National Neutropenia Network Family Conference July 12, 2014

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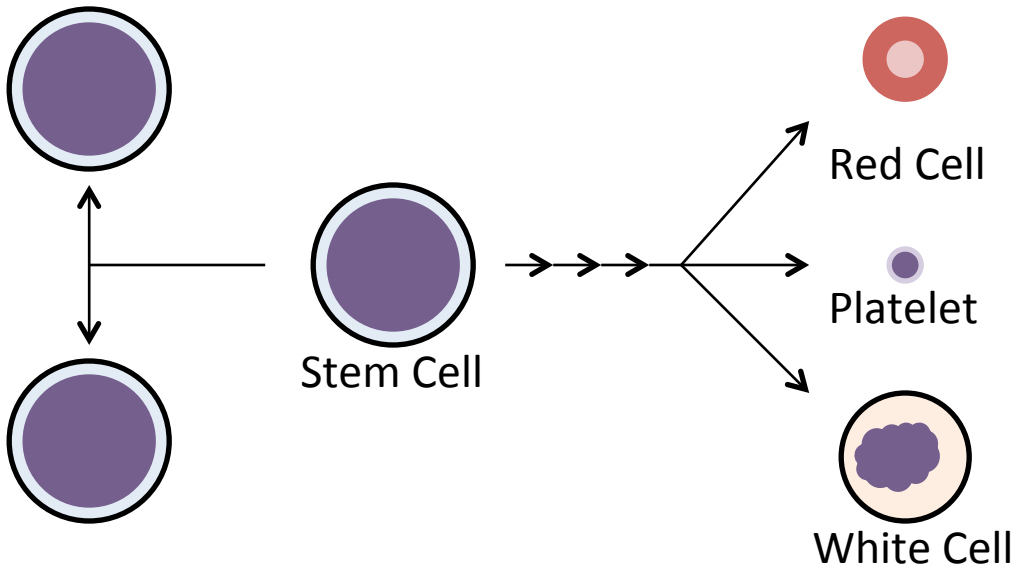
University of Michigan

Transplant Definition

- Hematopoietic Stem Cell Transplant (HSCT)
  - Infusion of blood “stem cells” into a recipient patient



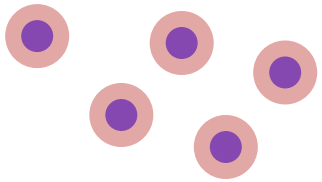
Donor Source of Hematopoietic Stem Cells

- Autologous: Use patient's own cells
  - Typically given in patients receiving high dose chemotherapy to "rescue" patients from toxic side effects
- Allogeneic: Use donor's cells
  - Used in a variety of diseases (cancer, red cell disorders, bone marrow failure, metabolic disorders, **NEUTROPHIL DISORDERS**, immune deficiencies)
- Donor sources include collection of stem cells from the bone marrow, peripheral blood, or umbilical cord

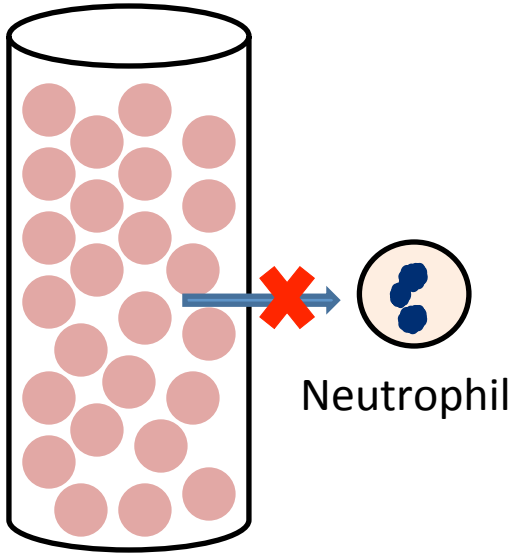
Stem Cell Transplant Process

Recipient

Immune System



Bone Marrow



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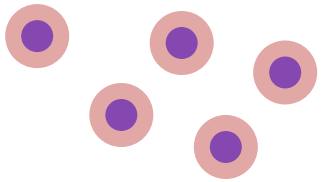

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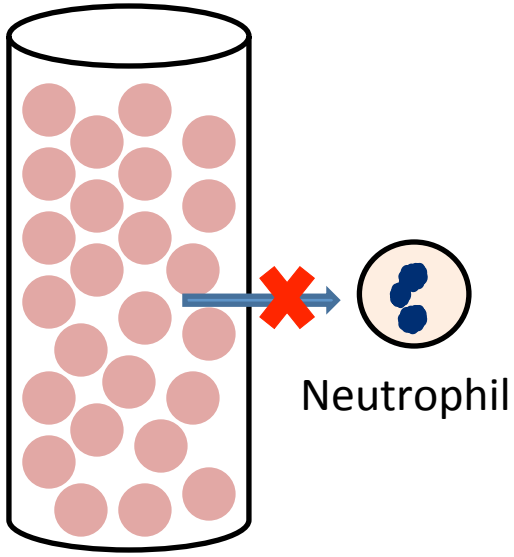
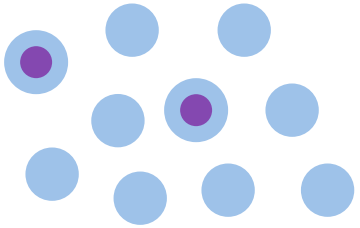
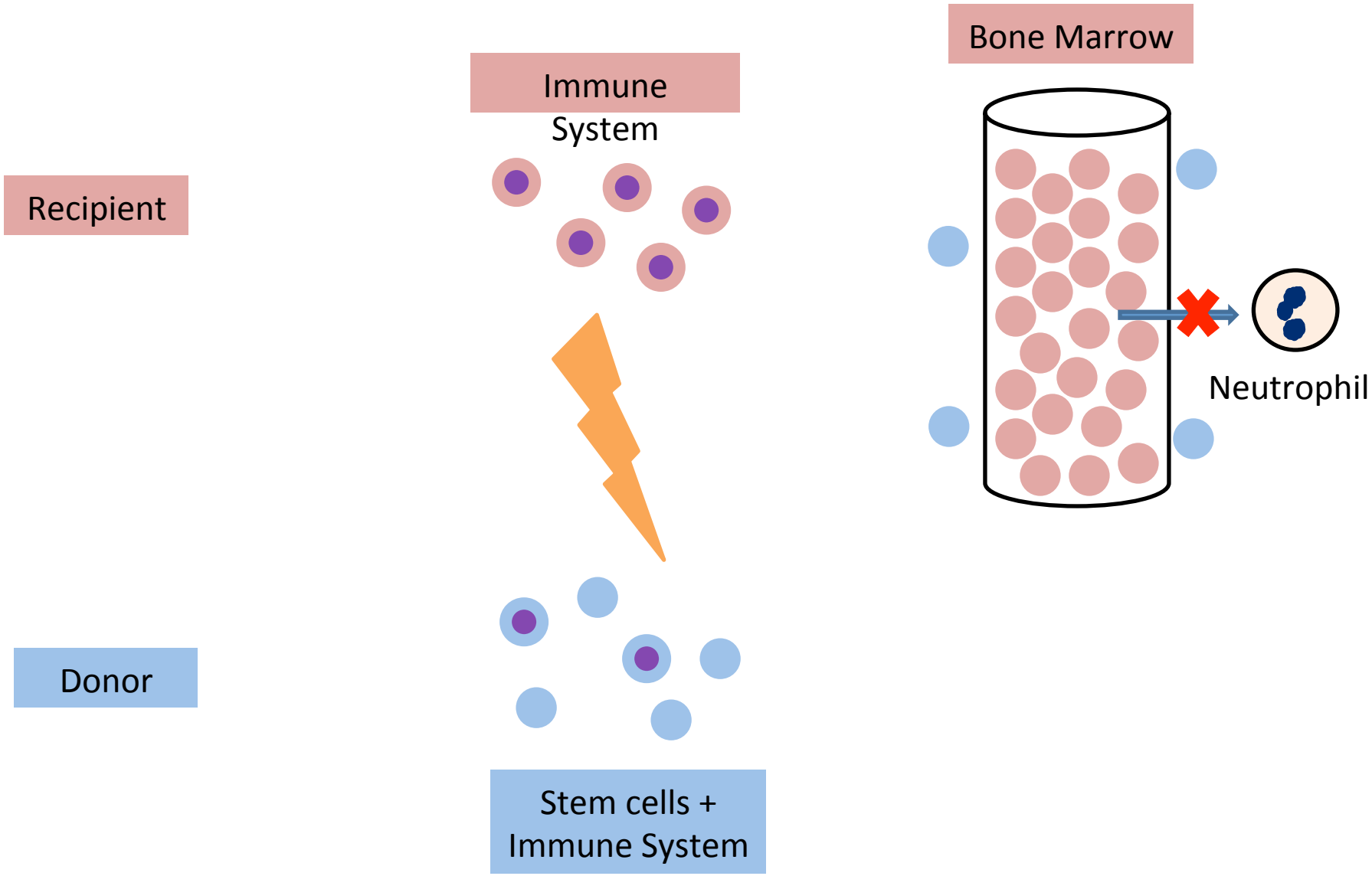


Donor



Stem cells + Immune System

Stem Cell Transplant Process



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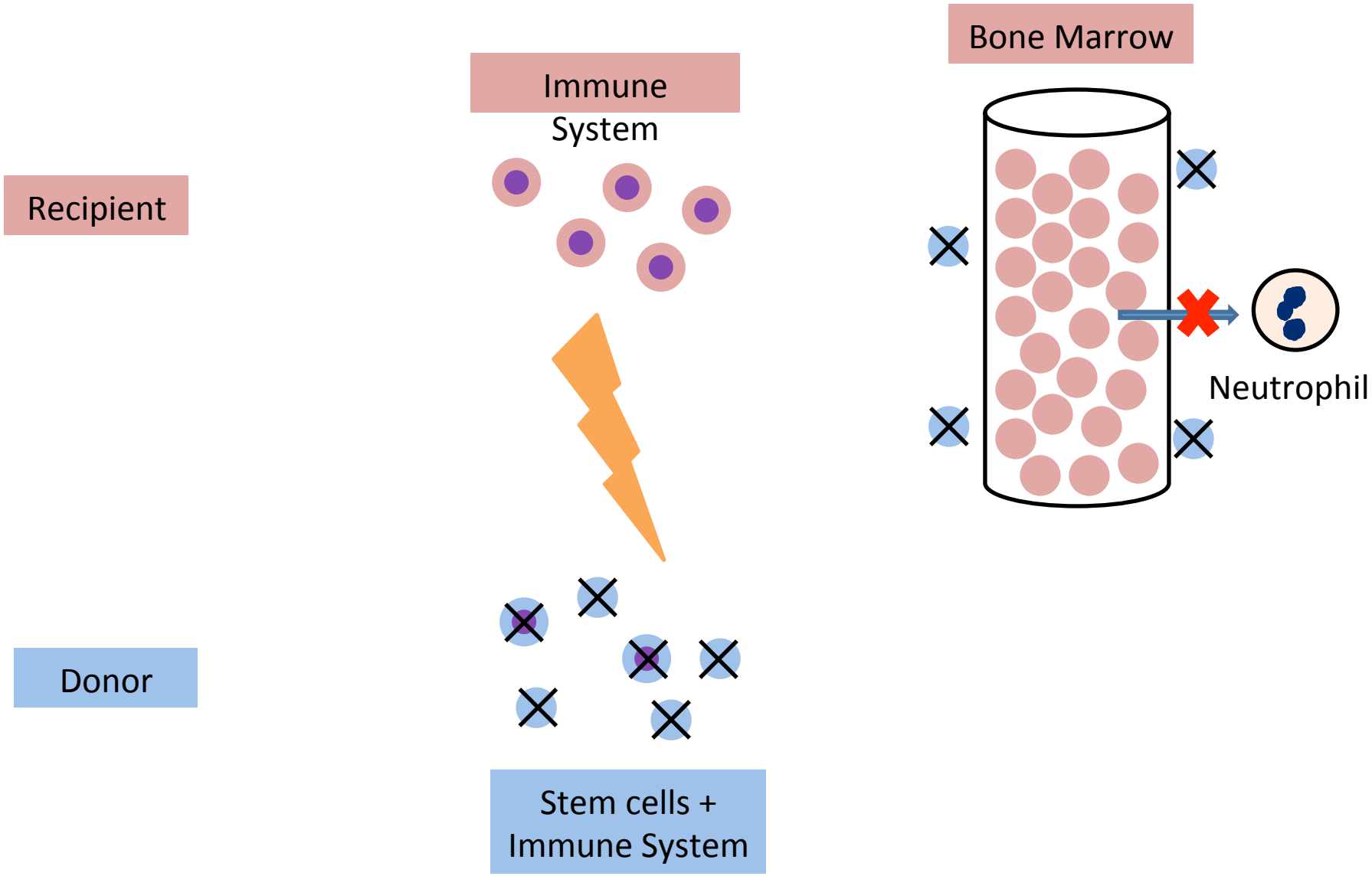


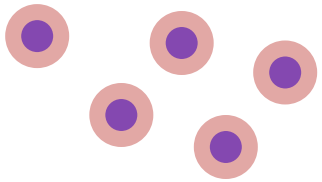
Transplant Requirements: Conditioning

- Eliminates/weakens recipient bone marrow and immune system
- Myeloablative
  - Irradicates marrow and immune system
  - Increased toxicity to the patient
- Reduced Intensity
  - Less organ toxicity and therefore expands the use of transplant to sicker patients
  - Less conditioning therapy can result in increased risk of donor cells not growing in the patient recipient

Stem Cell Transplant Process

Recipient

Immune System



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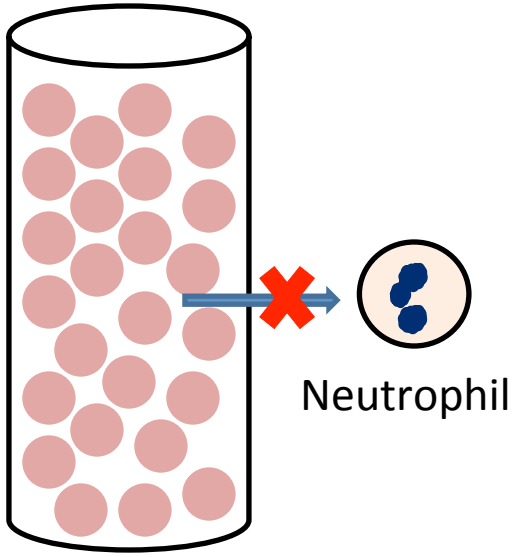

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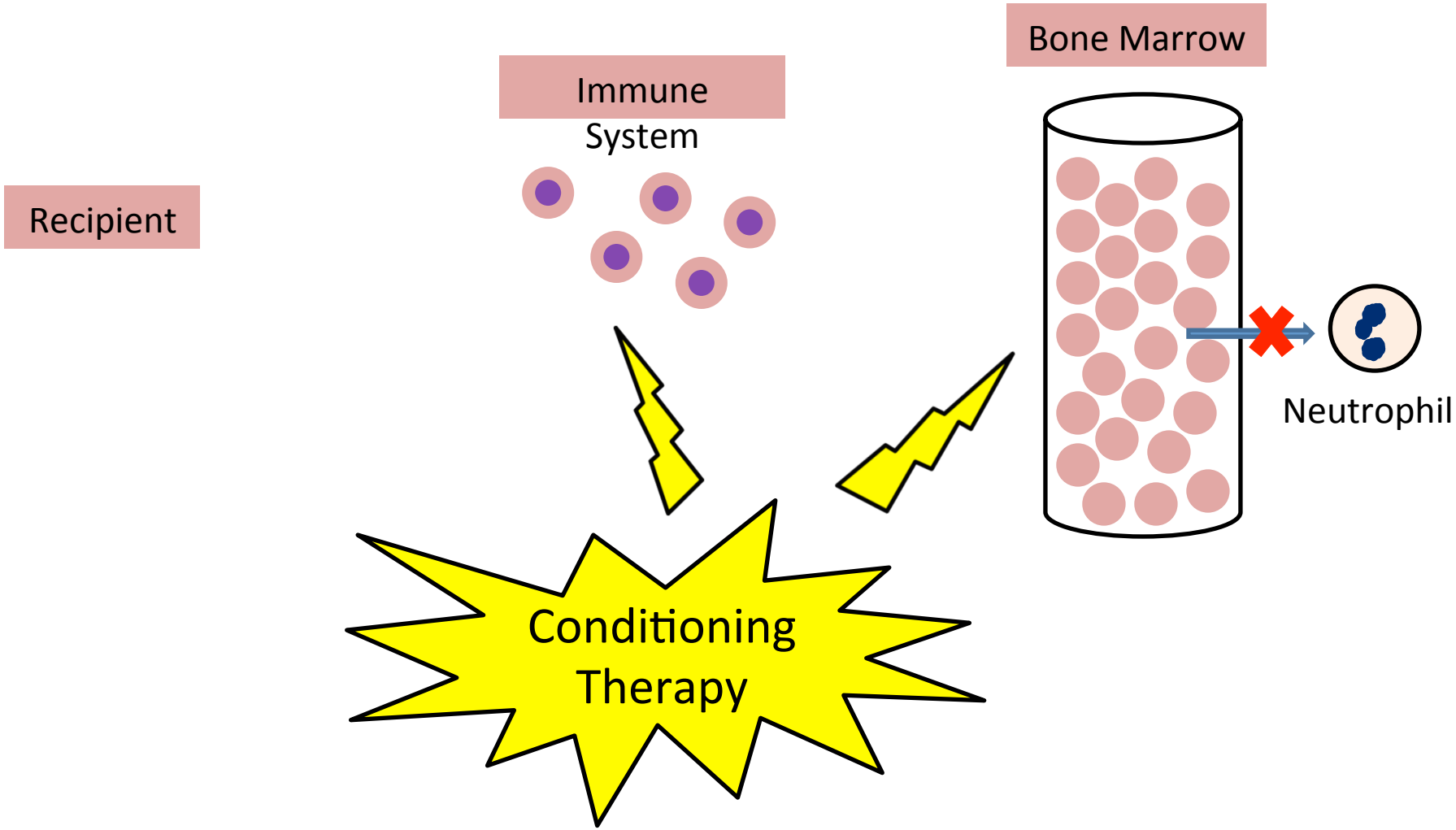

Stem Cell Transplant Process

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Immune System

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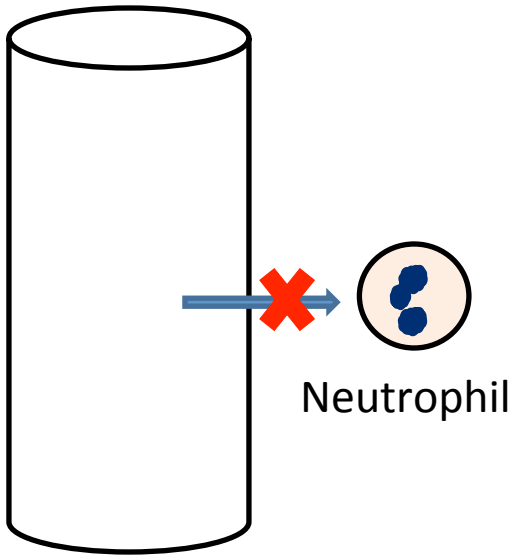

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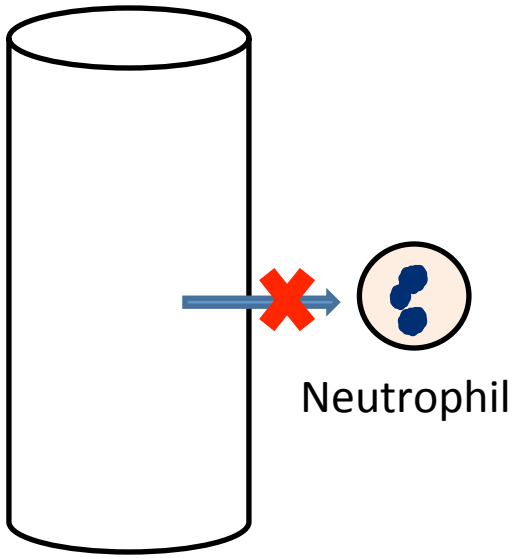

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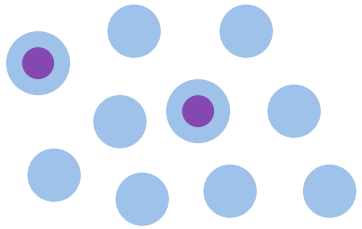

Stem cells + Immune System

Stem Cell Transplant Process

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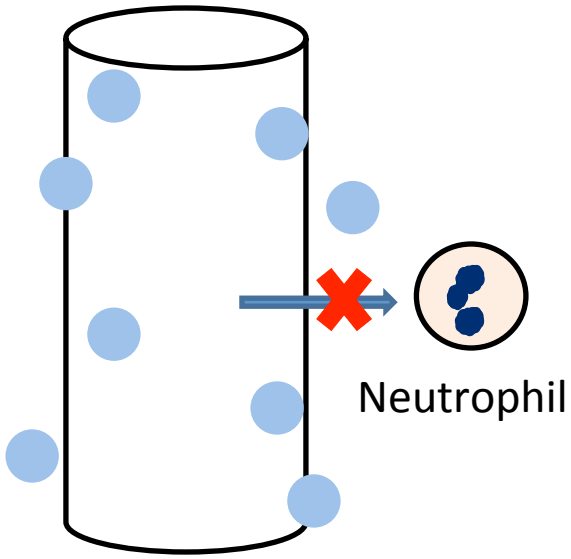

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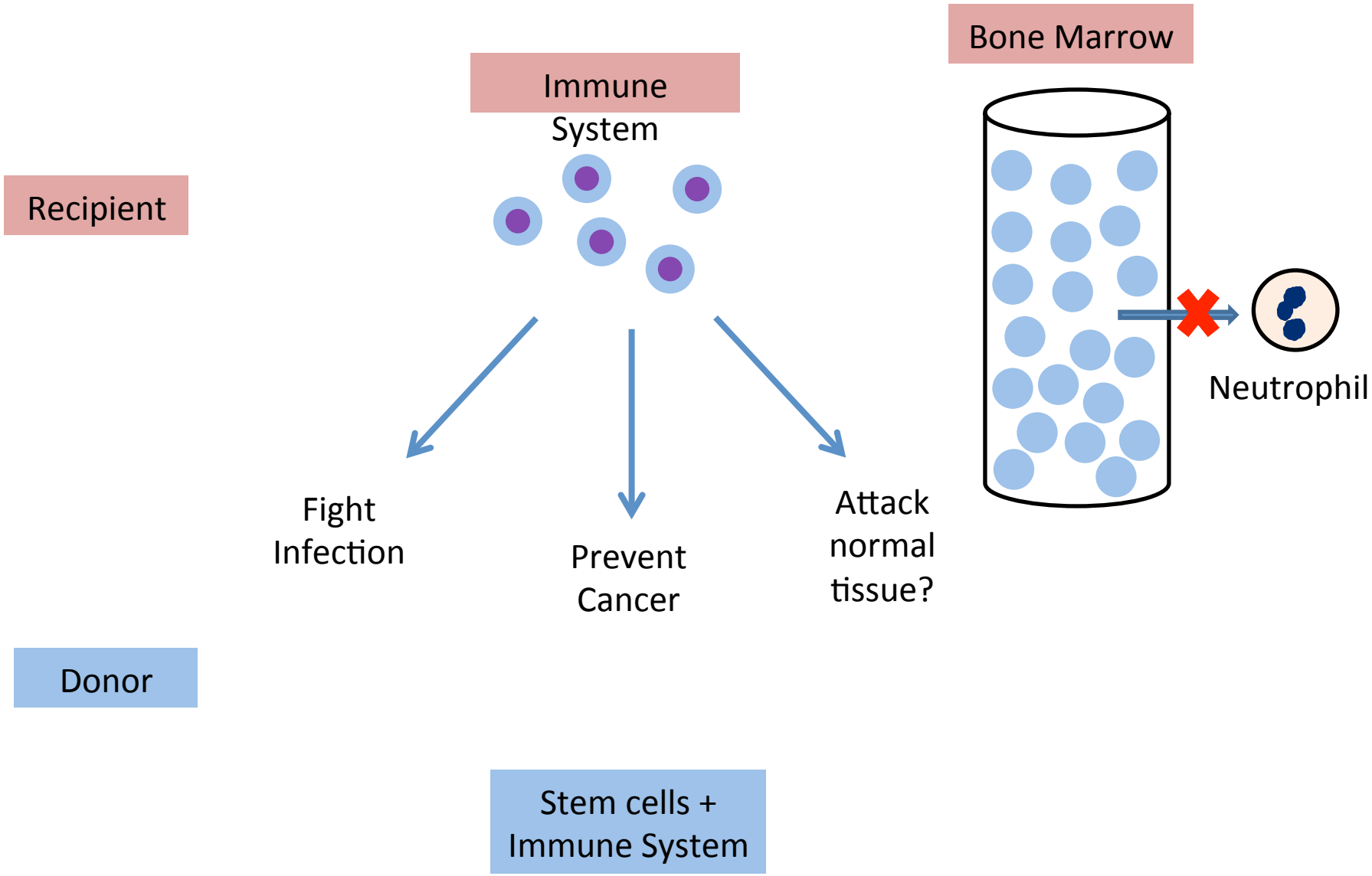
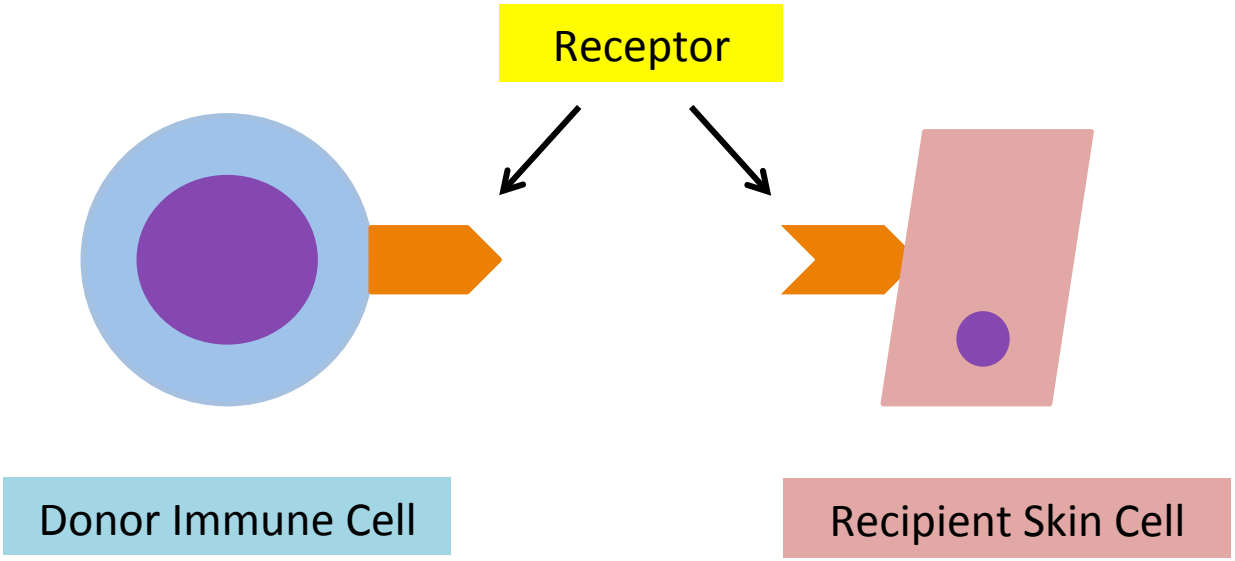


Finding an immune system match



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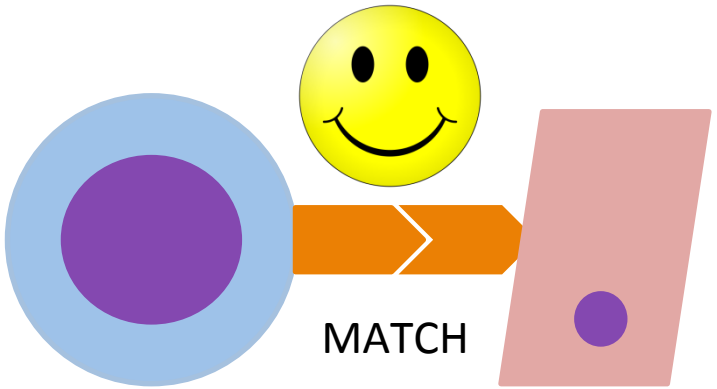
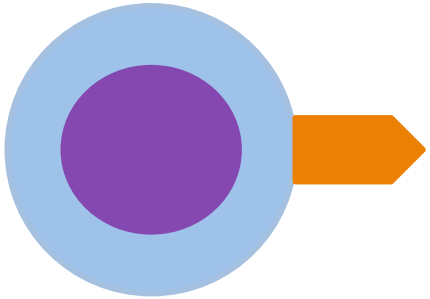


Donor Immune Cell

Recipient Skin Cell

Finding an immune system match



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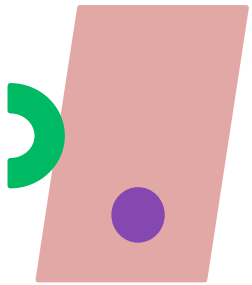

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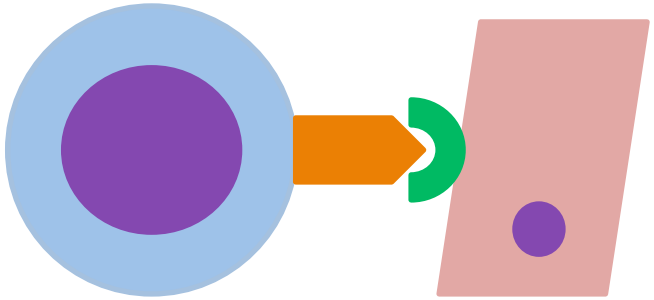

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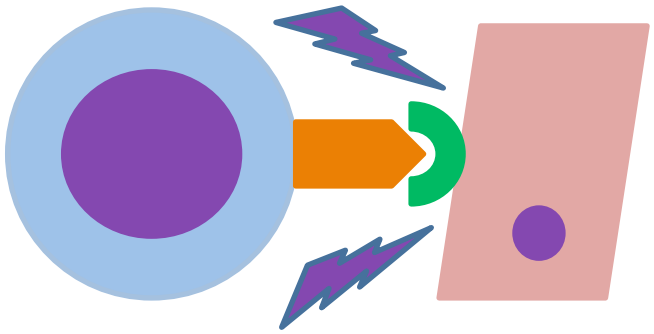

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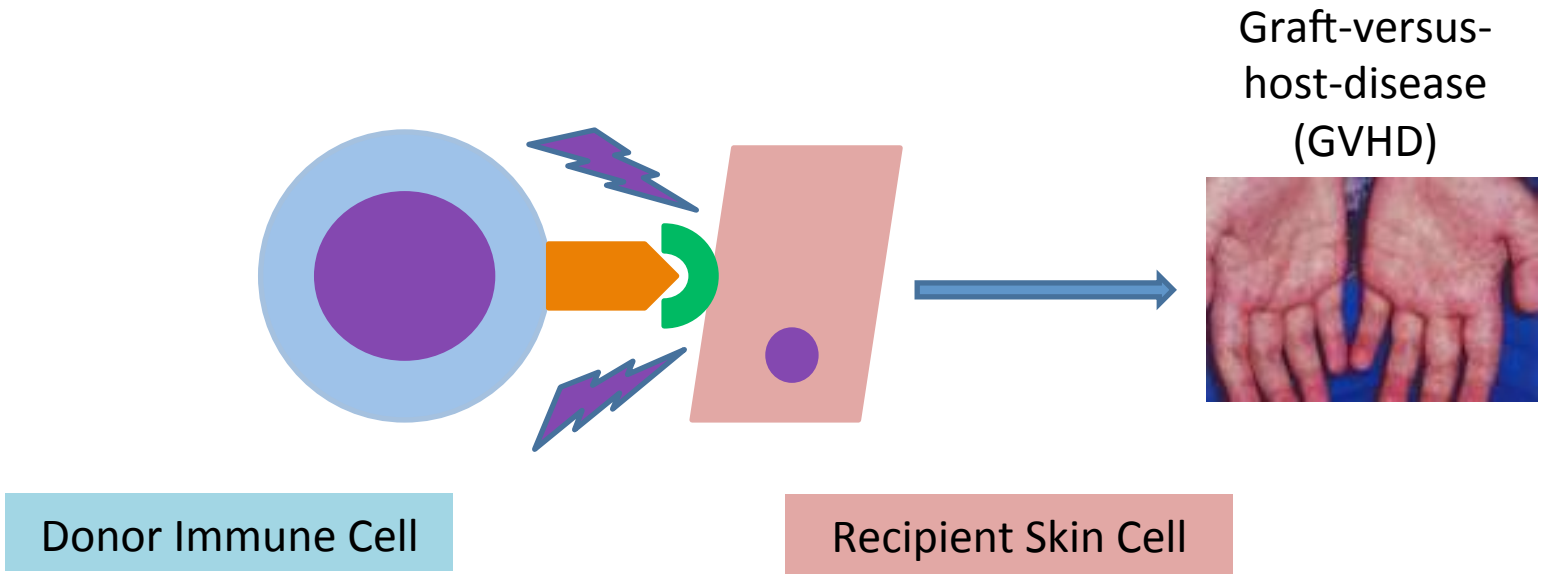

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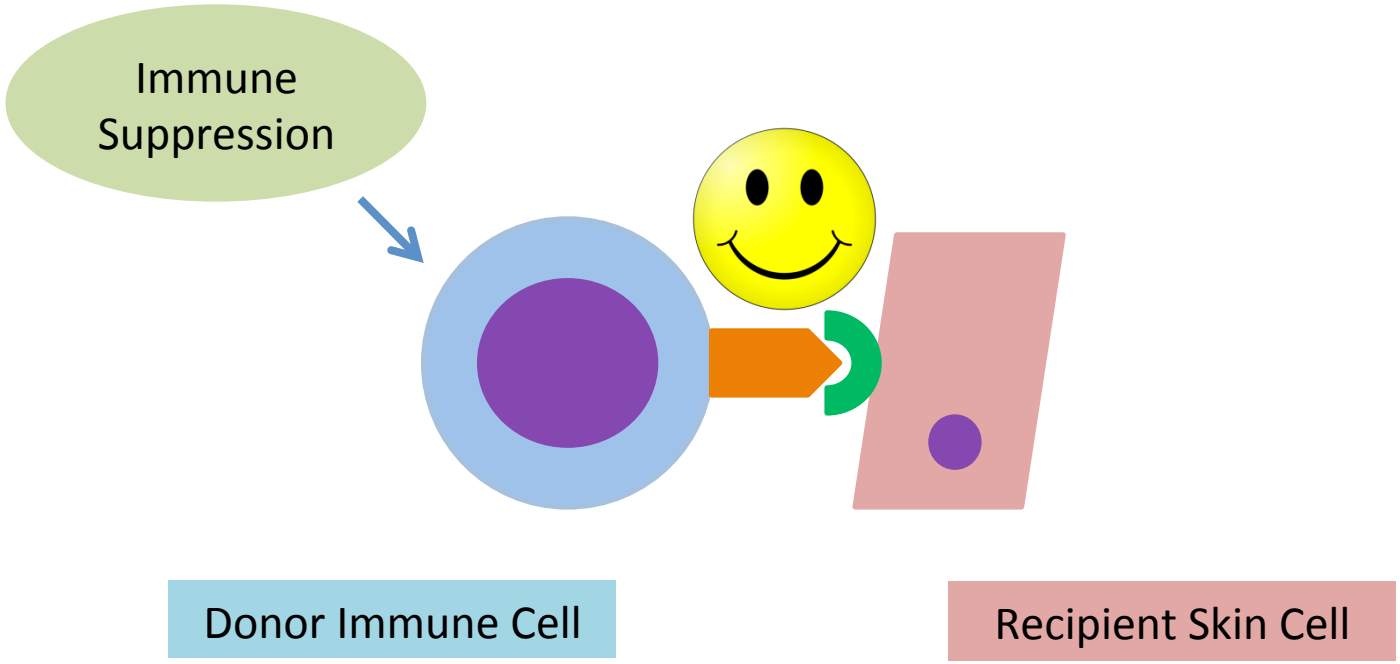

GVHD prevention and treatment

- Patients are started on immune suppression shortly before stem cell infusion
  - Goal is to wean off immune suppression starting around 6 months after cells infused if no evidence of GVHD
- GVHD can occur early (in first couple months) and/or late (several months after transplant)
  - Treatment is additional immune suppression (typically steroid based)

Indications for Transplant in SCN

- Absolute Indications
  - No response to GCSF
  - Malignant transformation to AML/MDS
- Indications to consider transplant if a good match is available
  - Poor response to GCSF (high doses with ANC < 2000)
  - Mutation causing SCN associated with poor outcomes

Transplant in SCN without AML/MDS

- The outcome of HCT in patients who have not developed MDS or leukemia is excellent

Summary of published HCT in SCN without MDS or leukemia*

Donor Source	Total Patients	Overall Survival	Event Free Survival
Matched Related Donor (MRD)	21	20/21 (95%)	18/21 (86%)
Matched Unrelated Donor (MUD)	8	7/8 (88%)	6/8 (75%)
Umbilical Cord	30	28/30 (93%)	13/17 (76%)
Total	59	55/59 (93%)	37/46 (80%)

Transplant in SCN with AML/MDS

- Patients who progress to MDS or leukemia do poorly
  - Patients with AML develop significant toxicity during induction chemotherapy
  - Currently recommended to avoid chemotherapy before conditioning therapy
  - Survival following HCT is historically poor

Summary of published HCT in SCN with MDS or leukemia[*]

Disease at transplant	Total Patients	Overall Survival	Event Free Survival
MDS	7	4/7 (57%)	4/7 (57%)
Leukemia	11	4/11 (36%)	3/11 (27%)