Graft versus Host Disease in Hematopoietic Stem Cell Transplant Patients
Duke University
OHMI use case

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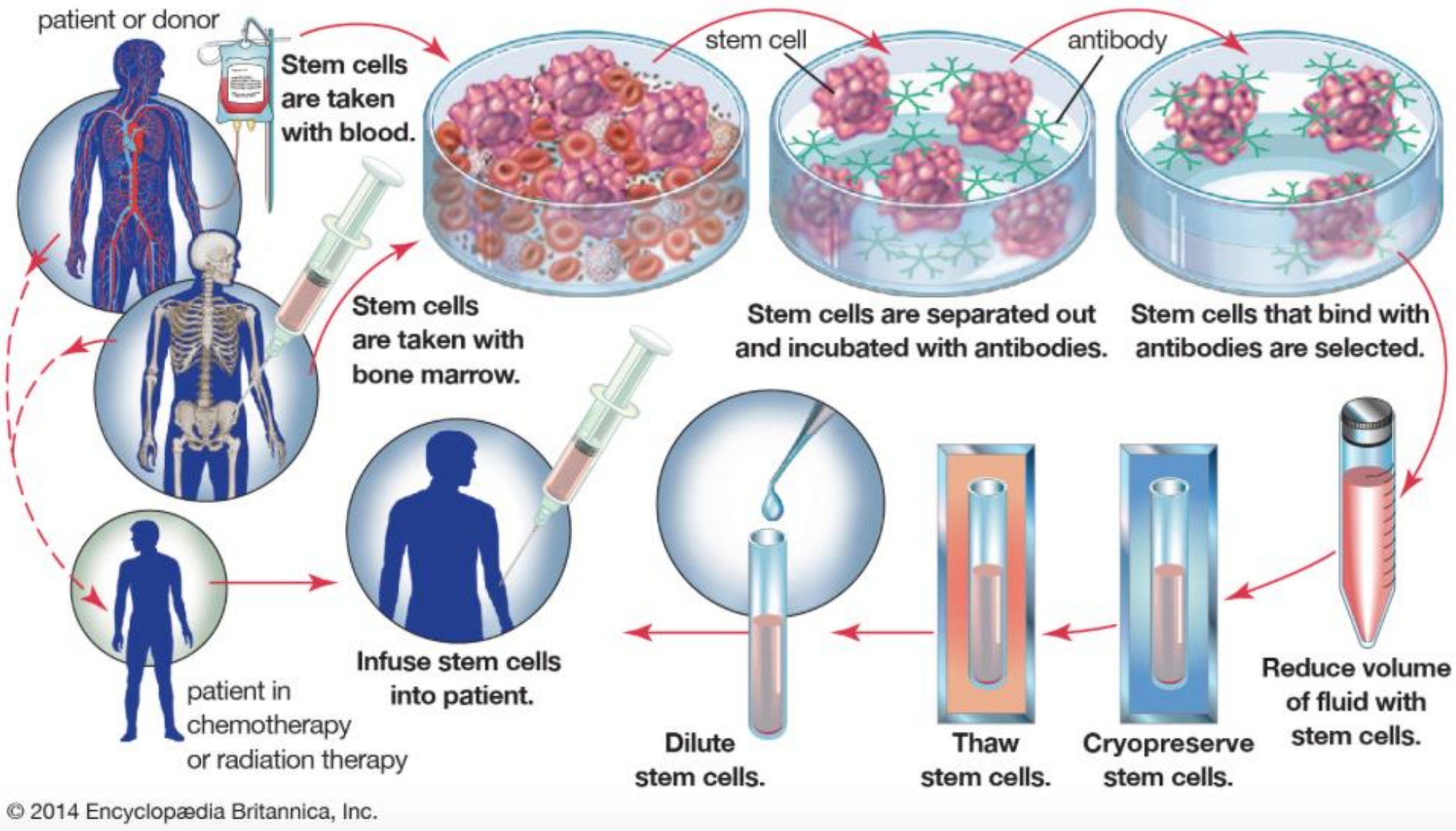
Duke Adult Bone Marrow Transplant Program is one of the nation's leading centers

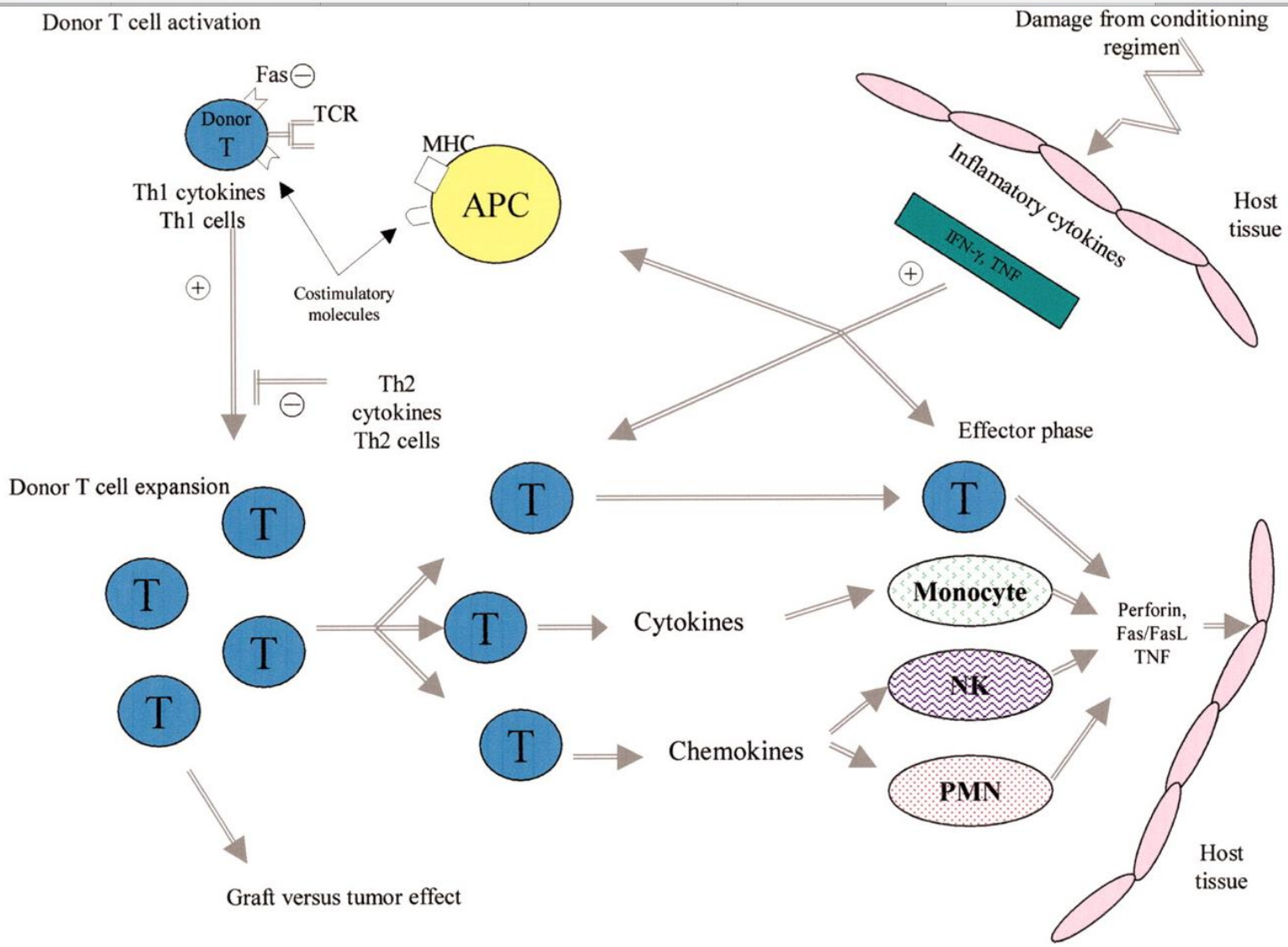
In June the program celebrated 30 years and 5000 transplants

Performs around 300 transplants annually

Hematopoietic Stem Cell Transplants are the major cause of Graft versus Host Disease (GVHD)

Hematopoietic Stem Cell Transplant

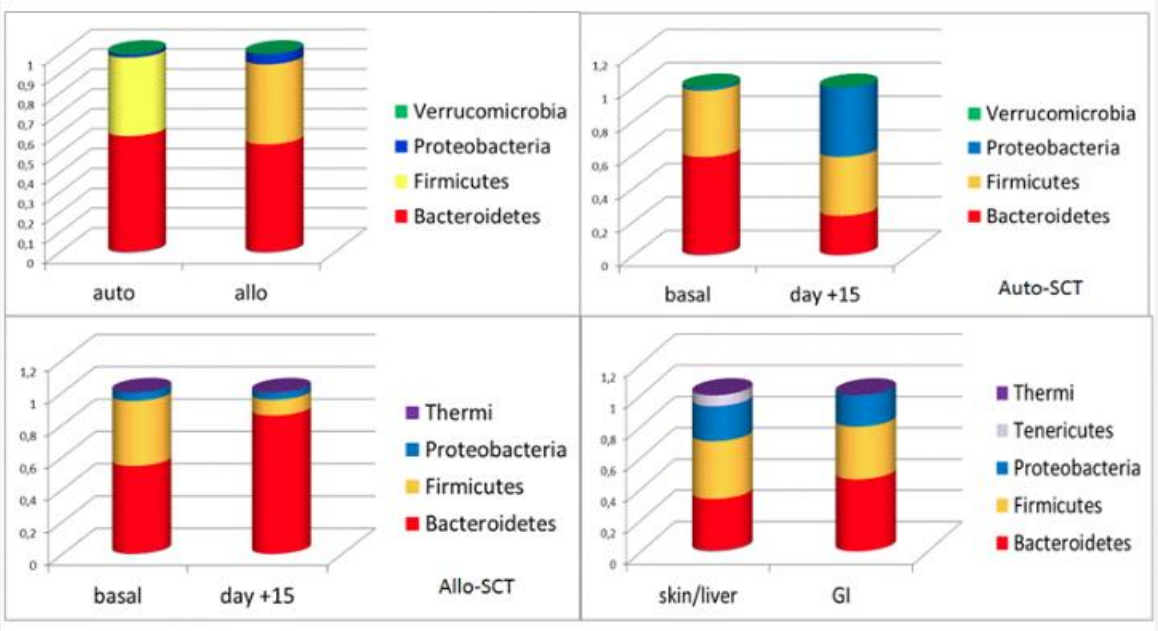




Three-Phase model of graft versus host disease GVHD

PMID:12359826 DOI:10.1146?annurev.med.54.101601.152339

HSCT AND MICROBIOME



Chiusolo P. et al ASH 2015

HSCT, chemotherapy and antibiotic treatment induce change in microbiome

Changes to the microbiome can include loss of bacterial diversity, intestinal domination or overgrowth of pathogenic bacteria

Data available at Duke

300 patients HSCT

1000 Stool Samples

Blood sample for monitoring immune reconstitution

Infection isolates (including organisms cultured from the bloodstream, tissue, body fluid, stool, or respiratory tract including sinuses) in the DUMC Clinical Microbiology lab

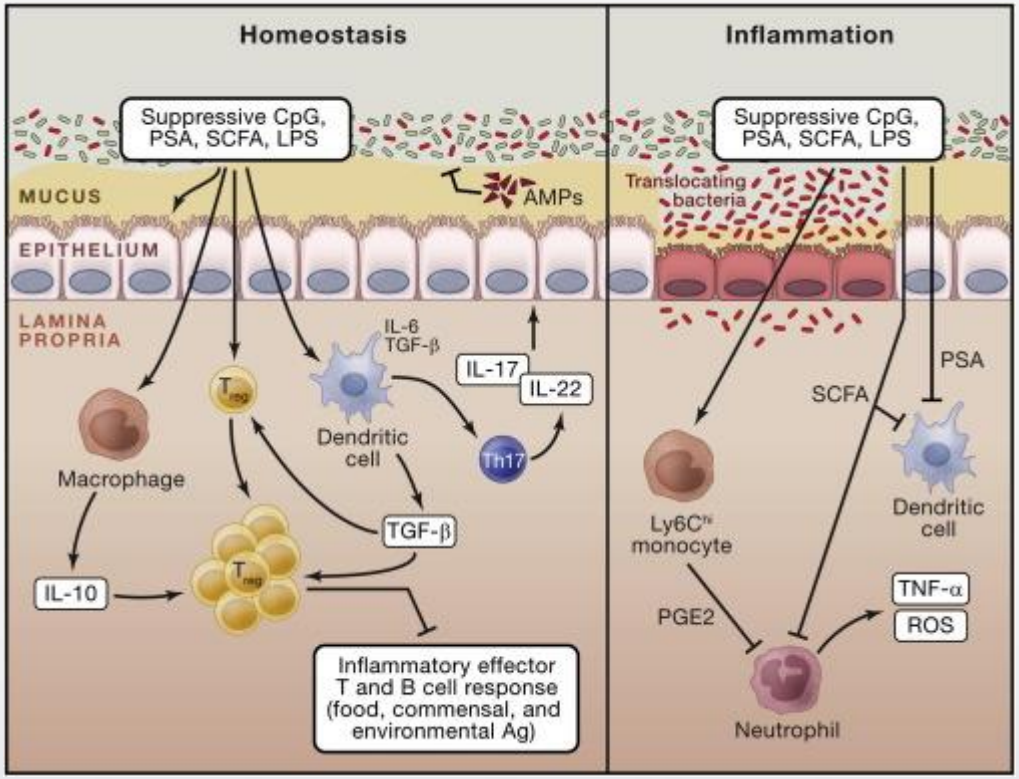
Goal of the study

Microbiome identification

Invasive infection

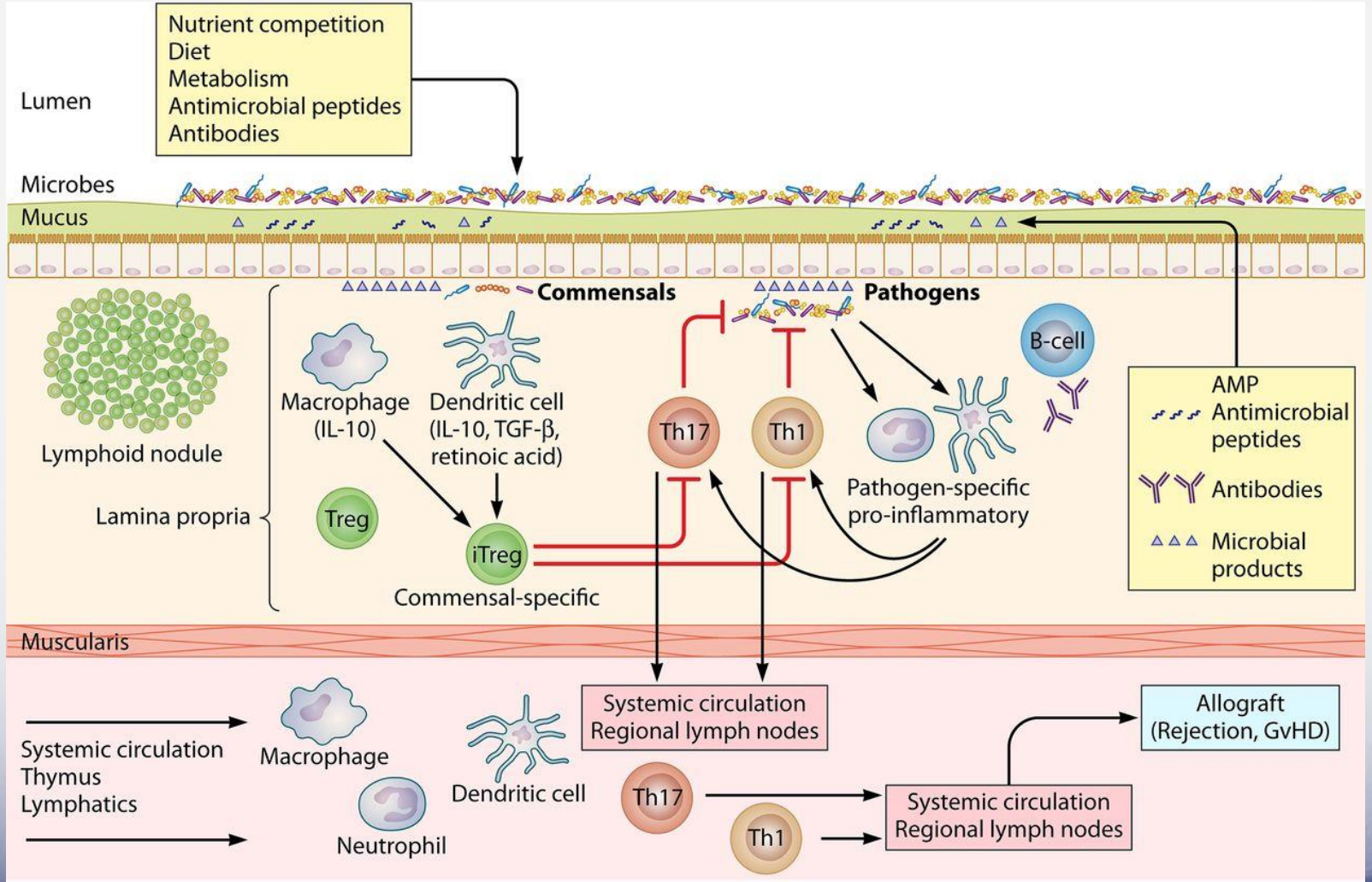
Immune reconstitution

Crosstalk between Microbiome and Immune system



Role of the Microbiota in Immunity and Inflammation null, Volume 157, Issue 1, 2014, 121–141
http://dx.doi.org/10.1016/j.cell.2014.03.011

The microbiome in alloimmunity.



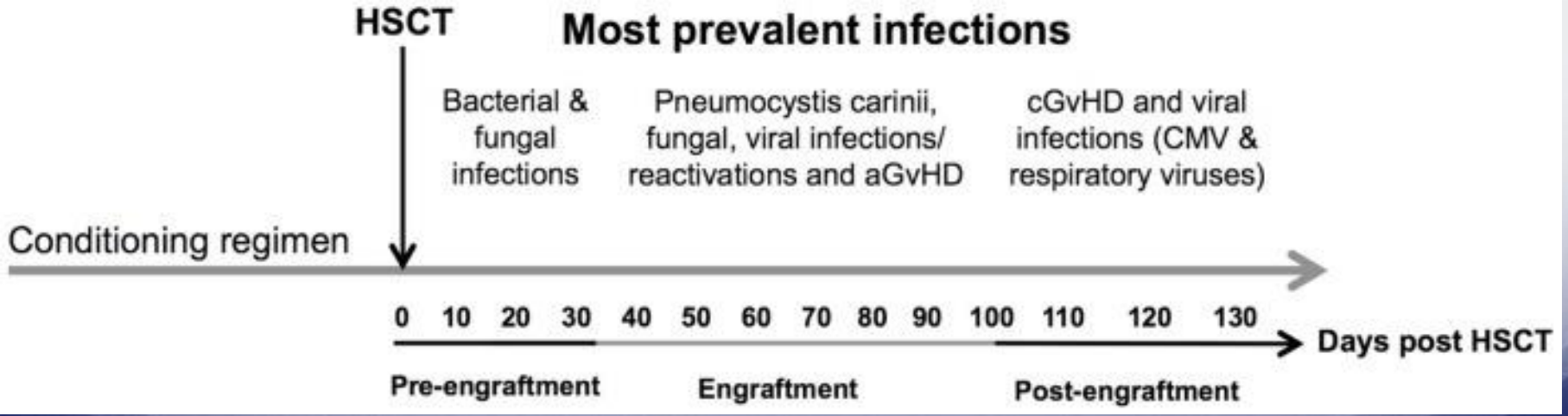
Anoma Nellore, and Jay A. Fishman Clin. Microbiol. Rev. 2016;29:191-199

Clinical Microbiology Reviews

Immune reconstitution after allogeneic HSCT.

Immune cells	Duration after allogeneic HSCT
Neutrophils >0.5 × 10^9/L	~14 days for PBSC, ~21 days for BM, and ~30 days for CB
NK cells	30–100 days
T cells	100 days
$CD19^+$ B cells	1–2 years

PBSC, peripheral blood stems cells; BM, bone marrow; CB, cord blood; NK cells, natural killer cells.



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Host and Microbiome are an Ecosystem

Factors that needs to be taken into consideration

Microbiome populations dynamics

Microbiome crosstalk with microenvironment

Microbial functions in the gut

Sr. No.	Genus-like taxa	Prevalence	General metabolic trait	Health association(s)
1	*Faecalibacterium prausnitzii*	100%	Produce butyrate, formate and lactate (Duncan *et al.* 2002)	Decreased abundance in Crohn's disease and colon cancer (Kang *et al.* 2010; Chen *et al.* 2012)
2	*Bifidobacterium*	99.50%	Produce lactate and acetate by utilizing various oligosaccharides (Turroni *et al.* 2008)	Widely used in probiotic preparations for health benefits (Turroni *et al.* 2008)
3	*Akkermansia*	96.26%	Dominant mucin degrader (Belzer and de Vos 2012)	Indicator of a healthy metabolic profile in humans (Dao *et al.* 2016)
4	*Prevotella melaninogenica*	89.53%	Acetate producer (Wu *et al.* 1992)	One of the tipping elements (Lahti *et al.* 2014)
5	*Ruminococcus bromii*	88.53%	Amylolytic activity (Ze *et al.* 2012)	Keystone species and healthy effects via breakdown of resistant starch (Ze *et al.* 2012)
5	*Bacteroides fragilis*	86.28%	Few strains have ability to degrade mucin (Tailford *et al.* 2015)	Anti-inflammatory effects and also opportunistic pathogen (Sansonetti 2011)

Lahti L, Salojärvi J, Salonen A et al. Tipping elements in the human intestinal ecosystem. Nat Commun 2014;5:4344, DOI: 10.1038/ncomms5344

CAPTURE THE FUNCTIONS

- COMMUNITY
- SPECIFIC LOCATION
- IMMUNE RESPONSE

“All happy families are alike; each unhappy family is unhappy in its own way.”
Leo Tolstoy's book Anna Karenina

In order to be happy family the family needs to have all the components but to be unhappy needs only one missing. There is only one way to be happy but different ways to be unhappy

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doi:10.1038/nmicrobiol.2017.121

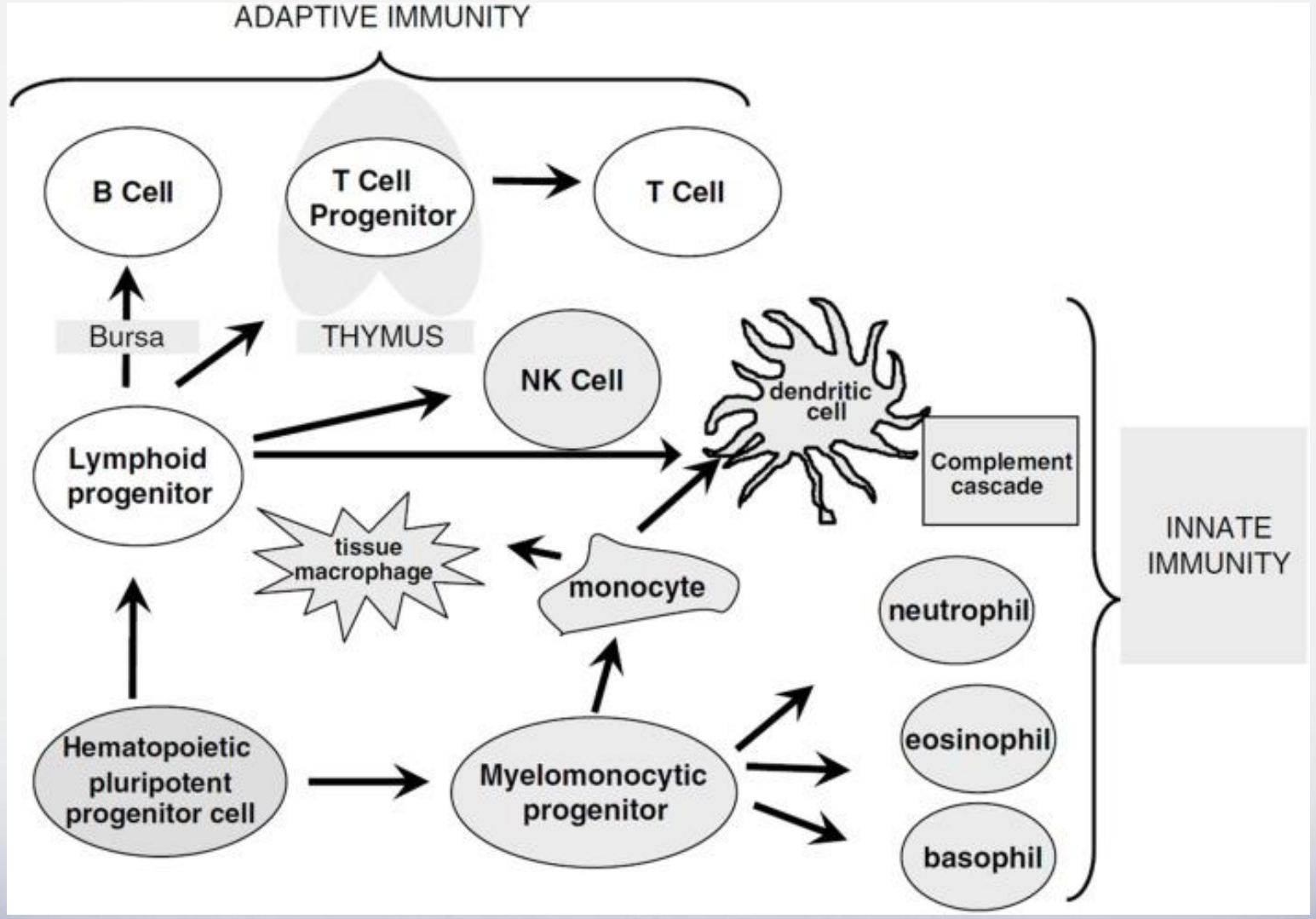

Thank you

APPROACH TO ONTOLOGY DEVELOPMENT

DEFINE THE BIOLOGICAL KNOWN FUNCTIONS PLAYED BY EACH MICROBIAL FAMILY

DEFINE THE KNOWN MICROBIAL MOLECULES THAT PARTICIPATE IN A SPECIFIC PROCESS

DEFINE THE INTERACTION BETWEEN THE MICROBIAL PARTS AND IMMUNE SYSTEM



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