:
- Enteric glial cells (EGC)
- Neurons (Hu)
- T cells (CD3, CD4, CD8)

Counting of T cells

Assessment of the area covered by glia
Results

In vitro

- **Nb of CD3/ganglion**
  - Threshold >7.7 T cells/ganglion
  - Crohn’s (n=20)
  - Control (n=9)
  - NS, p=0.175

**RT/qPCR**

- n=13

Western blot

- Threshold >1.7 T cells/ganglion

Immunocytochemistry: ICAM-1 labelling

- n=5
**Conclusion**

**In situ**

- T cells CD4+/CD8+ ↔ EGC

  Diagnostic threshold for Crohn’s disease:
  - >1.7 T cells/ganglion

  Predictive threshold for post-operative recurrence:
  - >7.7 T cells/ganglion

**In vitro**

- Inflammation EGC → Contact T cells/EGC
- Inflammation EGC → ICAM-1 expression

This suggests a role of EGC in the formation of plexitis, possibly through the binding of LFA-1 to ICAM-1

Further experiments will be carried out to confirm this possibility