Creation of a Human Immune System in a SCID Mouse Model Using Artificial Bone Marrow

By: Andrea Cantú

Background Information

Stem cells and Tissue Engineering

- Tissue engineering is the design and growth of cell tissues and organs outside of the human body.
- Stem cells are the primitive cells present in all organisms that can give rise to more stem cells and are the progenitors of all specialized cells in the body.
- Adult stem cells
  - found in infants, umbilical cords, placentas, teeth, and adult tissue
  - can renew themselves and have limited ability to differentiate into other types of cells, usually only the cell types found in their tissue of origin.
  - Little is known about adult stem cell identities, how they differentiate and mature, and their complete level of plasticity.
- Regenerative tissue engineering has many potential impacts on medicine and science.

SCID Mice

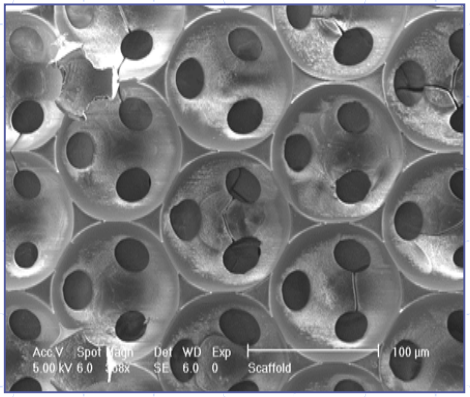
- SCID: severe combined immune deficiency
- mice are unable to make T cells or B cells
- rare and spontaneous mutation on chromosome 16.

Bone Marrow

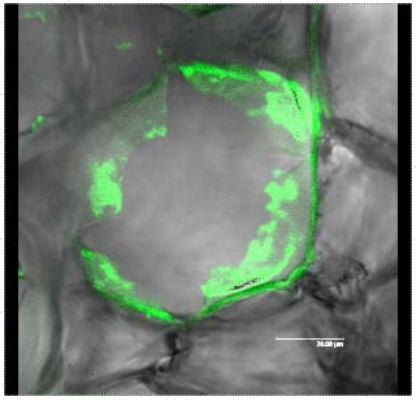
- the inner mass of a large bone
- contains two types of stem cells: hematopoietic and stromal
- matrix used was designed to be like human bone

Human bone marrow

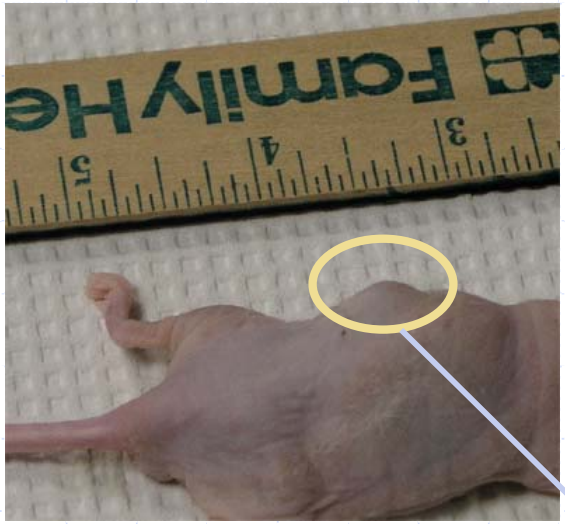
SEM ICC Scaffold

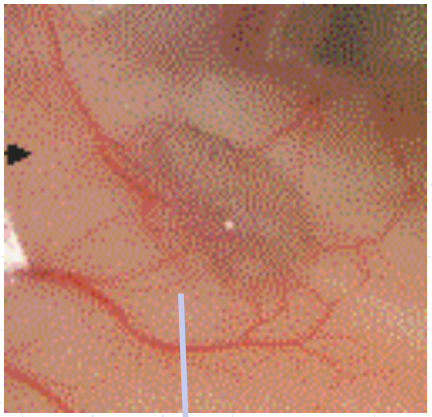


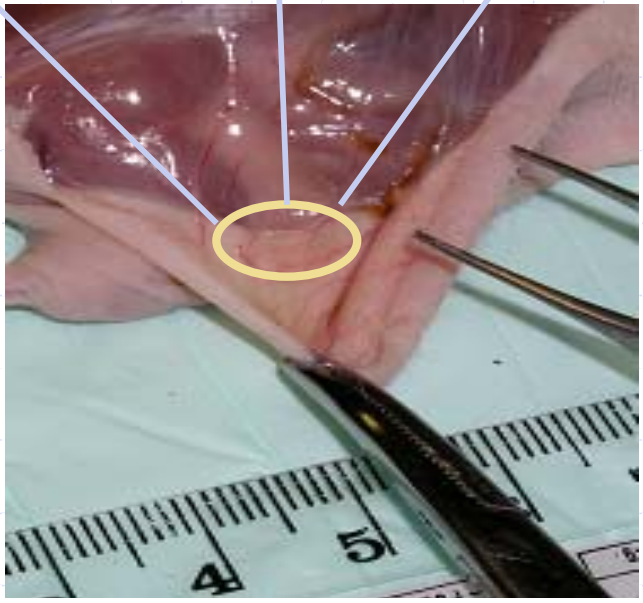
Stromal Cells on ICC Scaffold

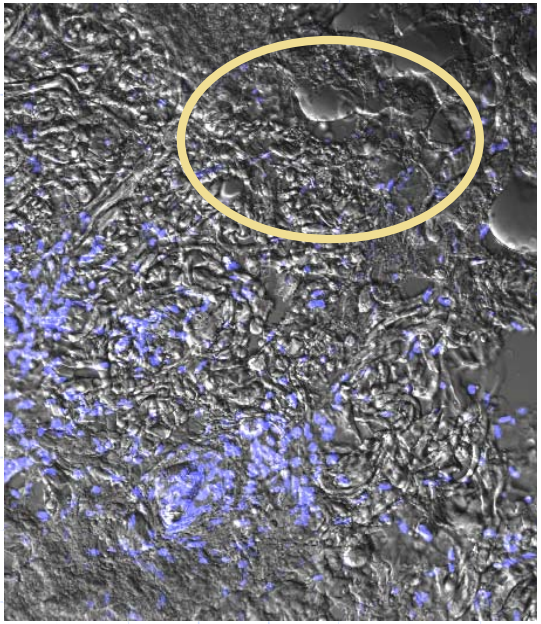


SCID B Cell Model







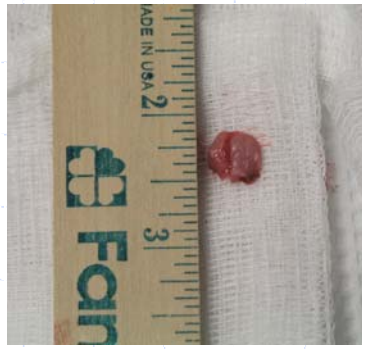


Method

SCID Mouse Model

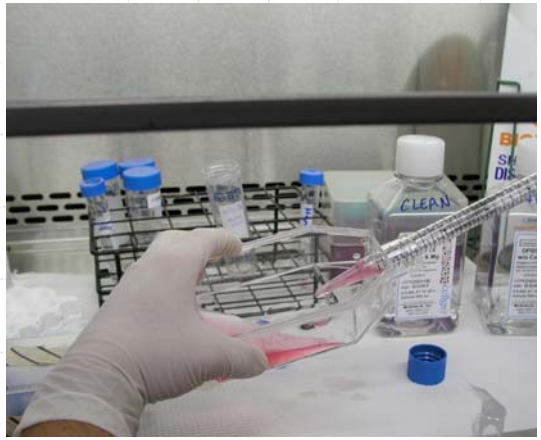
Implanted Matrix

Mouse Thymu



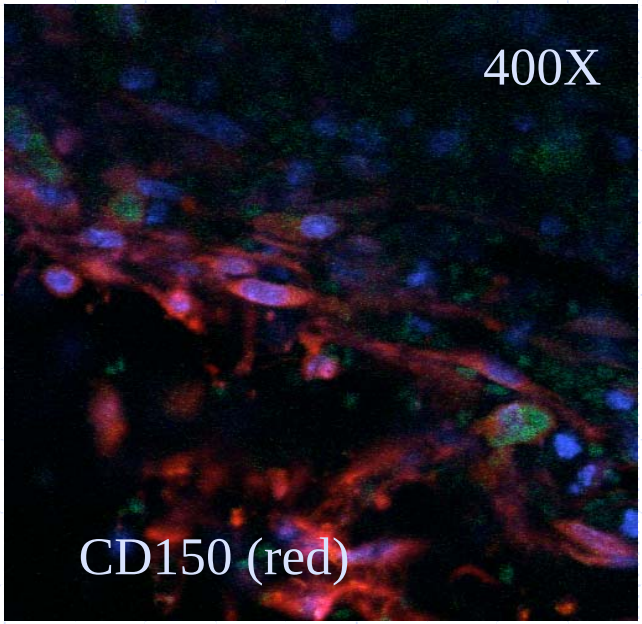
Cell Isolation from Mouse Spleen and Thymus Tissue

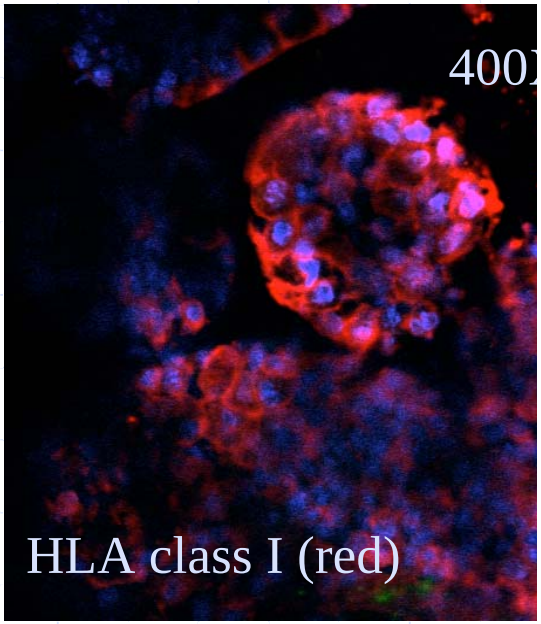
- Dissection and Chopping
- Wash PBS
- Digestion (Trypsin 0.1%)
- Trituration
- Filtration (200µm)

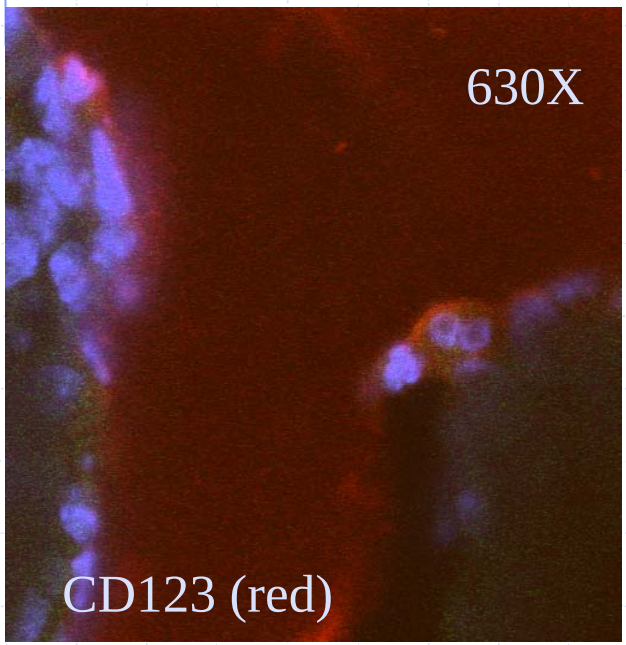


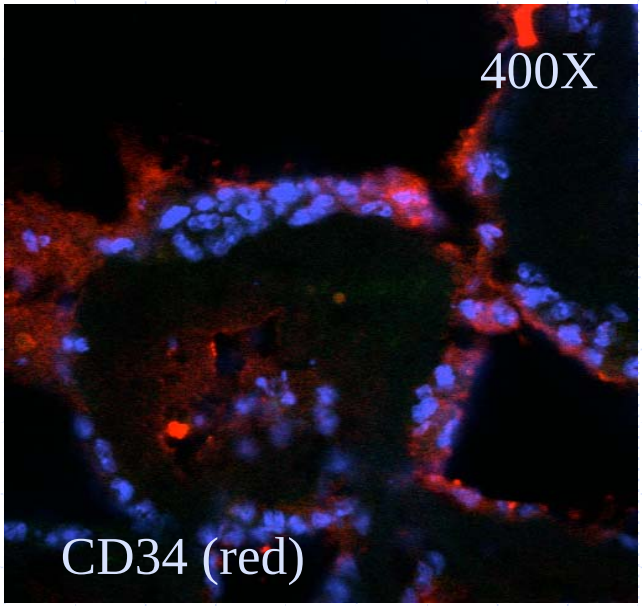
Matrix

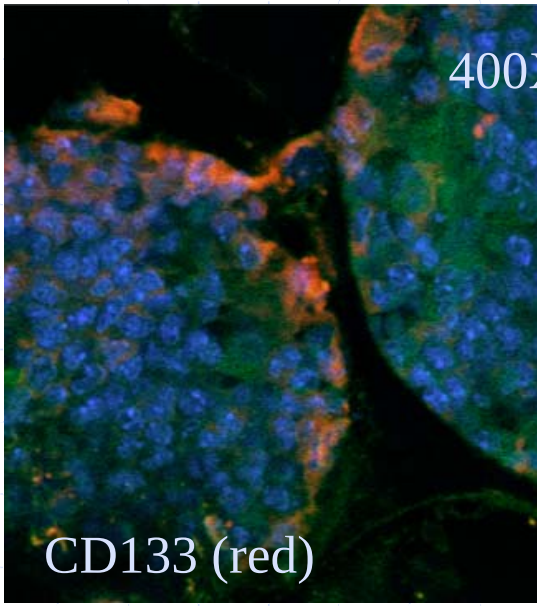
- Was seeded with CD34+/CFSE
- 7 day incubation on back of nude SCID mouse





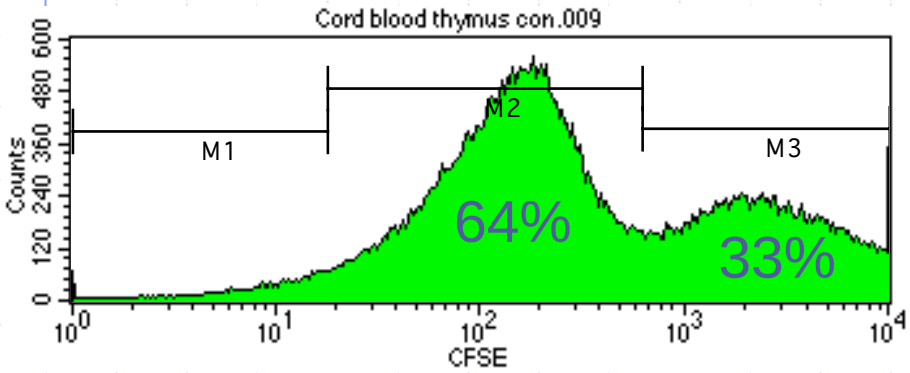


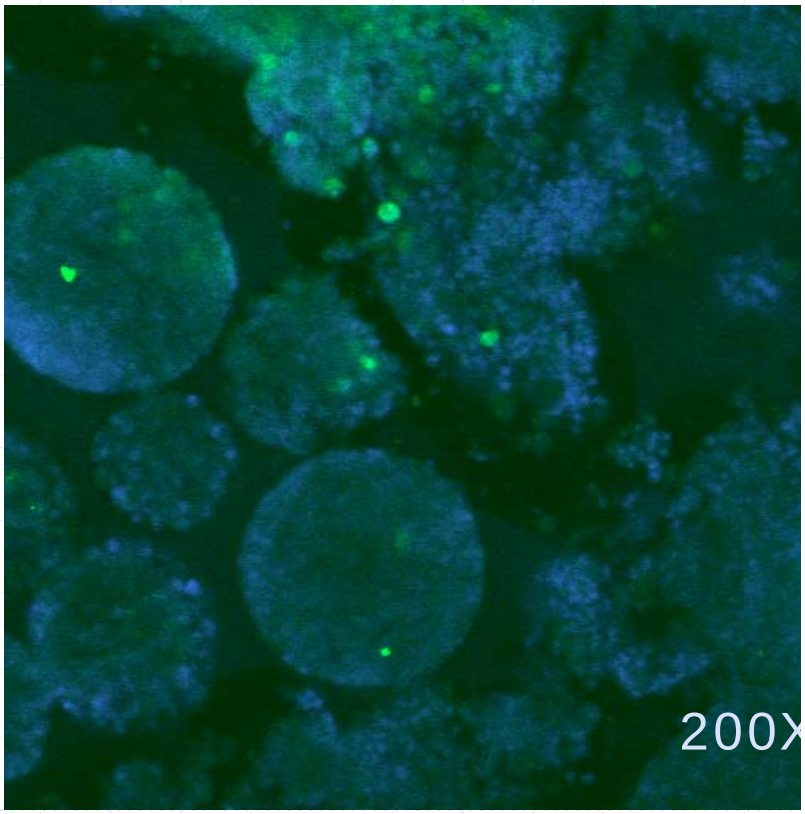




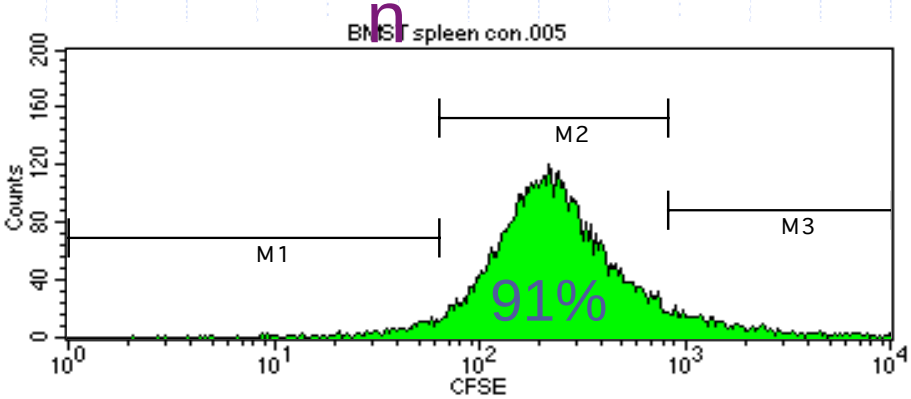
CFSE

Thymus

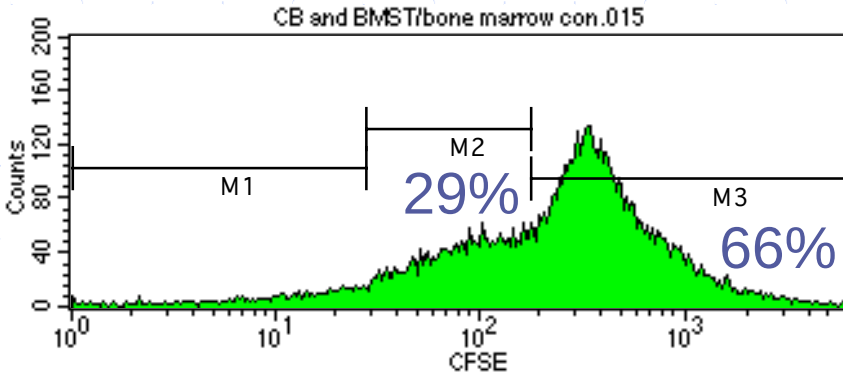




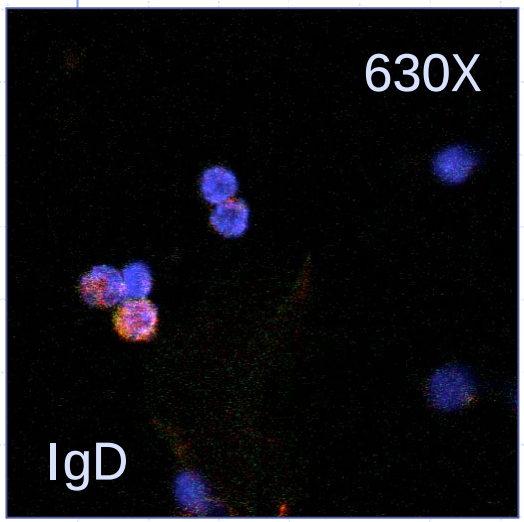
Splee n

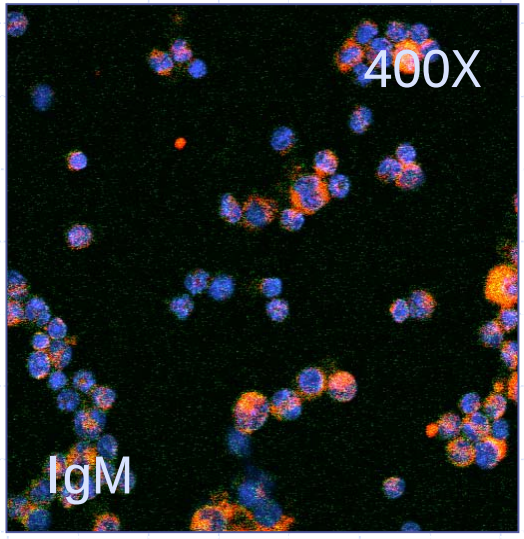


Bone Marrow



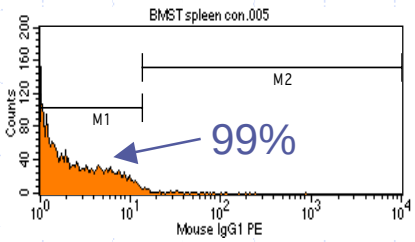
Spleen



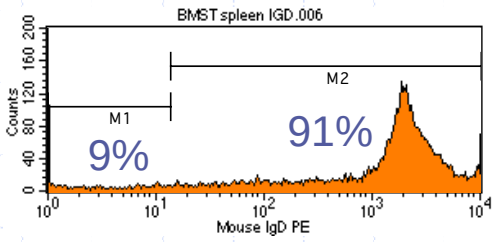


From Implanted Bone Marrow Cells

control



IgD



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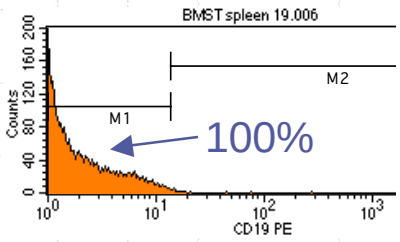

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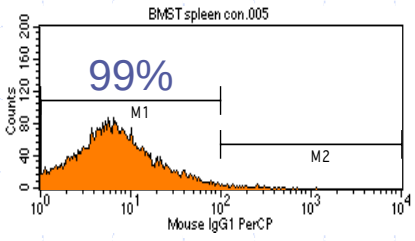

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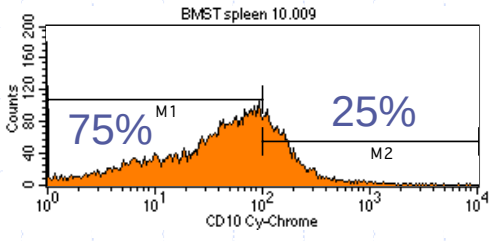

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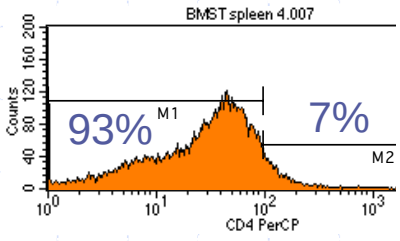
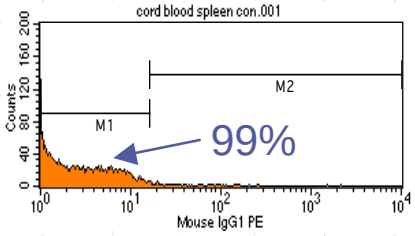


From Implanted Cord Blood Cells

control



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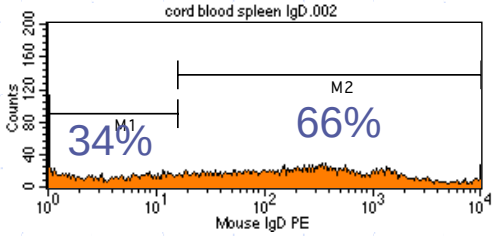

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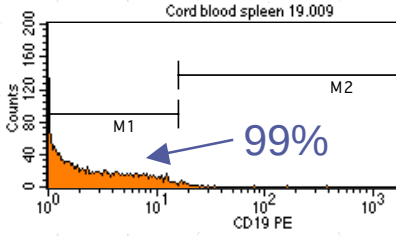

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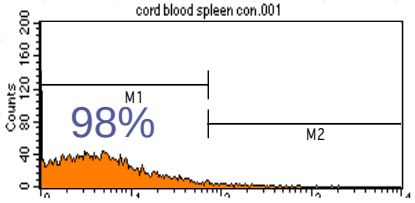

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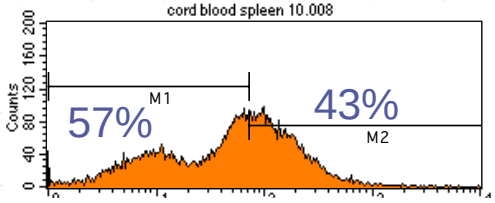

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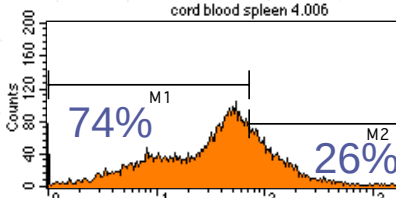
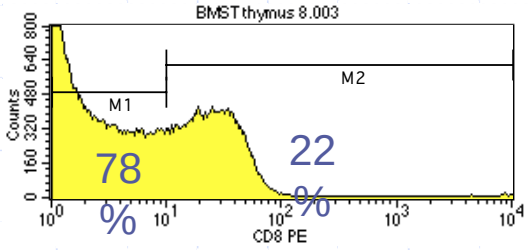


Thymus

Dissected thymus

From Implanted Bone Marrow Cells

CD8



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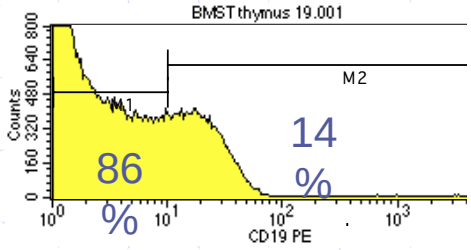

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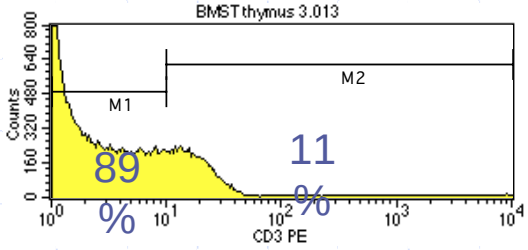

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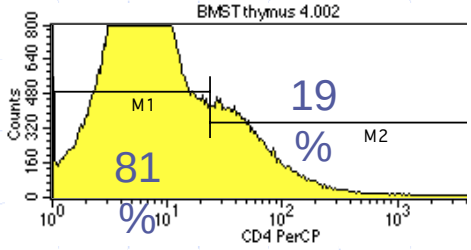
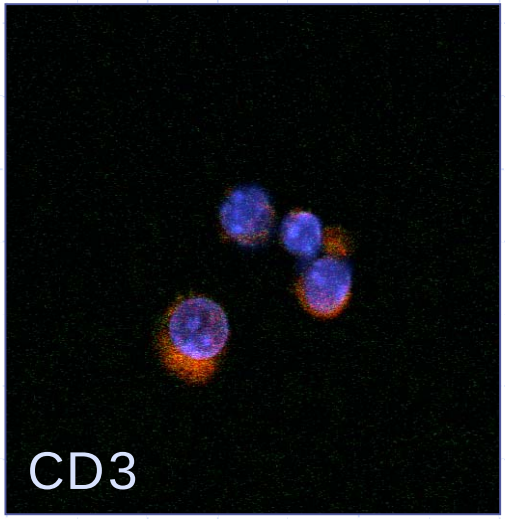


From Implanted Cord Blood Cells



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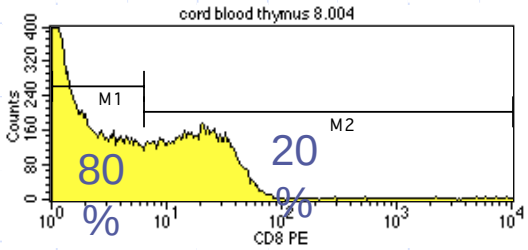

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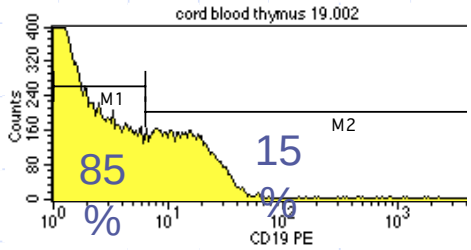

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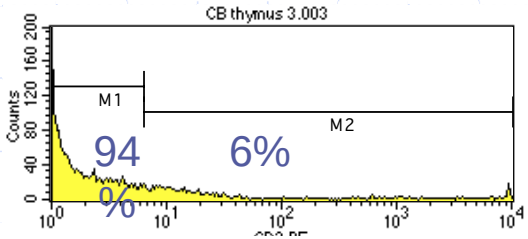

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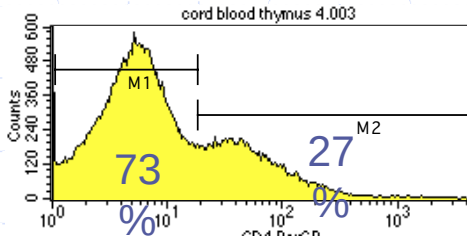

Conclusion

- This SCID mouse model created a source of mature cells and immature cells that may continue to differentiate.
- Not all of the progenitor cells differentiated and matured, making this a good source for immune cell production.
- CFSE staining showed migration of cells and exhibited the proliferation of the human cells throughout the mice.
- Many future applications of this information

References

- H.J. Rippon and A.E. Bishop. Embryonic Stem Cells. Cell Prolif., Vol 37, 23-34 (2004).
- University of California Center for Animal Alternatives http://www.vetmed.ucdavis.edu/Animal_Alternatives
- http://www.medterms.com
- http://www.stemcells.nih.gov

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