

Precision Health in IBD: Cell & gene therapy is on the horizon

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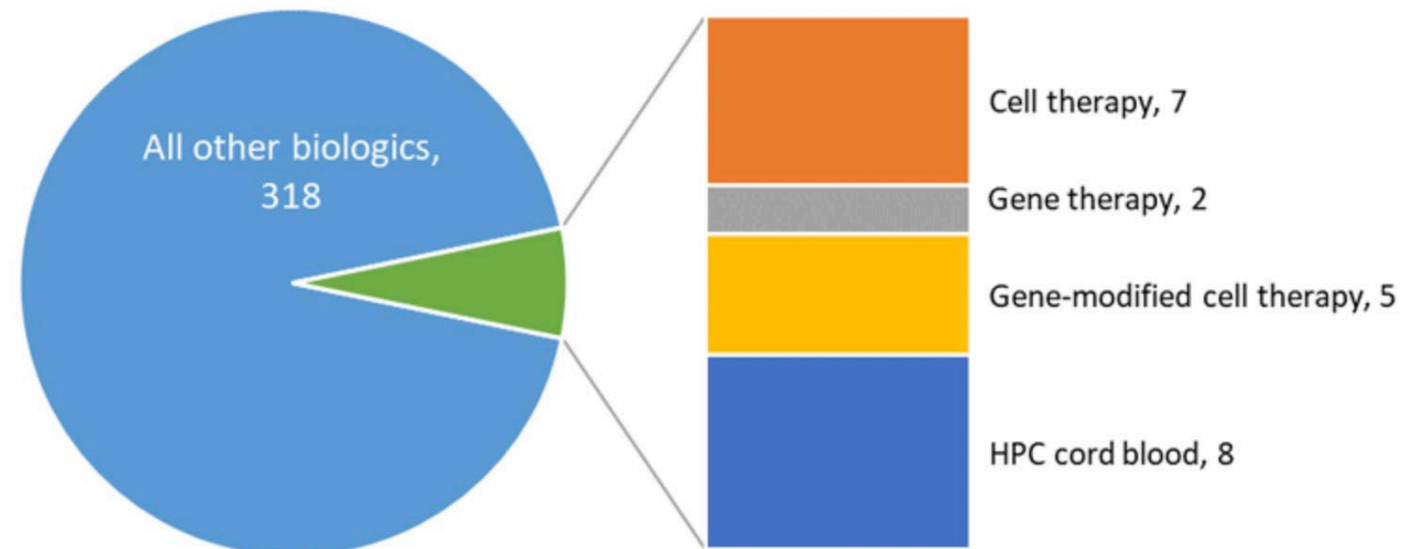
THE
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Cell and gene therapy is transforming medicine

- Living drugs
- Pioneered with BMT
- Solidified with cancer immunotherapy
- Poised for broad utility

Early Approvals Pave The Way For New Market Entrants

FDA approved cell and gene therapies



Source: FDA and Evaluate Pharma

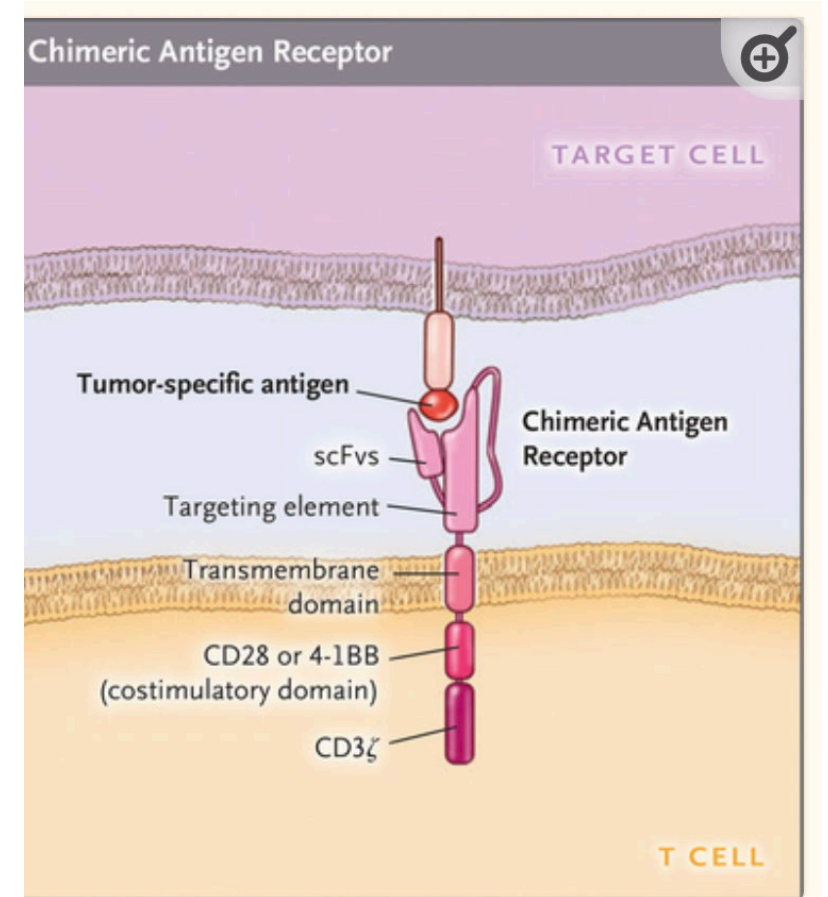
There are currently >1,000 clinical trials for cell and gene therapies registered with [ClinicalTrials.gov](https://clinicaltrials.gov)

The key cell & gene therapy success in cancer

CD19 CAR-T cells



Emily Whitehead, first child to receive CAR-T cell therapy



Now 6 FDA (3 Health Canada) approved
CAR-T cell therapies

Gut microbiome controls CD19 CAR-T cell response and toxicity

The gut microbiome and anti-PD-1 outcomes

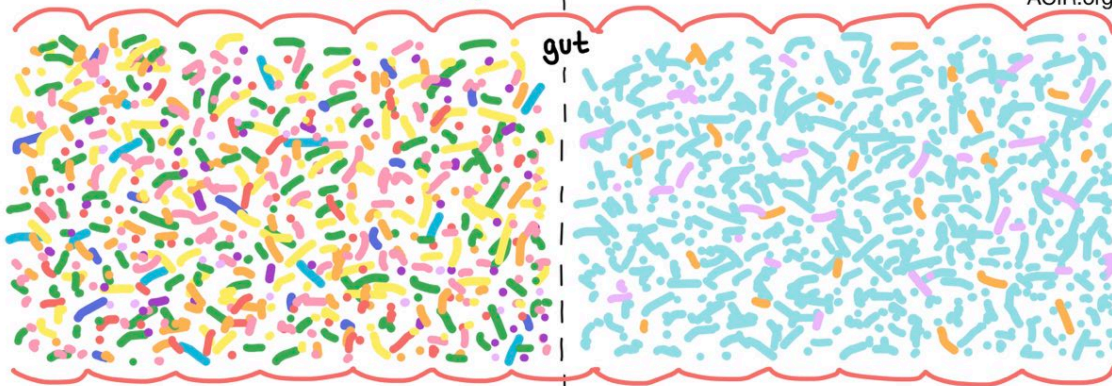
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High diversity
High proportion of
Faecalibacterium (G)
A. muciniphila (R)
and *E. hirae* (R)

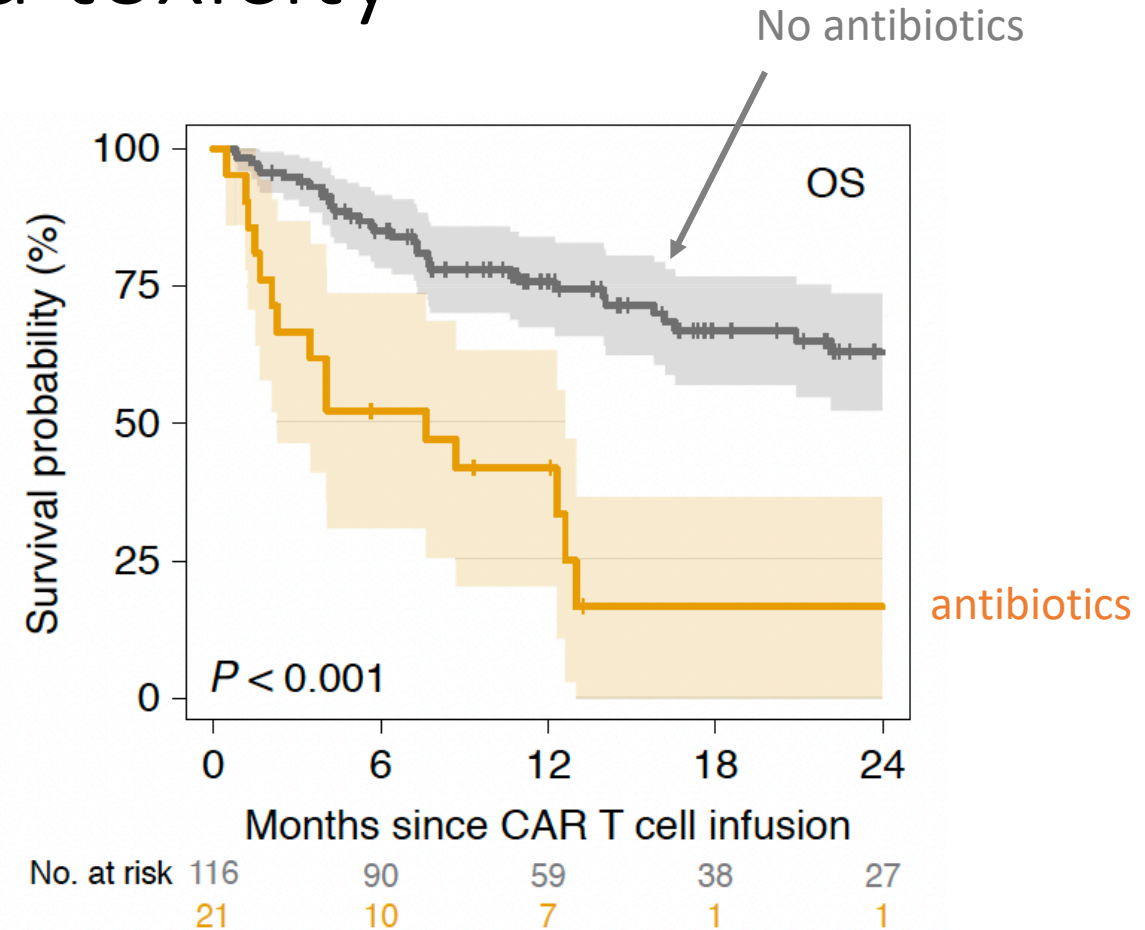
unfavorable

Low diversity/
Antibiotic use
High proportion of
Bacteroidales (G)

ACIR.org



Findings by Routy et al. (R) and Gopalakrishnan et al. (G)



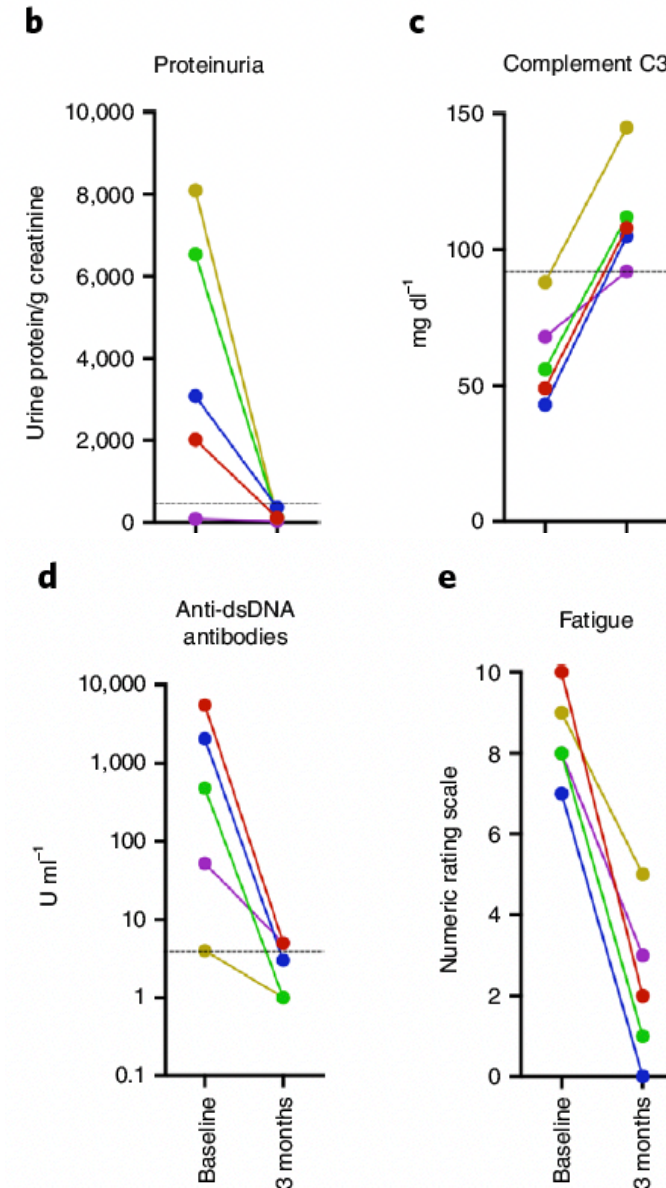
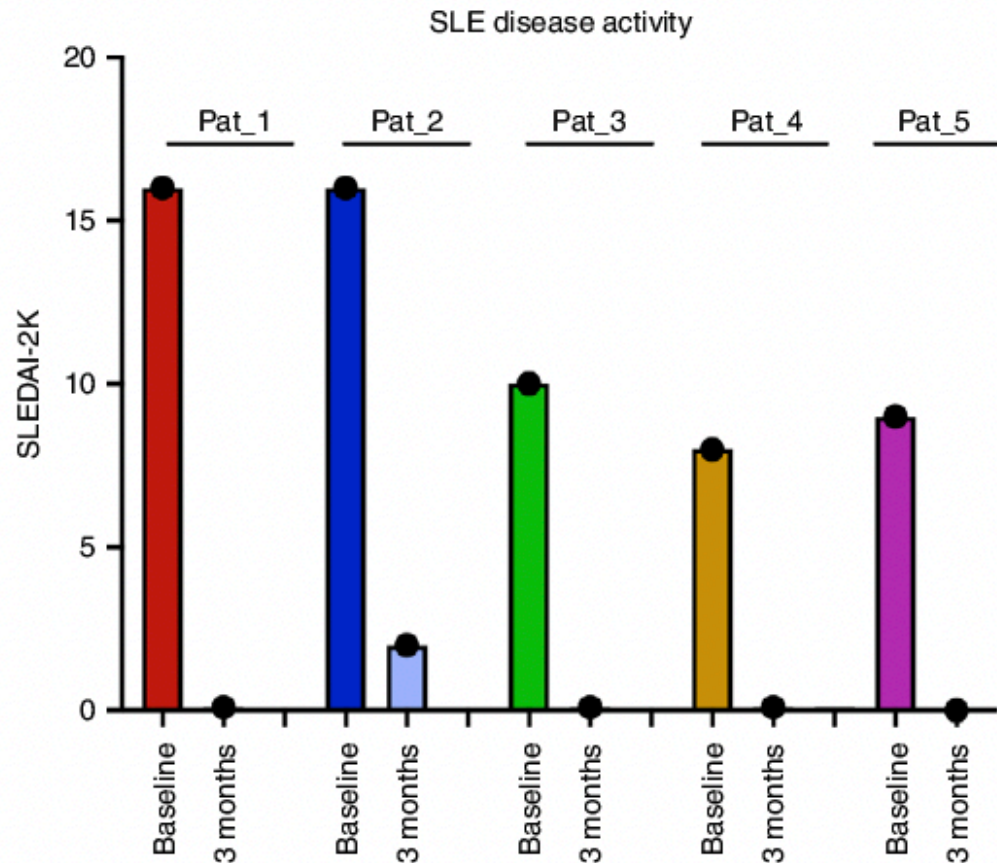
Smith....van den Brink, Ruella, Nat Med 2022

CAR-T cells: potential for transformative impact in autoimmunity

CD19-Targeted CAR T Cells in Refractory Systemic Lupus Erythematosus

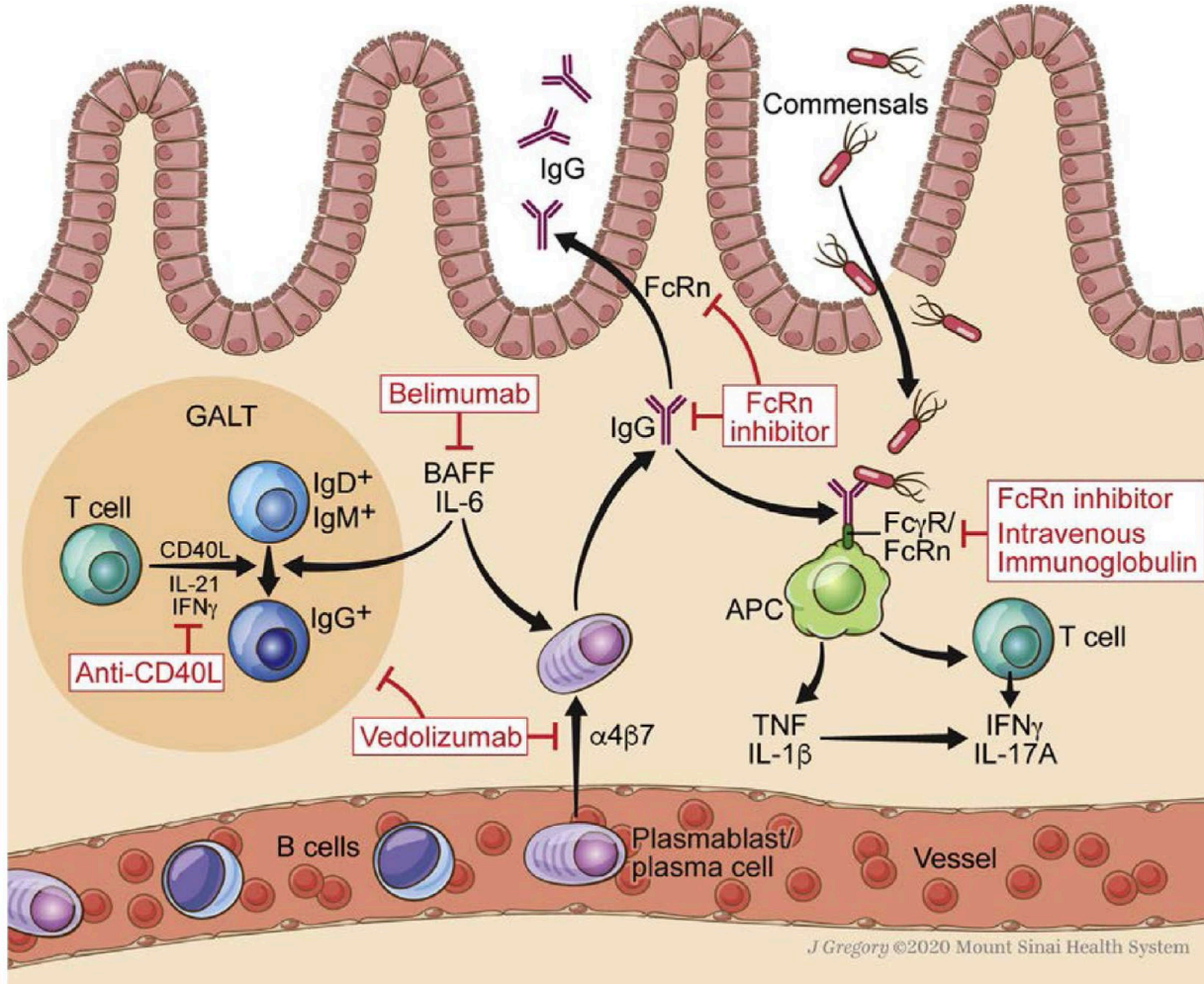
Mougiakakos, Mackensen, Schett et al

Nature Medicine, 2022



Is there a rationale to use CD19 CAR T cells in IBD?

- Patient profile?
- Conditioning?
- Concomitant therapy
- Risk of life-long B cell aplasia



CD19-CAR T cells in Canada

Decentralized Manufacturing (CLIC Point-of-Care Platform)



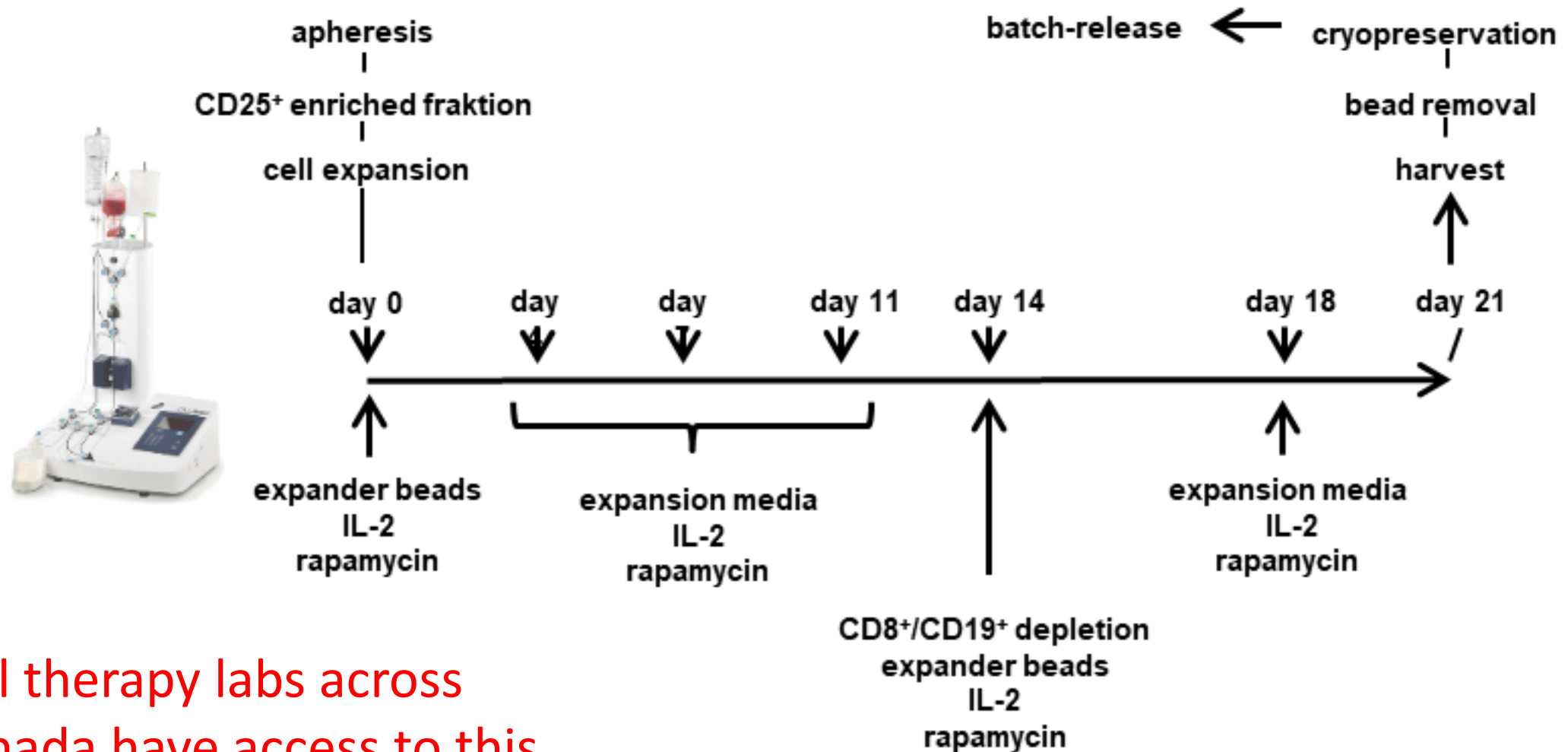
-  Therapeutics are 100% made-in-Canada
-  Lower costs: all processes completed within the same institution
-  Decreased timelines and faster patient delivery
-  Treatment at the point of care; standardized protocols across sites

Centralized Manufacturing



-  High costs: facility, marketing infrastructure, secure transport
-  Increased timelines due to product manufacture, transport, chain of custody
-  Complex manufacture and delivery process
-  Single manufacturing site - risk & vulnerability
-  Products need to cross U.S. border

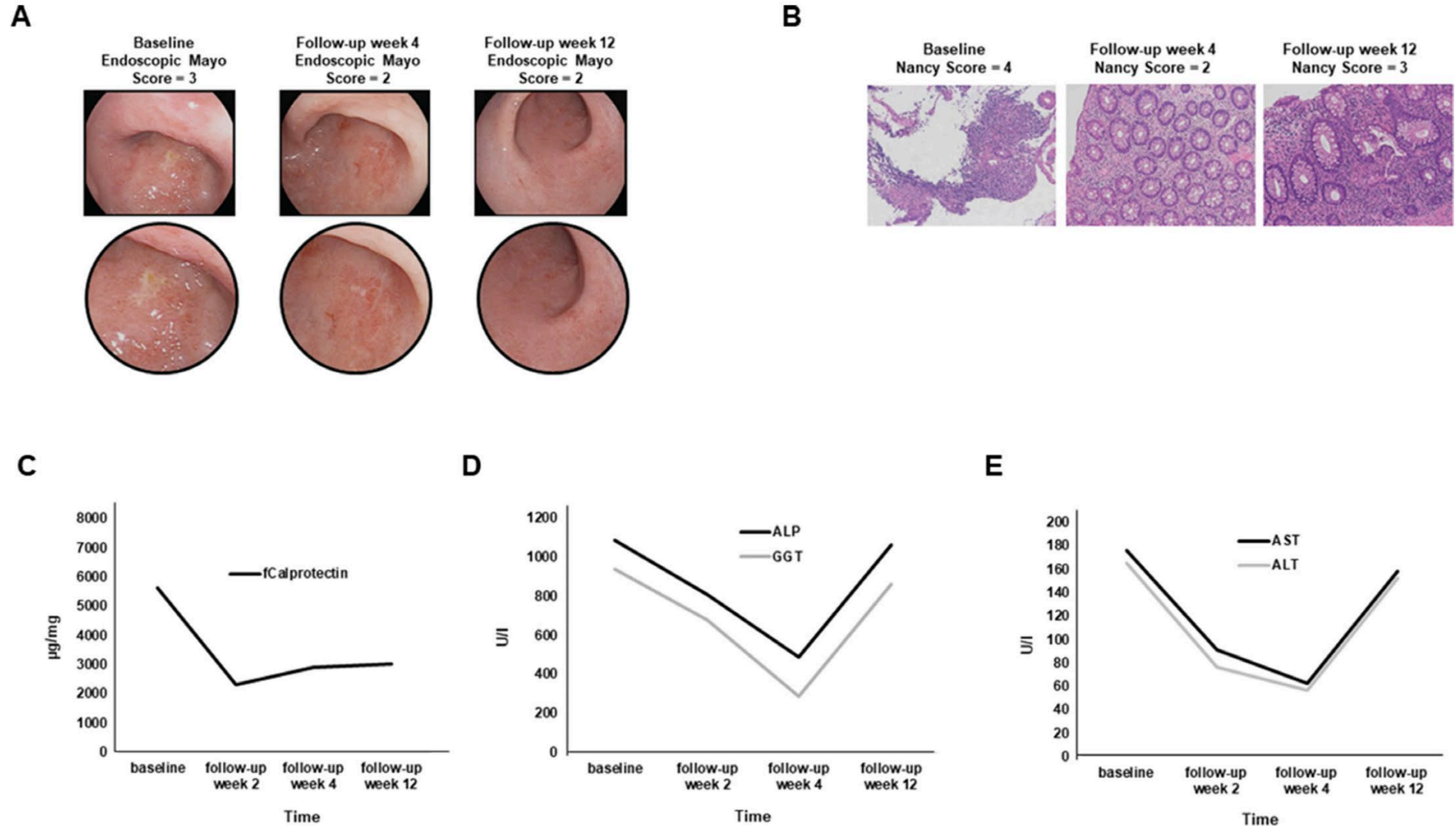
Unmodified Treg therapy is already happening in IBD



Cell therapy labs across
Canada have access to this
infrastructure

Phase I, open-label, fast-track Treg dose-escalation in UC

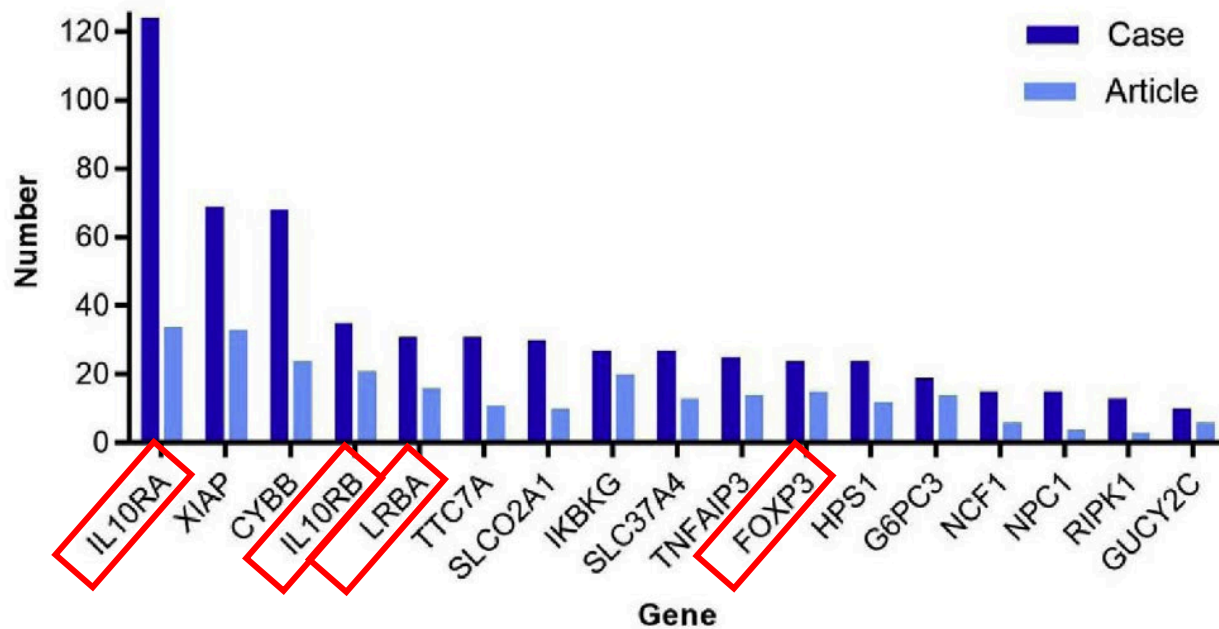
- $1 \times 10^6/\text{kg}$ (84 million) Tregs
- No pre or post conditioning



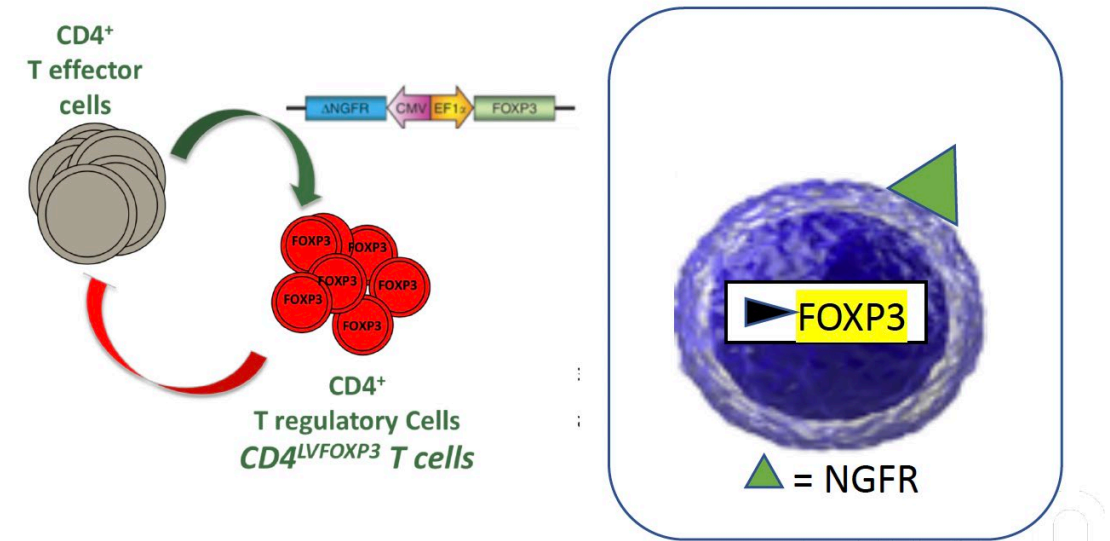
Voskens, ...,
Atreya, Neurath.
BMJ Open 2021

Rationale for genetically-modified Treg therapy in IBD

CD4⁺LVFOXP3 for IPEX



Nambu...Muisse et al, *Clinical Gastroenterology and Hepatology*. 2022



NIH U.S. National Library of Medicine
ClinicalTrials.gov

ClinicalTrials.gov Identifier: NCT05241444

Recruitment Status ⓘ : Recruiting
First Posted ⓘ : February 15, 2022
Last Update Posted ⓘ : June 10, 2022

Sponsor:

Bacchetta, Rosa, MD

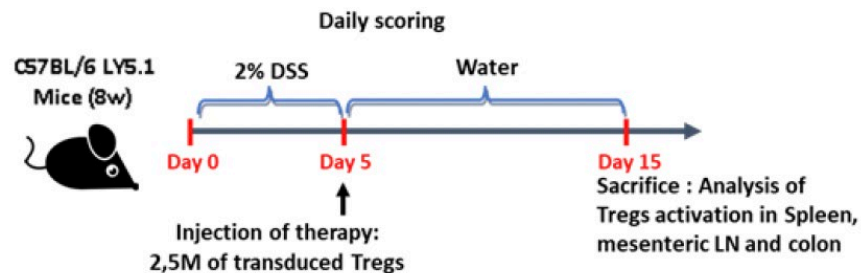
Collaborator:

California Institute for Regenerative Medicine (CIRM)

Information provided by (Responsible Party):

Maria Grazia Roncarolo, Stanford University

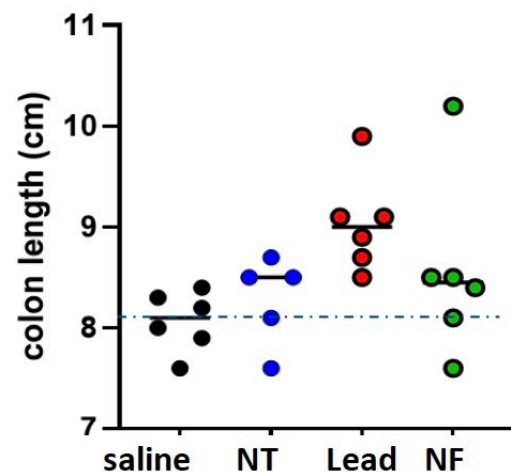
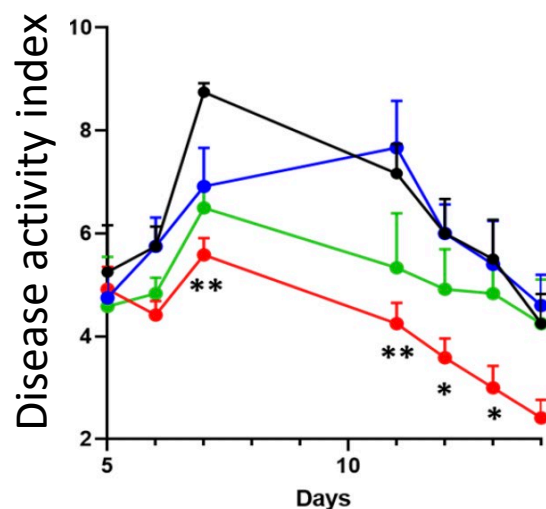
CAR-Treg therapy is on the horizon for IBD



HOME » NEWS AND TRENDS

GentiBio and Bristol Myers Squibb to develop engineered Treg therapies for inflammatory bowel diseases

BY JIM CORNALL
AUGUST 10, 2022 - 2 MINUTES



saline

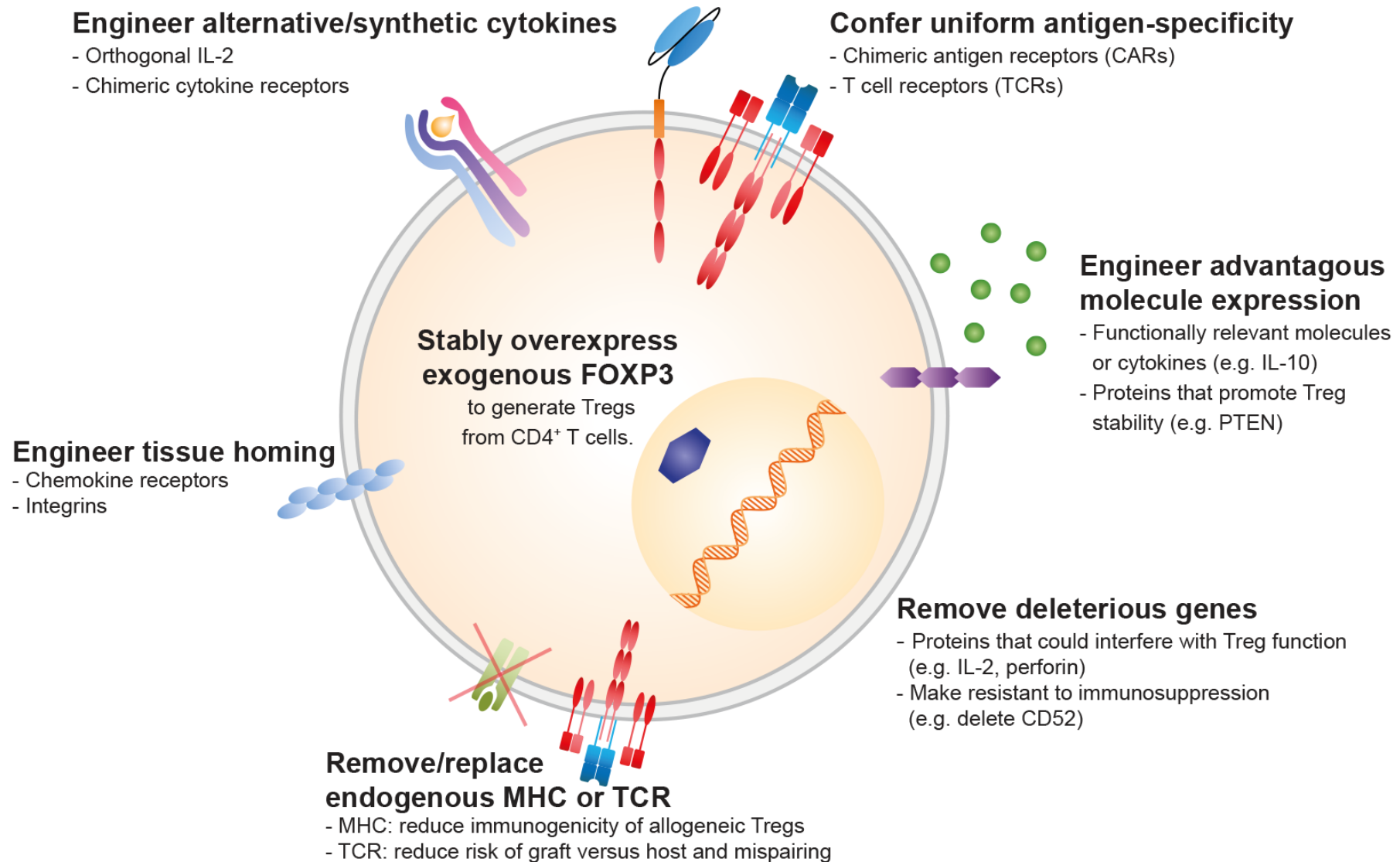
NT = non transduced Treg

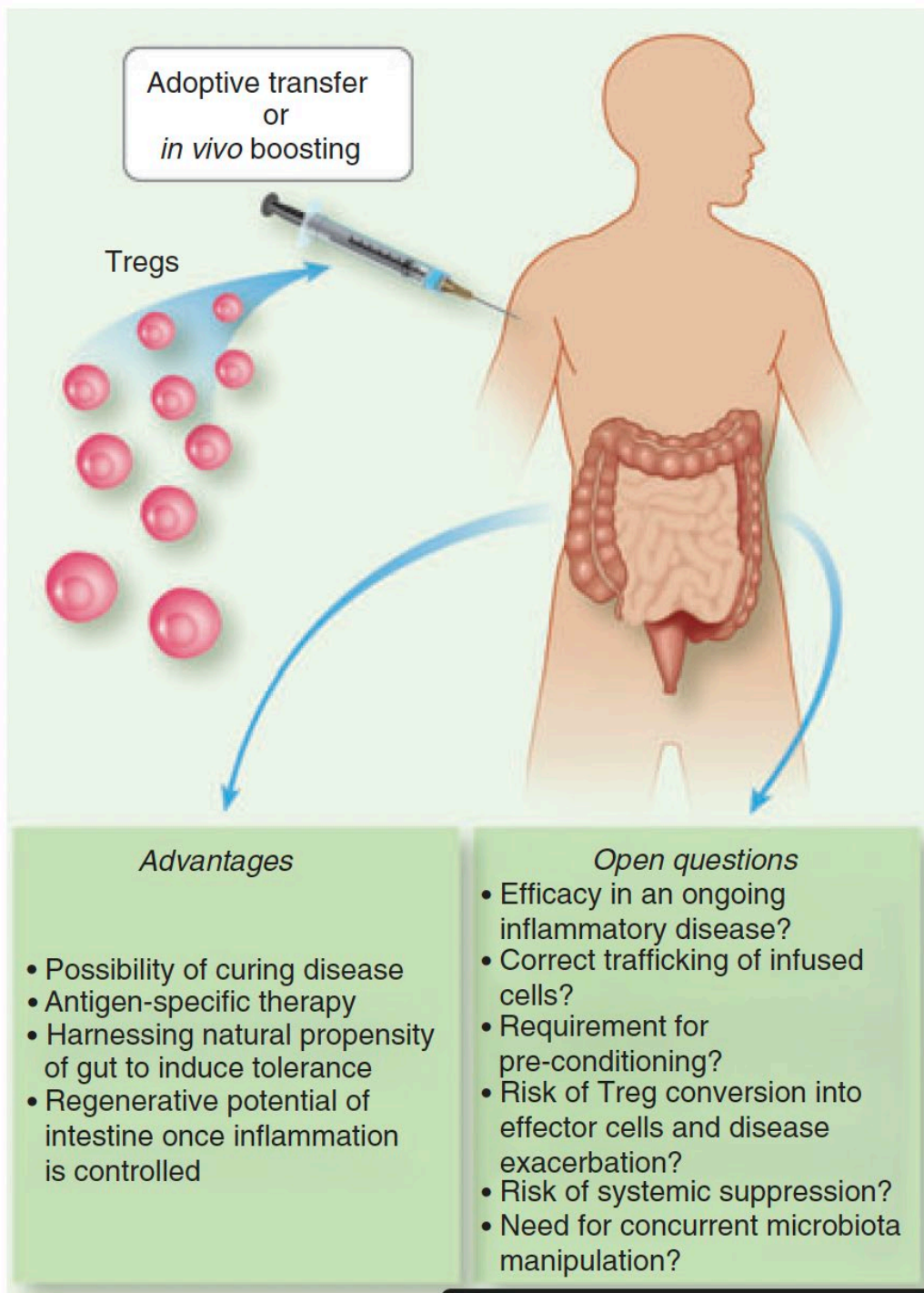
Lead = mIL23R CAR lead candidate

NF = Non-functional mIL23R-CAR



The future of Treg engineering





Discussion Points

- Rationale to use CD19 CAR-T cell therapy
- Interest in pursuing unmodified Treg therapy in Canada
- Pathway to genetically-modified Tregs
 - Patient population (biomarker stratified?)
 - Adjunct therapies
 - Markers of efficacy?
 - Cost/benefit