

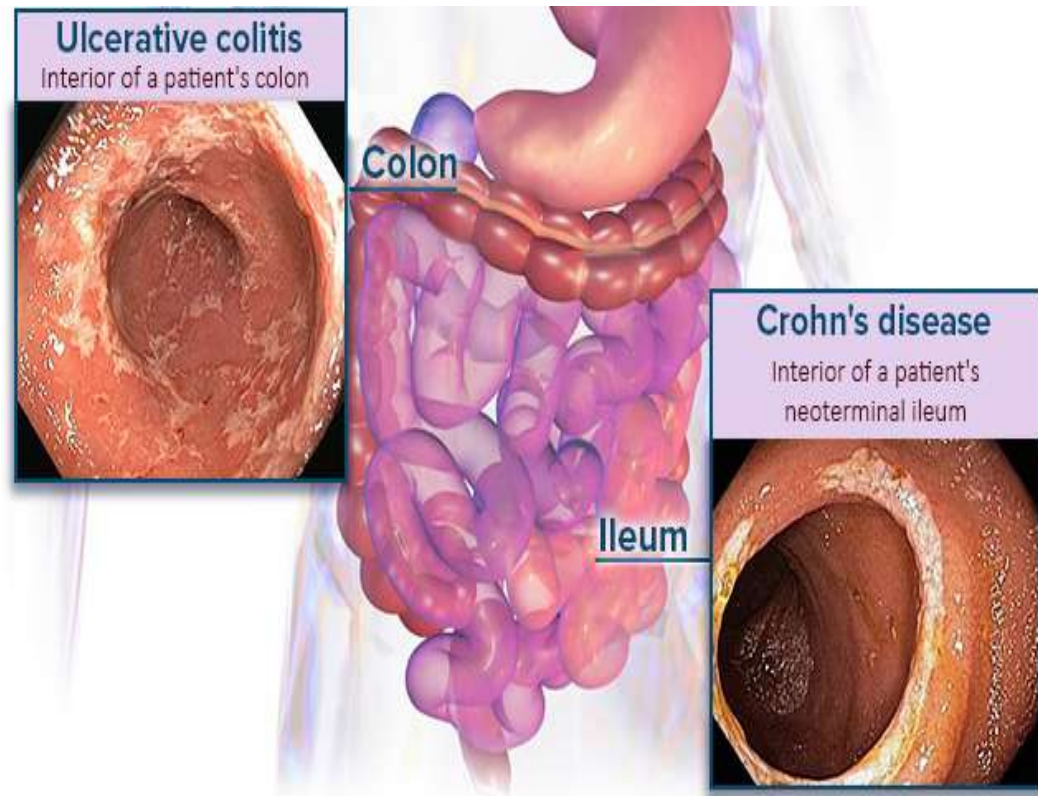
# Treatments for Pediatric IBD: What's On The Horizon?

Erin Lane, MD  
October 22, 2017



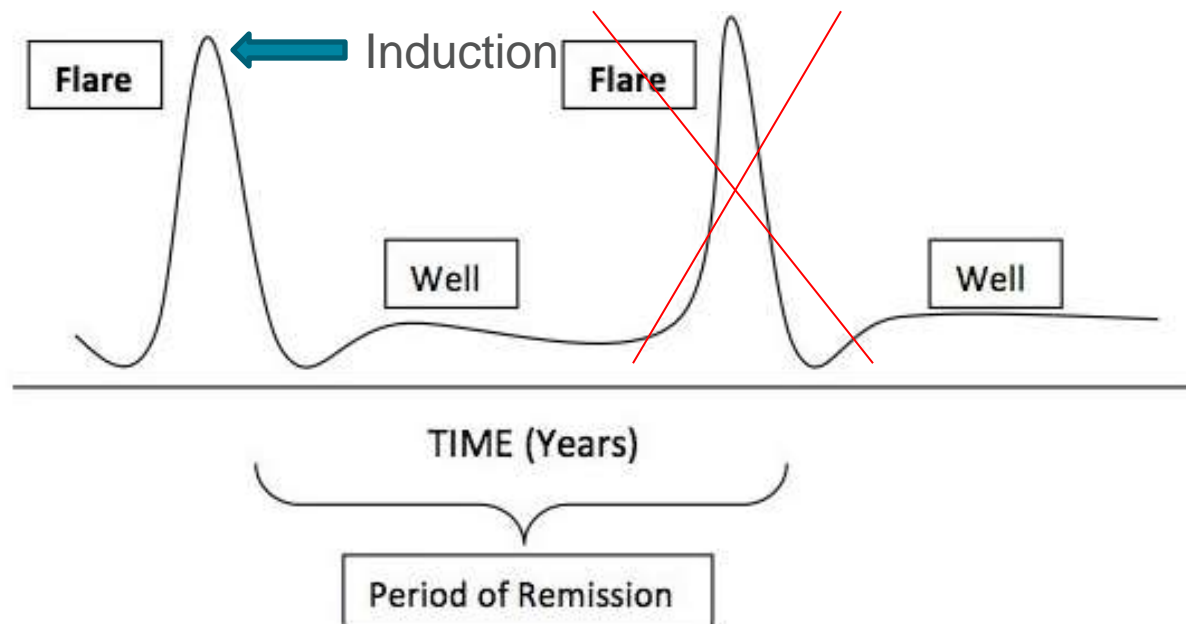
# IBD treatment: Goals of therapy

- Improved growth and nutrition
- Symptom improvement
- Normalization of labs
- Mucosal healing

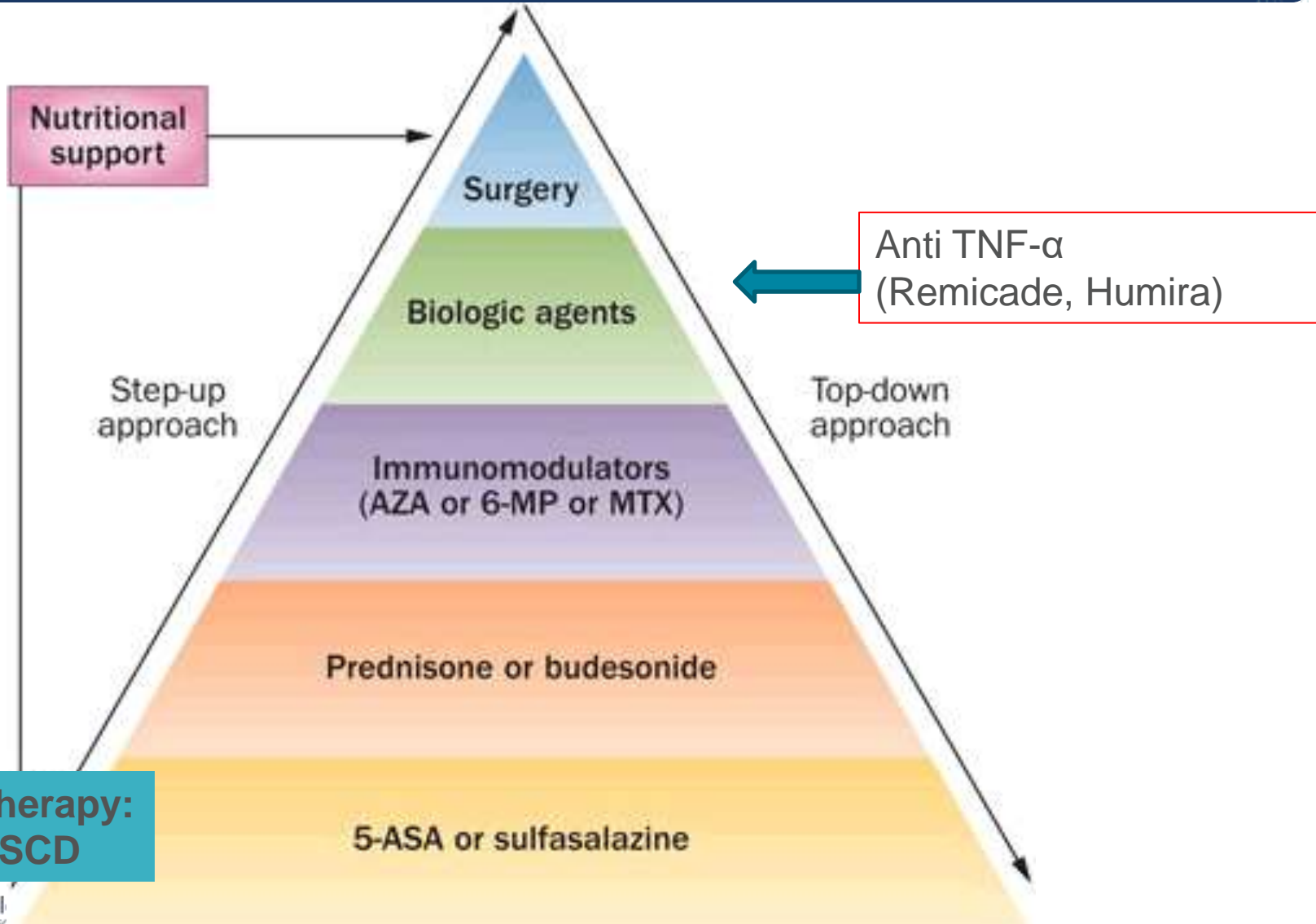


# IBD treatment: Goals of therapy

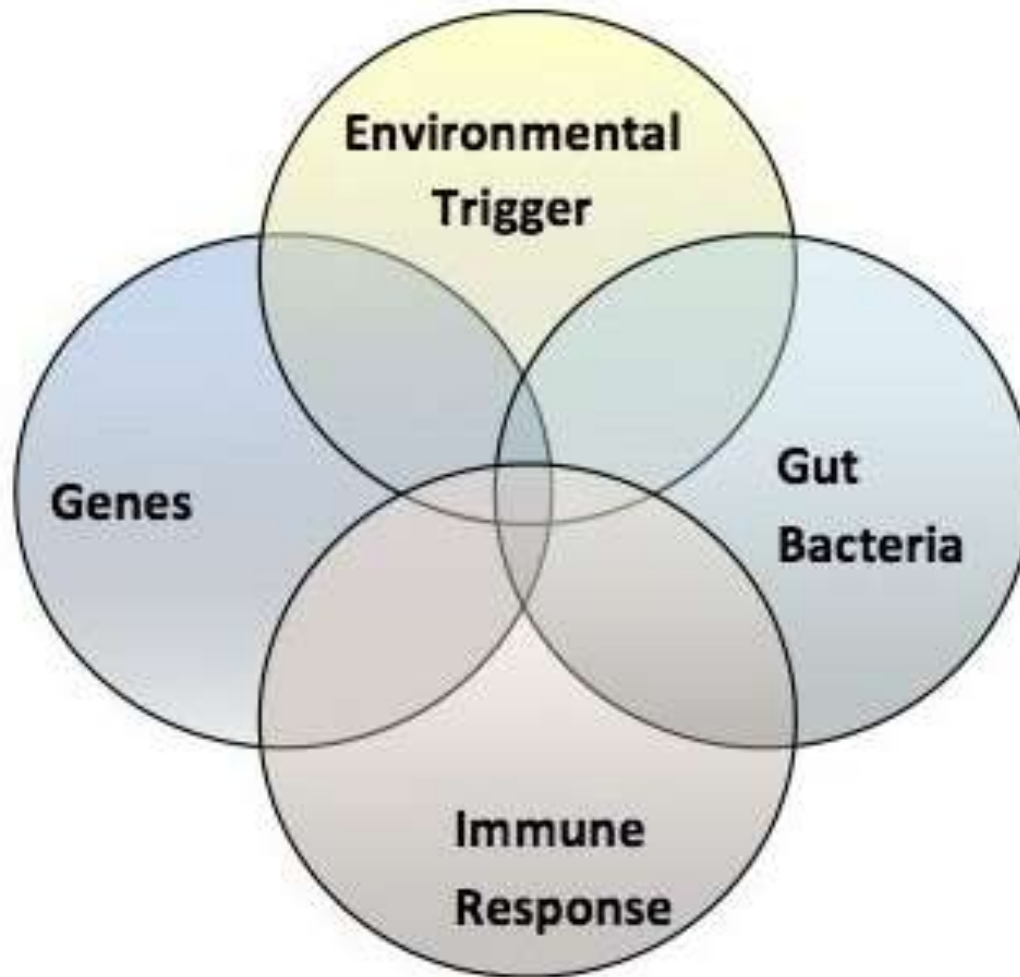
- 2 “step” process:
  - **Induction** of remission
  - **Maintenance** of remission



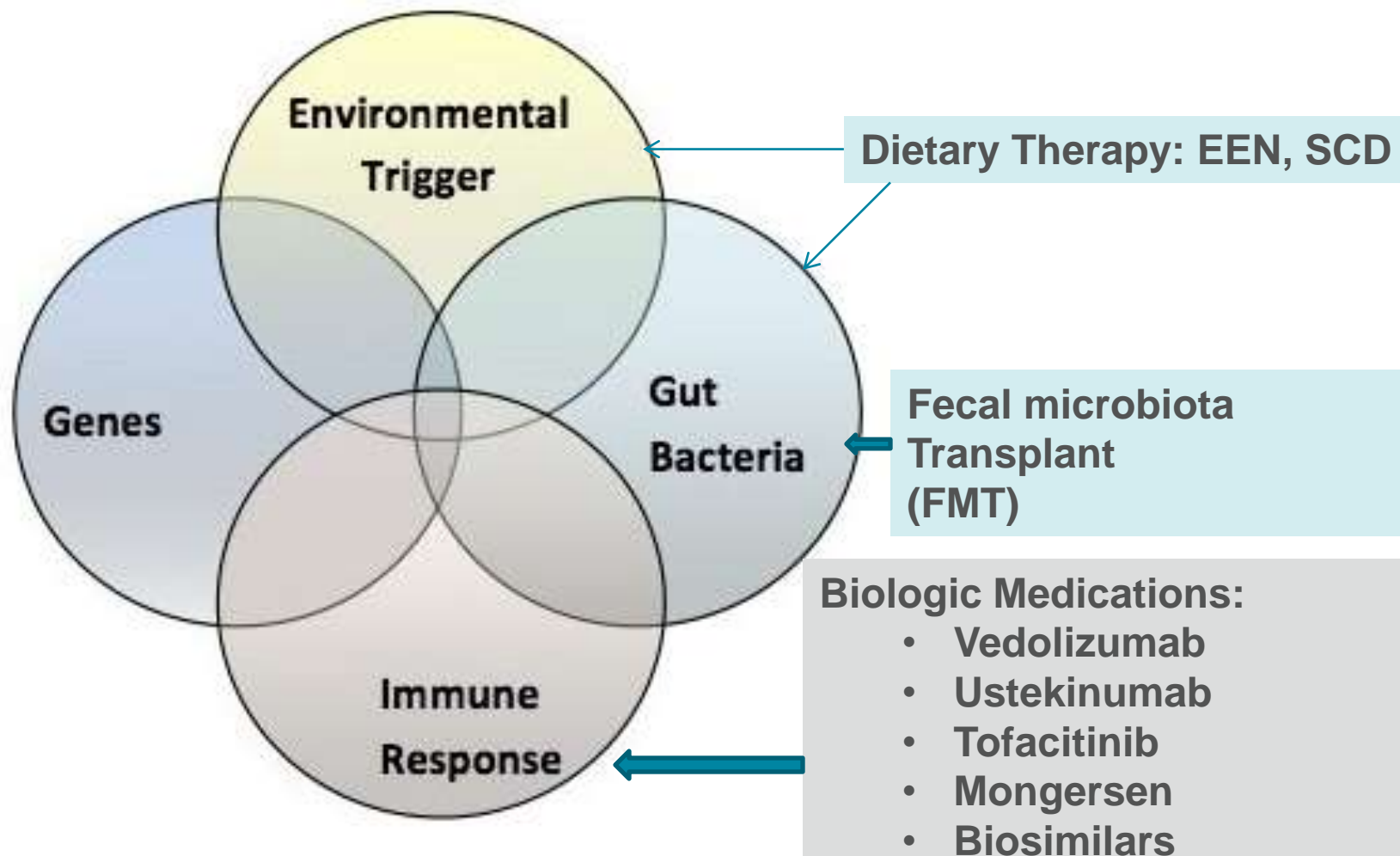
# IBD treatment: Current Strategies



# IBD treatment: Targets of therapy

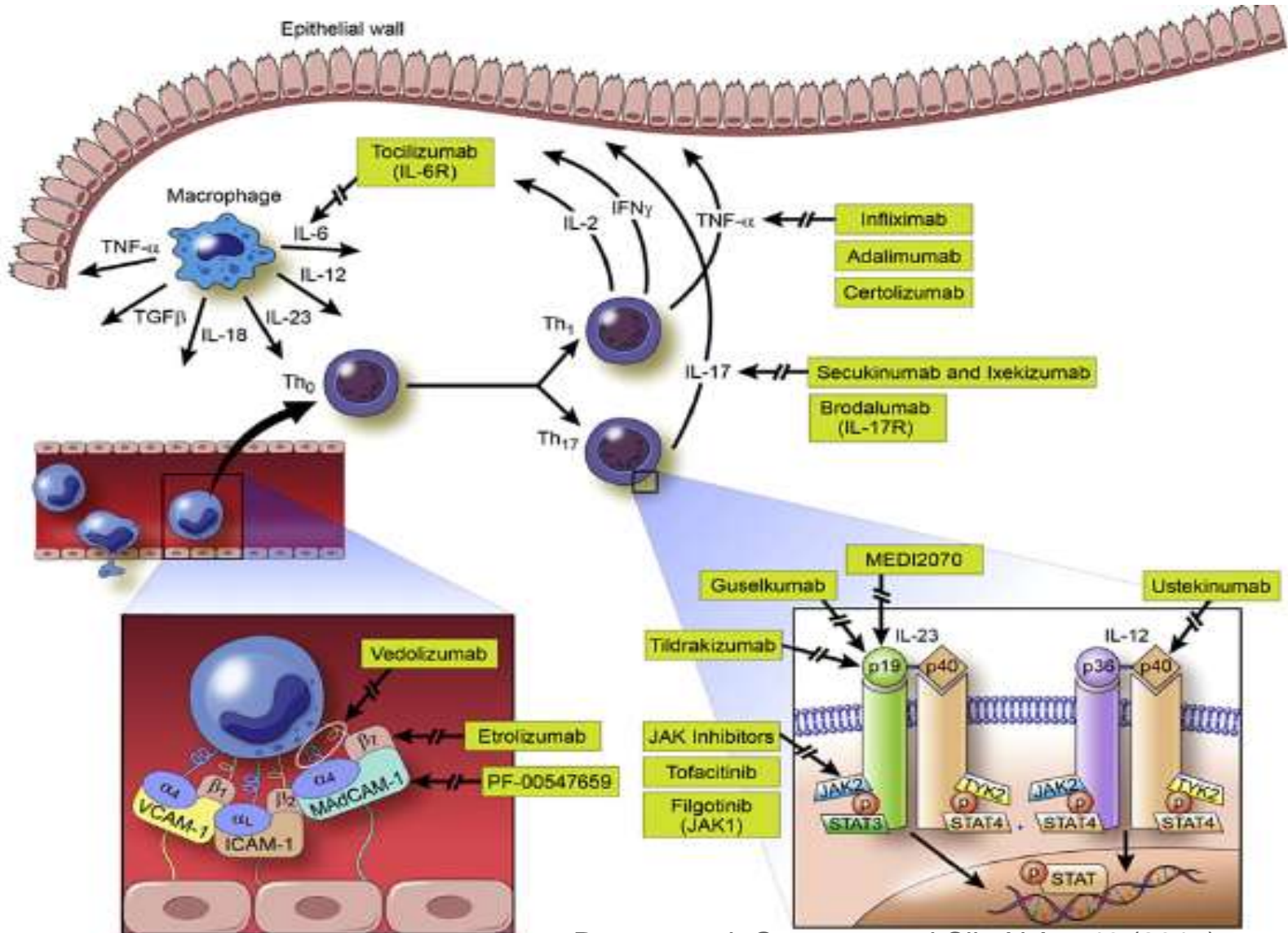


# IBD treatment: New Targets for Therapy





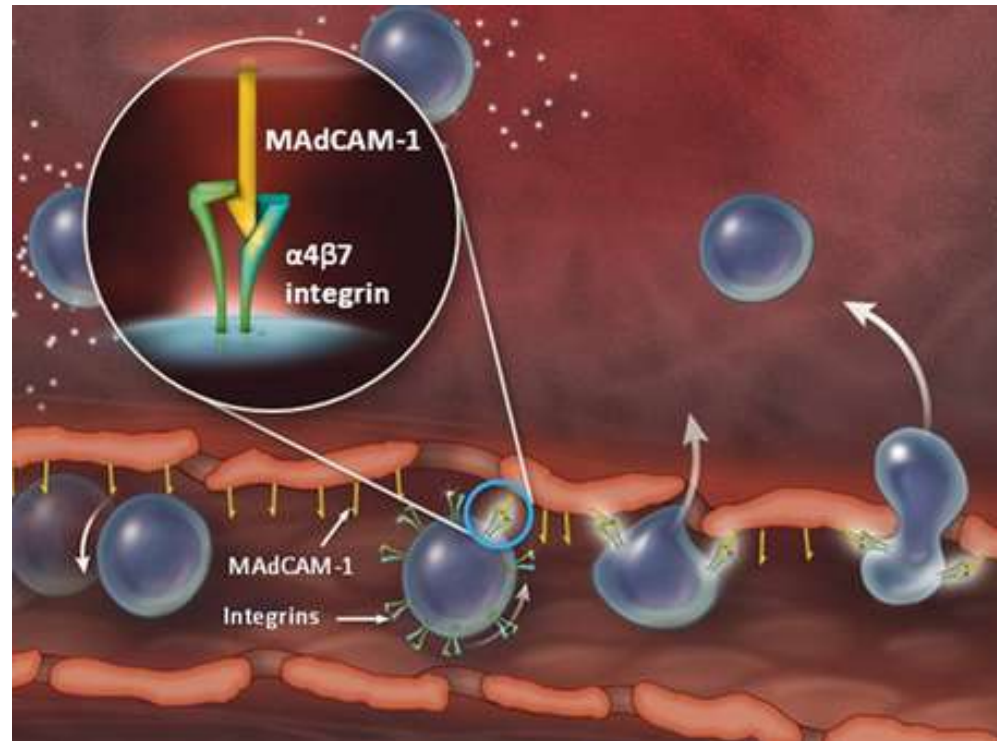
# Immunology



# IBD treatment: What's New?

## Vedolizumab (Entyvio)

- “Anti-integrin”
- Approved for adults with IBD
- Studies suggest it is efficacious and safe in kids
- Currently used “off-label” for pediatric IBD

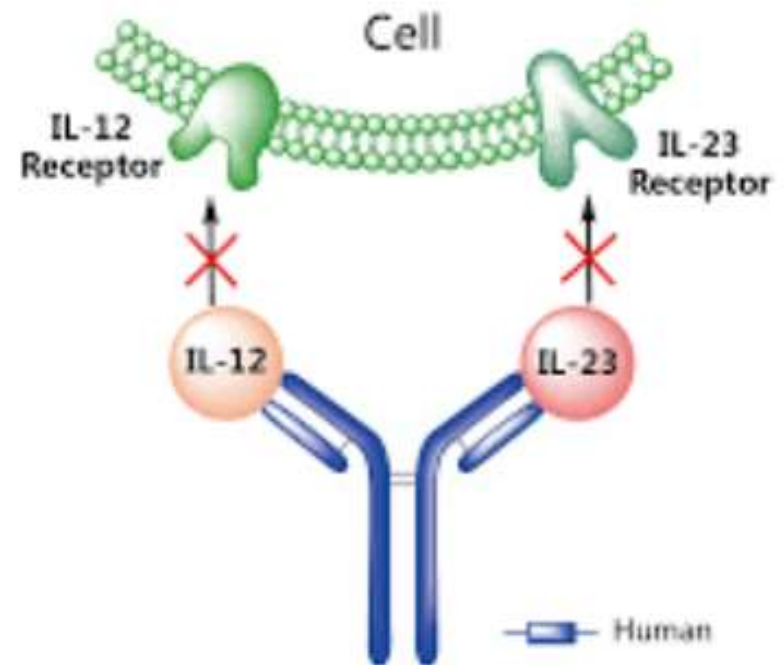




# IBD treatment: What's New?

## Ustekinumab (Stelara)

- Neutralizes IL-12 and IL-23, prevents development of activated T cells
- Approved for adults with Crohn's disease
- Approved for kids with psoriasis



# IBD treatment: What's New?

## Tofacitinib: (Xeljanz)

- Oral inhibitor of JAK 1, 2 and 3
- Blocks signaling of pro-inflammatory molecules
- Off-label use for ulcerative colitis



**ONCE-DAILY**

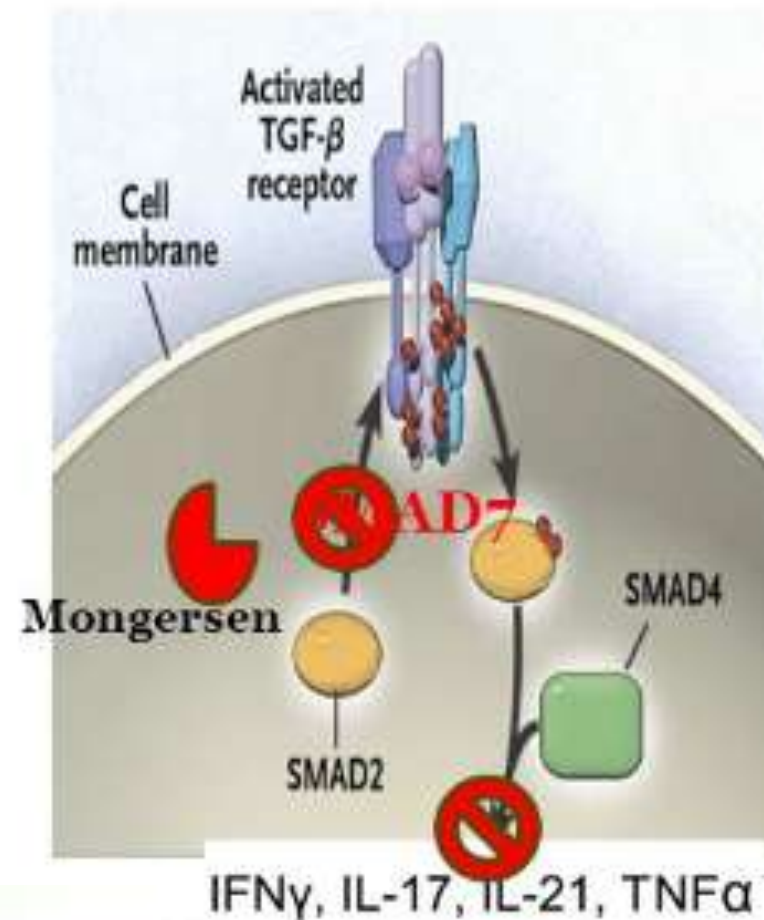
**XELJANZ<sup>®</sup> XR** 

[tofacitinib citrate]  
extended release • 11 mg tablets

# IBD treatment: What's New?

## Mongersen:

- Oral SMAD7  
Antisense  
Oligonucleotide
- Anti-inflammatory  
agent
- Clinical trials for adults  
with Crohn's Disease



# Biosimilars

## Biosimilars:

- Biological product approved based on showing it is highly similar to an FDA-approved biological product
- Potentially less expensive product



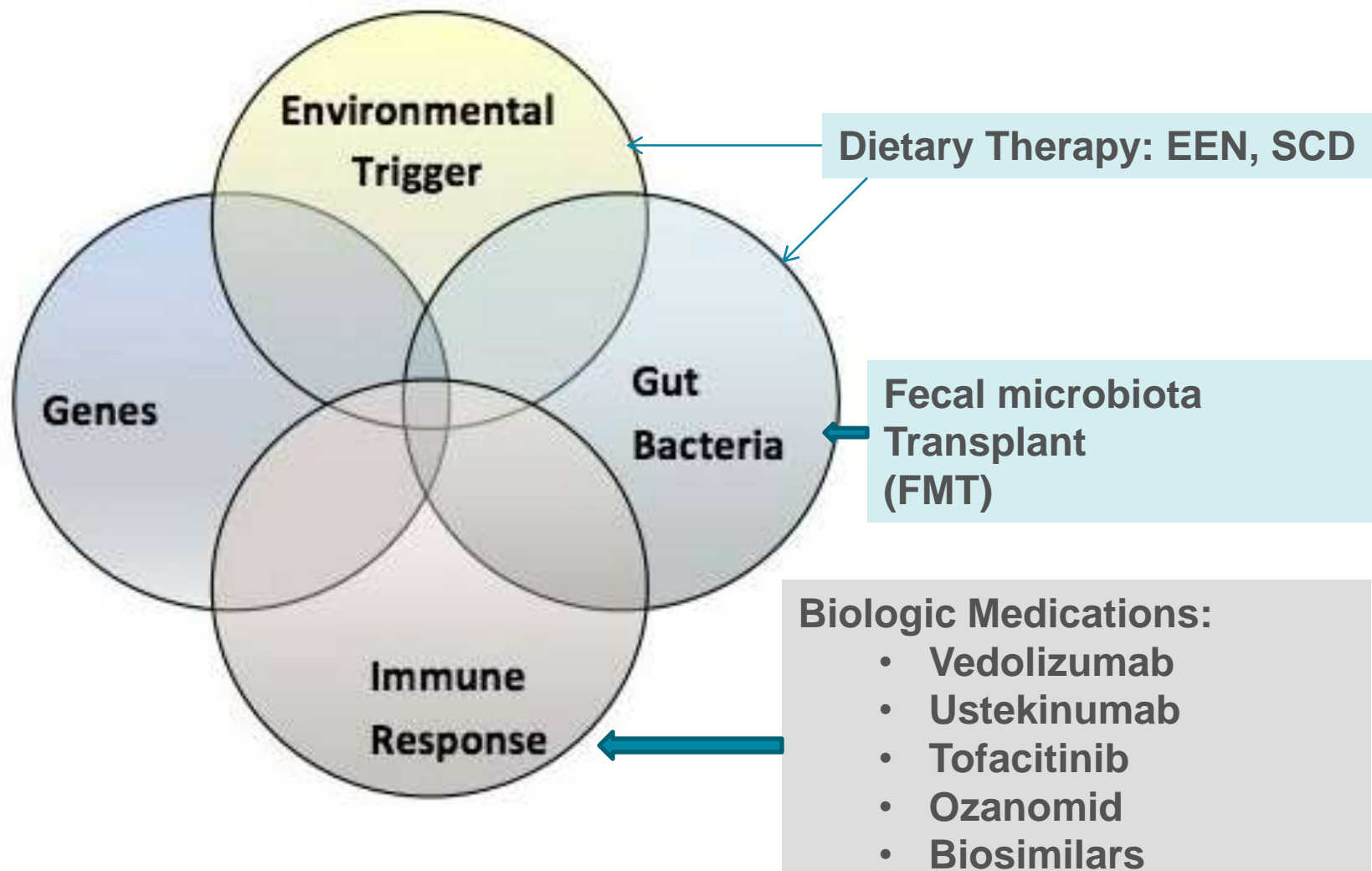
# IBD treatment: Special Considerations for Pediatric Patients

- Therapies approved for adults frequently used in pediatrics without sufficient data
- 2012: FDA implemented Pediatric Research Equity Act
- Pediatric Trials Network designed to boost pediatric clinical trials and product development





# IBD treatment: New Targets for Therapy



# IBD treatment: What's New?

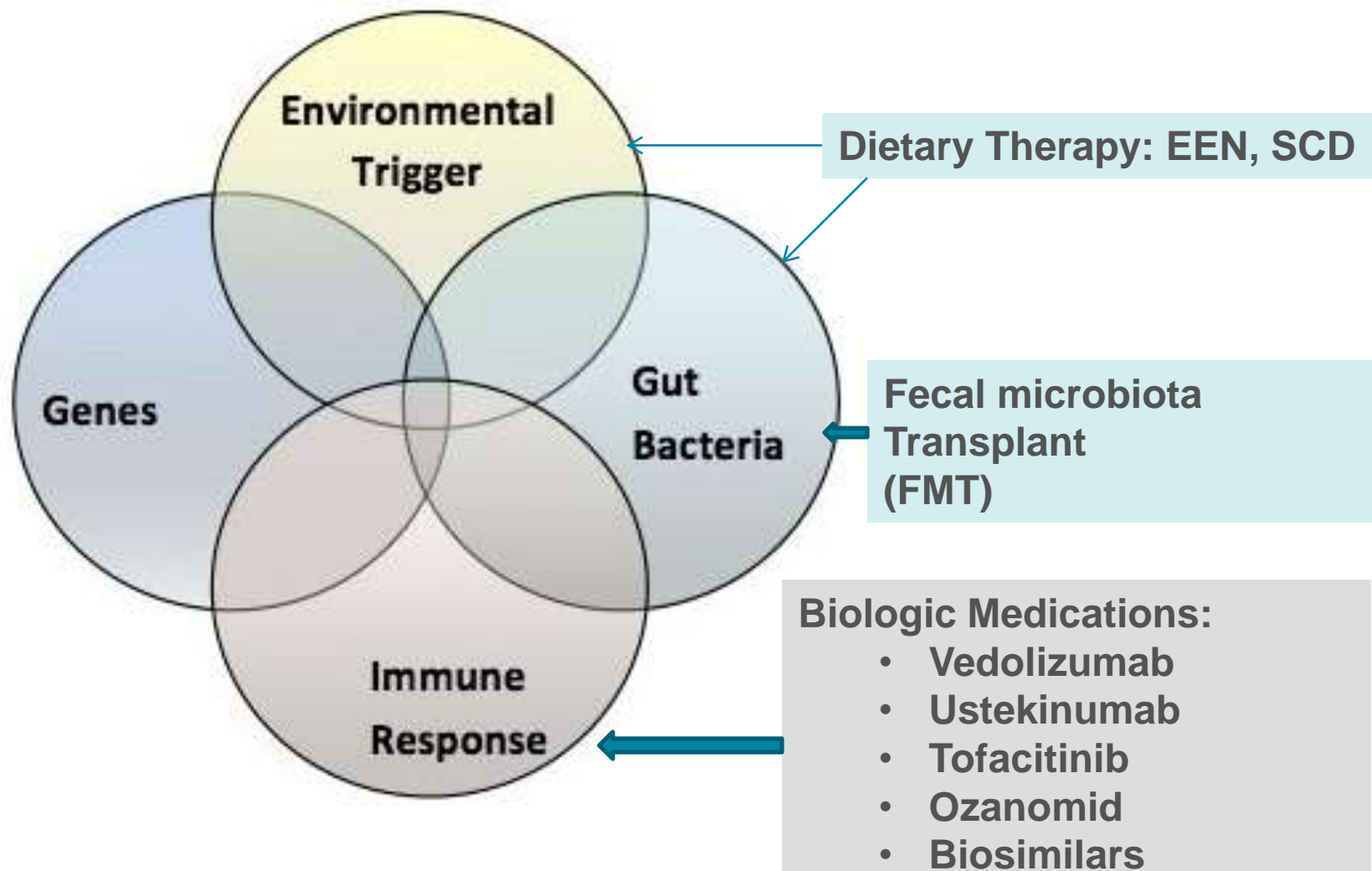
- **Dietary therapy:**

- Exclusive Enteral Nutrition (EEN)
  - Formula only diet
  - Works for both induction and maintenance of remission
- Specific Carbohydrate Diet (SCD)
  - Clinical remission demonstrated in study pediatric patients



Stay tuned! More to come on  
this...

# IBD treatment: New Targets for Therapy



# IBD treatment: What's New?

- **Fecal Microbiota Transplantation (FMT)**
  - Aim to restore “normal” intestinal bacteria by application of fecal microorganisms from a healthy subject into the GI tract of a patient
  - FMT is most effective treatment for recurrent *Clostridium difficile* infections
  - So far, FMT can only be recommended for treatment of C diff infection in IBD
  - FMT in the management of IBD remains uncertain



# Exciting Times for New Treatments in IBD!

**Table 1**  
New therapies for Crohn disease and their respective immunologic targets

|                                       | Target                       | Therapeutic Agent                                                                            |
|---------------------------------------|------------------------------|----------------------------------------------------------------------------------------------|
| <b>Extracellular</b>                  |                              |                                                                                              |
| (1) Leukocyte migration               | $\alpha_4\beta_7$ Integrin   | Vedolizumab, Abrilumab (AMG 181)                                                             |
|                                       | $\beta_7$ Integrin           | Etrolizumab                                                                                  |
|                                       | MAdCAM-1                     | PF-00547659                                                                                  |
|                                       | CCR9                         | Vercimon                                                                                     |
|                                       | S1P receptor                 | Ozanimod                                                                                     |
| (2) Cytokine inhibitors               | TNF- $\alpha$                | Infliximab<br>Adalimumab<br>Certolizumab pegol                                               |
|                                       | IL-12/IL-13<br>(p40 subunit) | Ustekinumab<br>Briakinumab                                                                   |
|                                       | IL-23 (p19 subunit)          | Tildrakizumab (MK-3222)<br>Guselkumab, Brazikumab<br>(MEDI2070), Risankizumab (BI<br>655066) |
|                                       | IL-17A                       | Secukinumab<br>Ixekizumab                                                                    |
|                                       | IL-17R                       | Brodalumab (AMG 827)                                                                         |
|                                       | IL-6R                        | Tocilizumab                                                                                  |
|                                       | (3) Antiinflammatory agents  | F8-IL-10<br>SMAD7                                                                            |
| <b>Intracellular and Intranuclear</b> |                              |                                                                                              |
| (1) JAK inhibitors                    | JAK1, JAK2, JAK3             | Tofacitinib                                                                                  |
|                                       | JAK1                         | Filgotinib, Upadacitinib (ABT-494)                                                           |
|                                       | JAK1, JAK2                   | Baricitinib                                                                                  |



Thank You  
Questions?

