




# Crohn's Disease

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# What is Crohn's Disease? (1)

- Chronic inflammation of gastrointestinal (GI) tract due to:

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Imbalance between  
inflammatory  
mediators

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Genetics and  
environmental factors

- Symptoms:
  - Rectal bleeding
  - Abdominal Pain
  - Diarrhea, nausea and vomiting



Image from: <http://emedicine.medscape.com/article/172940-overview>

# Prevalence/Epidemiology of Disease (1)

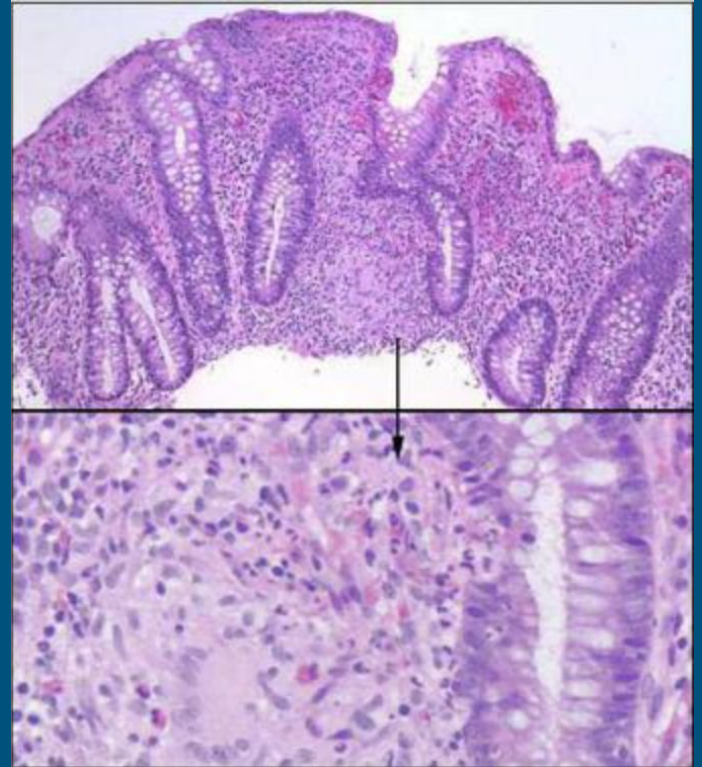
- Epidemiology
  - Adults= 201/ 100,000 adults
  - Children= 43 /100,000
- Increased rates in:
  - Upper socioeconomic classes
  - Influenced by increased access to health care
  - European Jewish population



Image from:  
[https://www.jhmicall.org/GDL\\_Disease.aspx?CurrentUDV=31&GDL\\_Disease\\_ID=291F2209-F8A9-4011-8094-11EC9BF3100E&GDL\\_DC\\_ID=D03119D7-57A3-4890-A717-CF1E7426C8BA](https://www.jhmicall.org/GDL_Disease.aspx?CurrentUDV=31&GDL_Disease_ID=291F2209-F8A9-4011-8094-11EC9BF3100E&GDL_DC_ID=D03119D7-57A3-4890-A717-CF1E7426C8BA)

# Mechanism of Disease (2)

- Chronic inflammation from T-cell activation leads to tissue injury in GI tract
  - Activation of type 1 T-helper (Th1) cells from defective regulation
- Activity of ulceration of superficial mucosa
  - Encourages invasion of deep mucosal layers by inflammatory cells



# Risk Factors (3-5)

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- Family history
- Environment
- Measles virus
- Breastfeeding

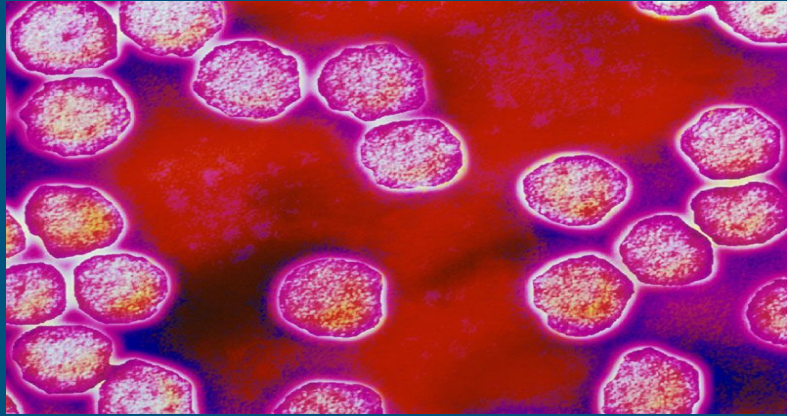


Image from: <https://www.thinglink.com/scene/769336703558090752>



Image from: <http://mom.girlstalkinsmack.com/family/the-relationship-of-mother-and-baby-after-child-birth.aspx>

# Exacerbating Factors (6-9)

- Intercurrent infections
  - Upper respiratory tract and enteric infections
- Smoking
- Stress
  - Controversial but anecdotal evidence
- Oral contraceptives
  - Preliminary evidence



Image from:  
<http://www.nbcnews.com/health/health-news/only-15-percent-u-s-adults-now-smoke-cdc-finds-n579646>



Image from:  
<http://www.exercisemed.org/research-blog/oral-contraceptives-exert.html>

# Medications

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# What is Prednisone? (10-13)

- Glucocorticoid receptor agonist
- Prevent digestive inflammation

**Recruitment  
of  
inflammatory  
immune cells**

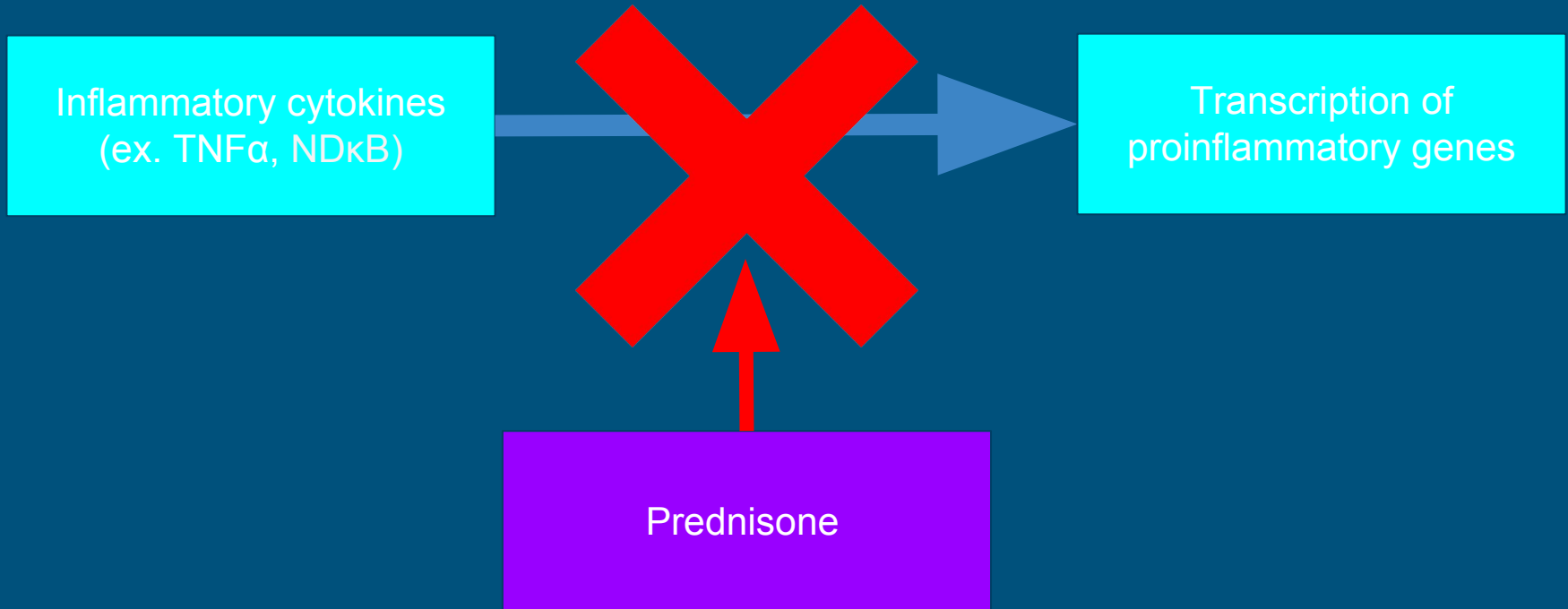


Image from:  
<http://www.millersurgery.co.uk/conditions/crohns-disease-and-colitis/>

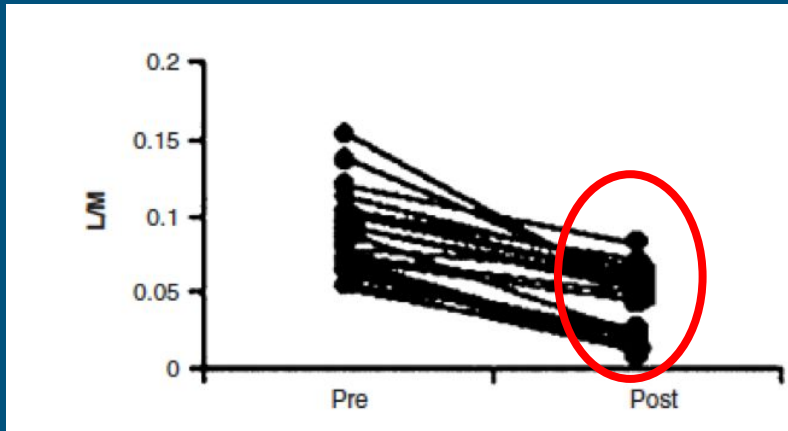


# Mechanism of Action (14,15)

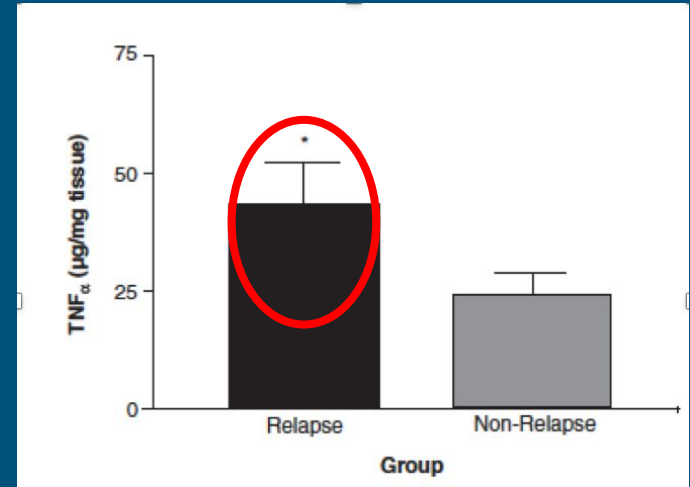
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# Effectiveness of Prednisone- Wild et al. (16)



Decreased L:M ratios by 50%=  
improved intestinal permeability

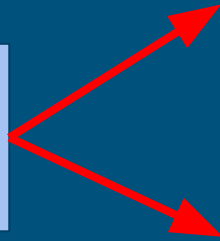


Decreased TNF $\alpha$  levels in  
non-relapsed individuals

# Side effects: Immunosuppressant Effect (17)

- Typically:

Pro-inflammatory  
cytokines



Vasodilation

Leukocyte migration  
to infection site



- Prednisone side effects:

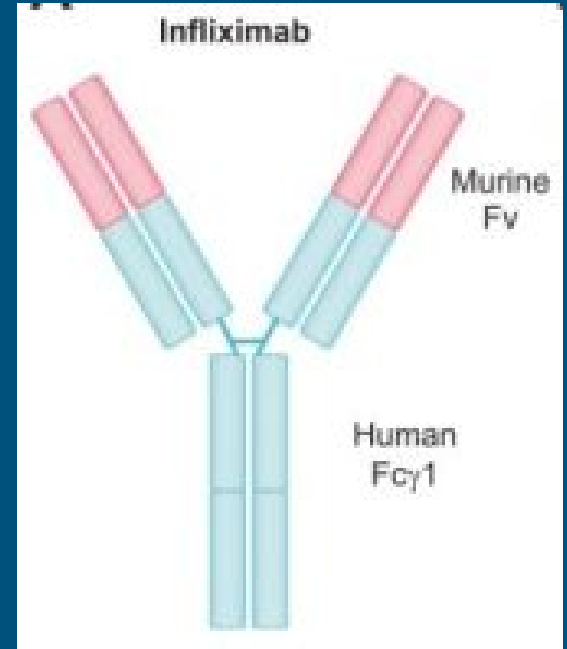
- High blood pressure
- Increased susceptibility to infection



# What is Infliximab/Remicade? (18)

- Monoclonal antibody that works against TNF- $\alpha$
- Apoptosis of T-lymphocytes and monocytes
- Down regulation of other pro inflammatory cytokines

**Decreases  
inflammation  
AND induces  
apoptosis**



# Mechanism of Action

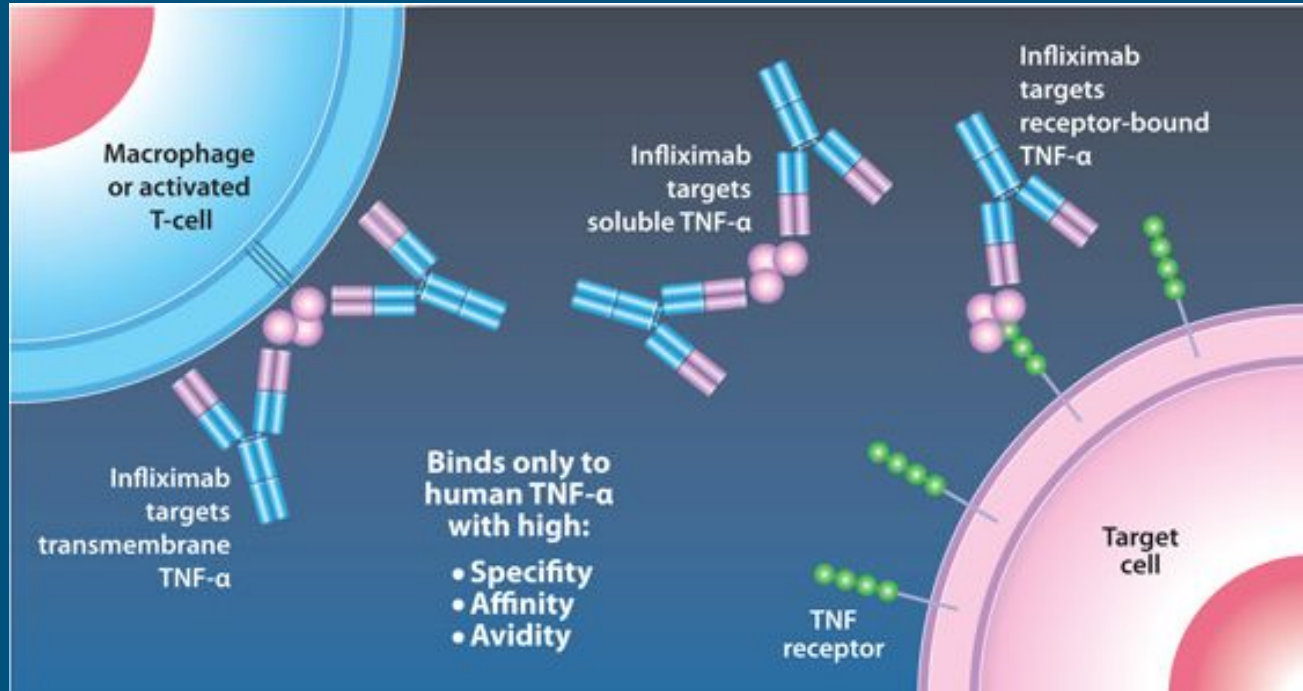
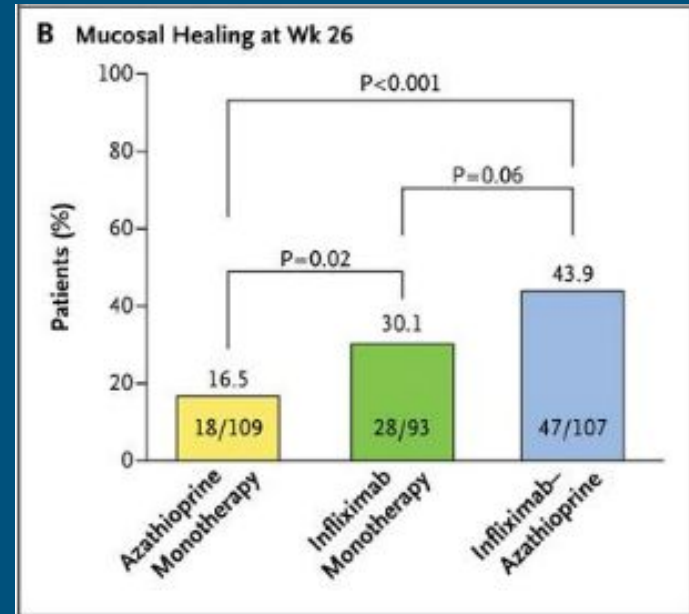
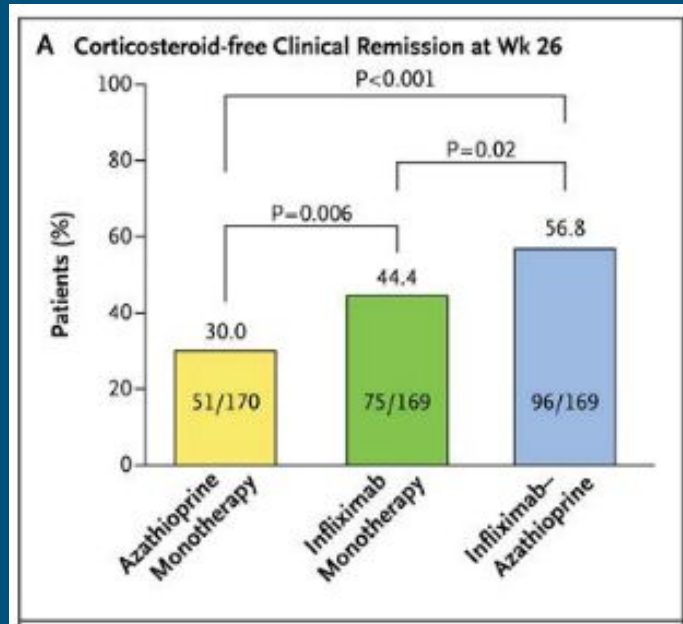


Image from: <http://www.peterbullartstudio.co.uk/webcontent/wp-content/gallery/technical/technical30.jpg>

# Effectiveness of Infliximab (19)



# Side Effects (20, 21)

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- Most serious: higher risk of infection associated with mycobacteria
- Tuberculosis
- Lymphoma
- Acute and delayed hypersensitivity reactions

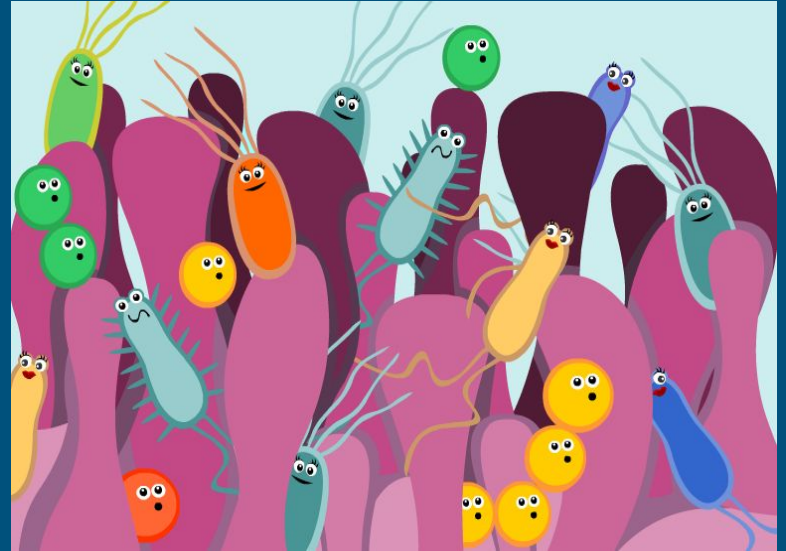


Image from: <http://allergiesandyourgut.com/wp-content/uploads/2016/01/gutbacteria8.png>

# Current Research

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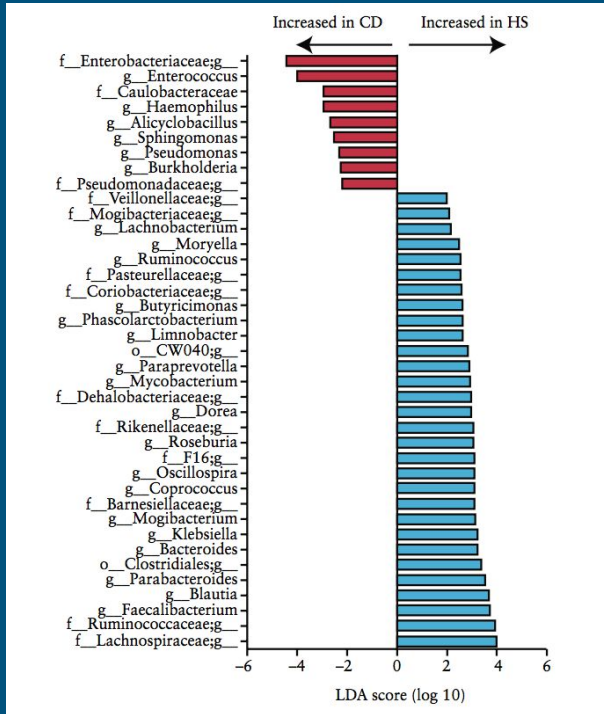


# Bacteriome and Mycobiome Research (22, 23)

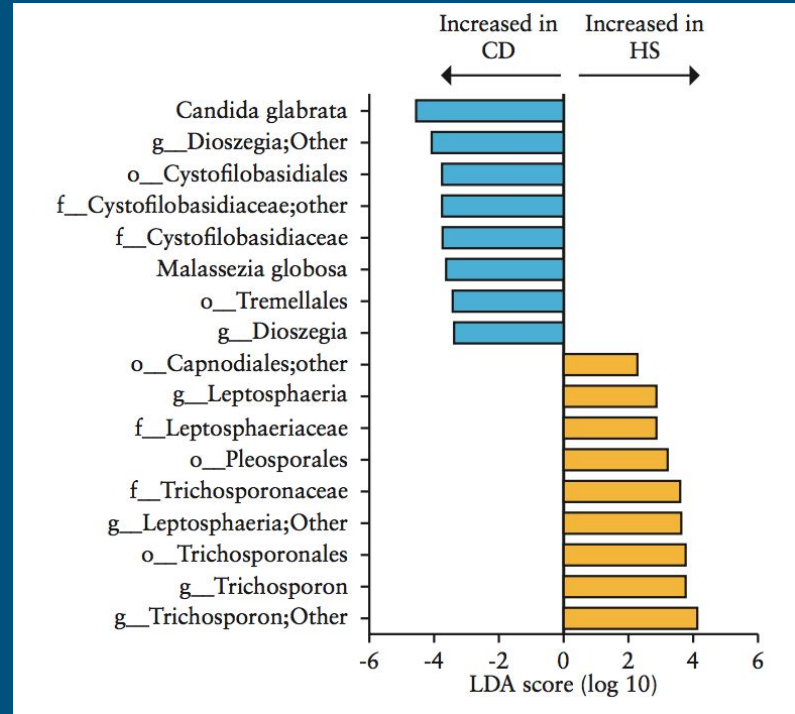
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- Dysbiosis associated with several diseases, particularly inflammatory bowel diseases [IBD]
- Liguori et al. (2015) analyzed bacterial and fungal composition of mucosa-associated microbiota of Crohn's Disease patients (CD) and healthy subjects (HS)
- Hoarau et al. (2016) identified fungal and bacterial species associated with CD dysbiosis

# Liguori et al., 2015

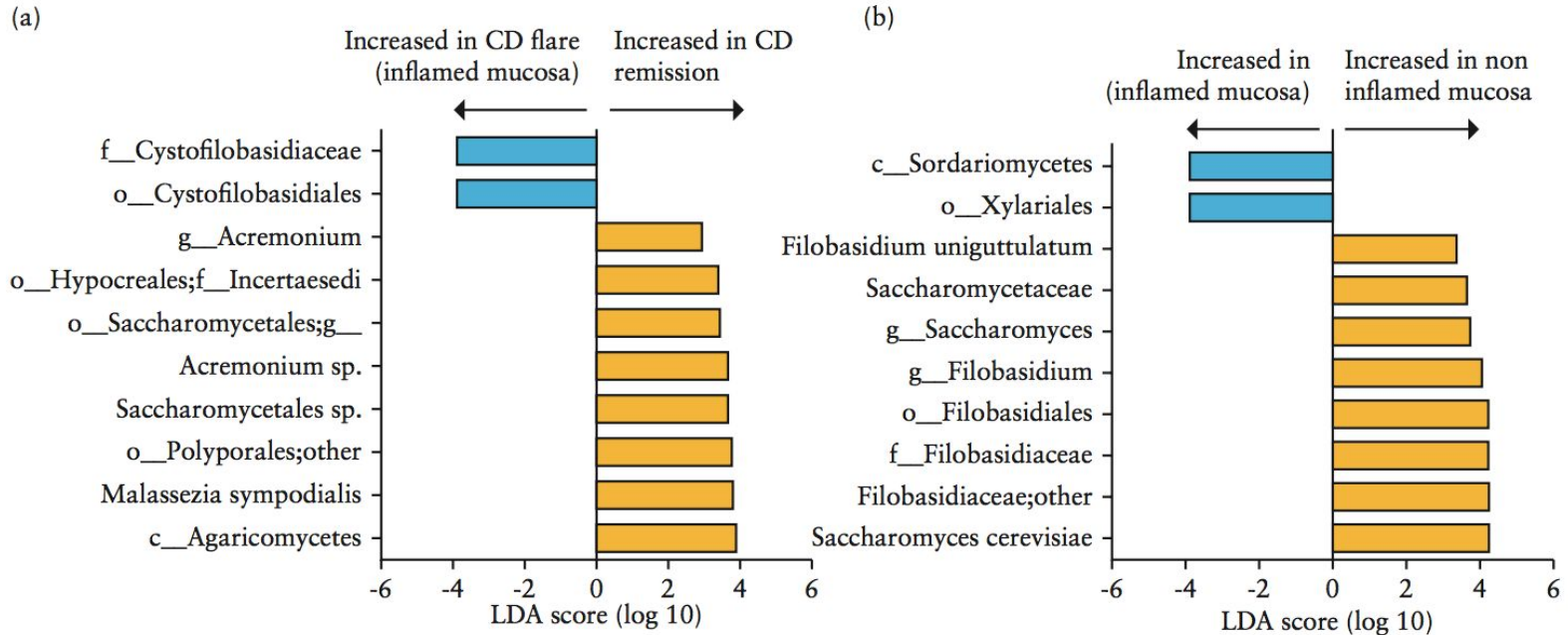


(Liguori et al., 2015)



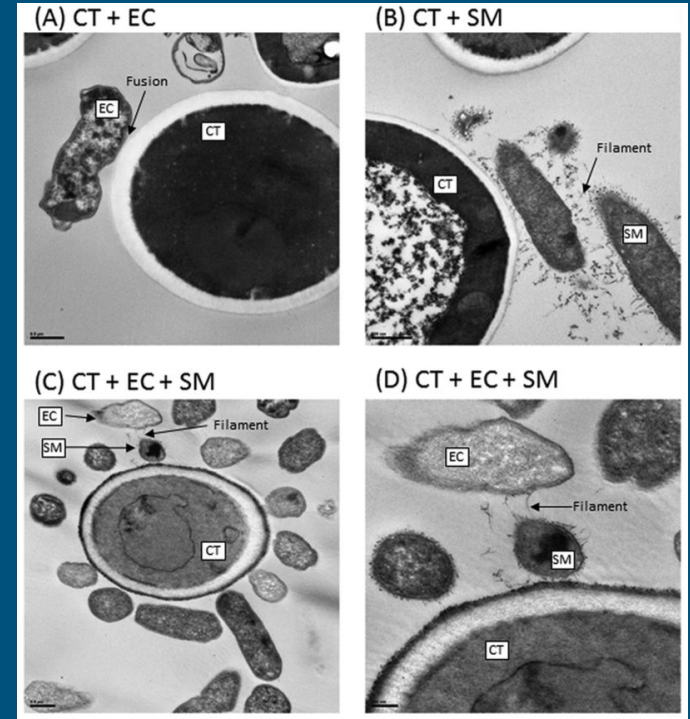
(Liguori et al., 2015)

# Liguori et al., 2015



# Hoarau et al., 2016

- *Candida tropicalis* abundance is significantly increased in CD patients
- Abundance of *Serratia marcescens* (*S. marcescens*) and *Escherichia coli* (*E. coli*) is elevated in CD patients
- Interactions between *C. tropicalis* and potential bacterial pathogens play an important role in CD



(Hoarau et al., 2016)

# Conclusion

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