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Improving the diagnosis, treatment and quality of life of people affected by primary immunodeficiency through a community empowered by advocacy, education and research.
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SCID Compass Toolkit

Now available in these languages!

- Arabic
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- Portuguese
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https://scidcompass.org/provider-publications
WELCOME!

Moderator: Ami Shah, MD
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Panelists:
Mort Cowan, MD
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Immune Deficiency Foundation
Mixed Chimerism: What does that mean?

Ami J. Shah (moderator)
Mort Cowan (panelist)
Robertson Parkman (panelist)
Ken Weinberg (panelist)
What are Chimerisms?

• A chimera is any individual whose body is a mixture of cells that came from both themselves and another individual.

• Therefore, anybody who received a transplant from someone else is a chimera, or is “chimeric”.

• For example, someone who got a kidney transplant is a chimera of their own cells and their donor kidney.

• A bone marrow chimera is someone who has their own cells (for example, their skin, heart, brain) but in addition has blood-forming cells from a transplant donor.
Bellerophon (on Pegasus) Killing Chimera

Greek plaque in Rhodes, c. 270 BCE
Two Different Cell Types In the Graft Make T Cells in the Recipient

**“Baby Cells”**
- Stem cells “HSC”
- “Committed Progenitors”

**“Grownup Cells”**
- T Lymphocytes

### Hematopoietic Stem and Progenitor Cells (HSPC)
- Take months to grow up to become a mature T cell
- Don’t cause GVHD
- Stem cells make all types of blood cells, not just T-cells
- Stem cells live a long time (entire life of the recipient)

### Mature T Lymphocytes
- Can fight infection soon after transplant
- Can also cause GVHD
- Mostly taken out in a “T-cell depleted” transplant
- Won’t last as long as transplanted stem cells
Chimerism after Transplant for SCID

• Every successfully transplanted child with SCID is a chimera.

• If all of their blood cells after transplant come from their donor, then they are a “full chimera”, or have “full donor chimerism.”

• If some of their blood cells come from their donor and others are their own, then they are a “mixed chimera”, or have “mixed chimerism.”

• Whether someone has full or mixed chimerism depends on
  1. What kind of SCID they had (do they have some types of lymphocytes or not?)
  2. What medications they got before transplant (“conditioning”)
  3. What type of graft they got (“T-cell depleted” or “unmanipulated”)
Different Types of Cells in the Graft Need Different Types of Pre-Transplant Conditioning in Order to Grow

“Baby Cells”

- Stem cells “HSC”
- “Committed Progenitors”

“Grownup Cells”

- T Lymphocytes

Hematopoietic Stem and Progenitor Cells (HSPC)

- In order to grow, they need to have space made in the bone marrow by certain types of conditioning medications given before transplant.
- **Examples:** Busulfan, treosulfan, anti-Kit antibody

Mature T Lymphocytes

- In a baby with SCID, mature T-cells in the graft can usually grow, perhaps with some conditioning to suppress the immune system further.
- **Examples:** ATG, fludarabine
Patient 1

• Patient is a 7 month old male with X linked SCID. At diagnosis he had 0 T cells, 95 B cells and 45 NK cells

• who had an unconditioned (no chemotherapy) transplant from his sister at 4 months of age.

• At day 100, his chimerism showed:
  • T cells: 100% donor chimerism
  • B cells: 4% donor chimerism
  • NK cells: 7% donor chimerism
• What does it mean that the T cells are from the donor?  
  • but the B and NK cells are primarily from the recipient?

• Why will the lack of donor B cells mean that I will need IVIG?

• Will I always need IVIG?
Patient 2

• 6 month old child with Omenn’s syndrome. At birth he had
  691 T cells
  0 B cells
  5 NK cells

He went to transplant very quickly. He received only chemotherapy (Busulfan, Cytoxan) conditioning regimen followed by a T cell depleted haploidentical transplant from his father.
Day 100

• He had mixed chimerism with 60% cells of the patient and 40% of the cells being of his father

• His sorted chimerism showed
  • T cells: 90% recipient and 10% donor
  • B cells 100% donor
  • NK cells 100% donor
• What does it mean in this situation that most of the T cells are of the recipient and the B and NK cells are of the donor?

• Why would that happen?

• What do you do in this situation? Do you have to do another transplant? Or what might you need to?
Patient #3

The patient is a 9 month old who was initially diagnosed after an RSV infection that brought him to the hospital quite sick.

He was found to have X SCID, but was not diagnosed from the NBS.

His initial testing showed that he was maternally engrafted (which means that he had some of mom’s T cells in his blood).

Because of his organ function, he received a reduced conditioning regimen of low dose Busulfan (ie. Not ablative) and low dose fludarabine. He did not receive any serotherapy (ie. ATG)
Day 100

• T cell chimerism:
  • 100% donor T cells

• B cell chimerism
  • 80 % donor chimerism

• NK cell chimerism
  • 90% donor chimerism
1 year

Stem cell chimerism: 70% donor, 30% recipient

He has
T cell count of 43
B cells: 85
NK cells: 140
• What does it mean that 70% of the cells are from the donor?

• Why are the T cell numbers low? What will that mean?

• What do you need to do in that case?
Conclusions:

• Chimerisms and what they mean can be complicated after transplant and depend on many factors:
  • Genotype (the type of SCID that you have: ie. X linked SCID vs RAG 1 vs many others)
  • Conditioning regimen that you received (myeloablative vs reduced intensity vs none)
  • Infections that you had prior to transplant

• It is important that if you do not understand, please ask your doctor to really explain them and what that means for your child for the short term and the long term.
Please feel free to reach out to any of us or your physicians if we can answer any of your questions

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THANK YOU!

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Additional Resources

• ASK IDF: www.Primaryimmune.org/ask-idf
  ○ 800-296-4433

• IDF Resource Center:
  • https://primaryimmune.org/resource-center

• IDF Support Services:
  https://primaryimmune.org/support-services

• IDF’s YouTube Channel
  ○ We record and upload all IDF Education sessions
  ○ https://www.youtube.com/user/IDFvideos
From all of us at IDF

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You make the IDF community stronger

Immune Deficiency Foundation