

# Prospects for cell-based therapies for ILD

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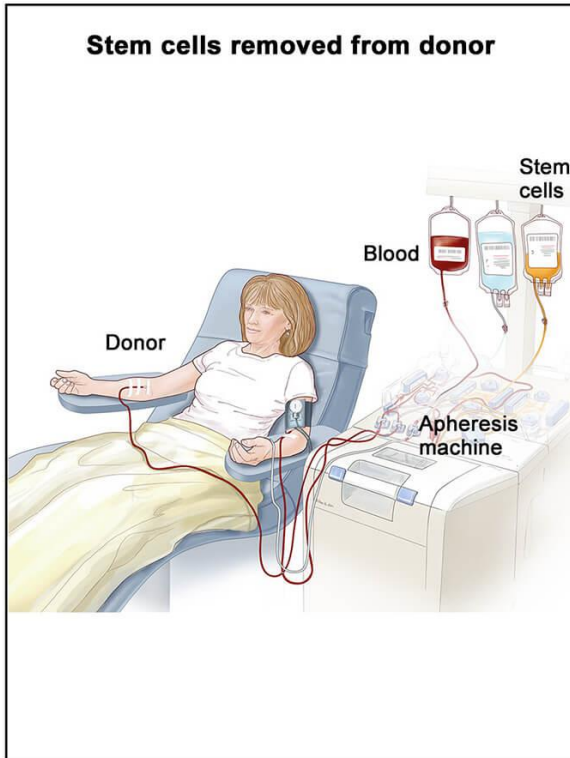
# Stem cells produce new cells

- Pluripotent stem cells:
  - Can generate cells of all types for any tissue (embryonic)
  - Can now be made from any cell from an adult person (induced)
- Adult stem cells:
  - Restricted to generating cell types for a specific tissue throughout life (normal adult physiology)
  - Dysfunction can result in diseases of aging (lose activity) or cancer (overactive)
- Adult progenitor cells:
  - Like adult stem cells but more limited capacity for making new cells
  - Dysfunction can result in cancer (e.g., leukemia)

# Stem cell diseases

- Blood stem cell failure (myelofibrosis) → anemia
- Blood progenitor cell 'overactivity' → leukemias
  
- 'stem cell transplants' = blood stem cell transplants
- Mainstay of modern medicine
  
- Leukemia: purify patient's own stem cells from blood, give chemotherapy to kill diseased progenitor and cancer cells, then infuse back blood stem cells
- Sickle cell anemia: collect blood stem cells from suitable donor, give chemotherapy to kill patient's stem cells, then transfuse donor blood stem cells
  - \*\* Immune suppression to prevent immune cells generated by donor stem cells from attacking patient tissues!

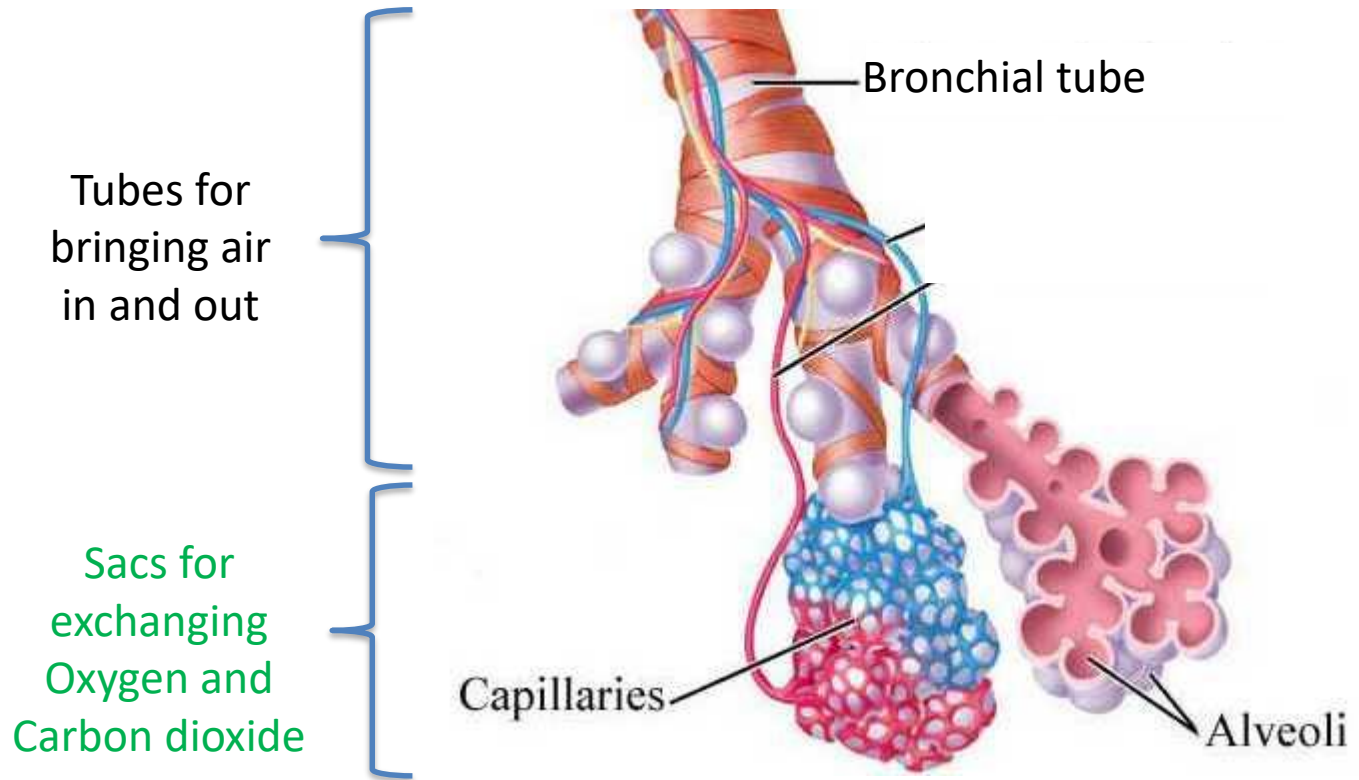
# Donor blood stem cell transplant



# Self versus Other

- Immune system
  - Recognizes ‘non-self’ cells and attacks them
- Re-transplanting your own stem cells:
  - Ideal because no need to suppress your own immune response
  - Sickle cell anemia → purify patient stem cells, use gene-editing to correct mutation in DNA, use chemotherapy to kill residual patient stem cells, then transfuse in “corrected” stem cells
- Transplanting in donor stem cells from another person:
  - Blood stem cells: Suppress foreign immune cells generated by donor blood stem cells from attacking you!
  - Non-blood stem cells: Immune suppression needed to prevent your own immune cells from killing the donor cells (but no worry about donor cells attacking you)

# Lung stem cells

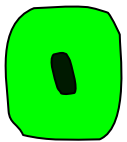


# Two types of cells in the air sacs



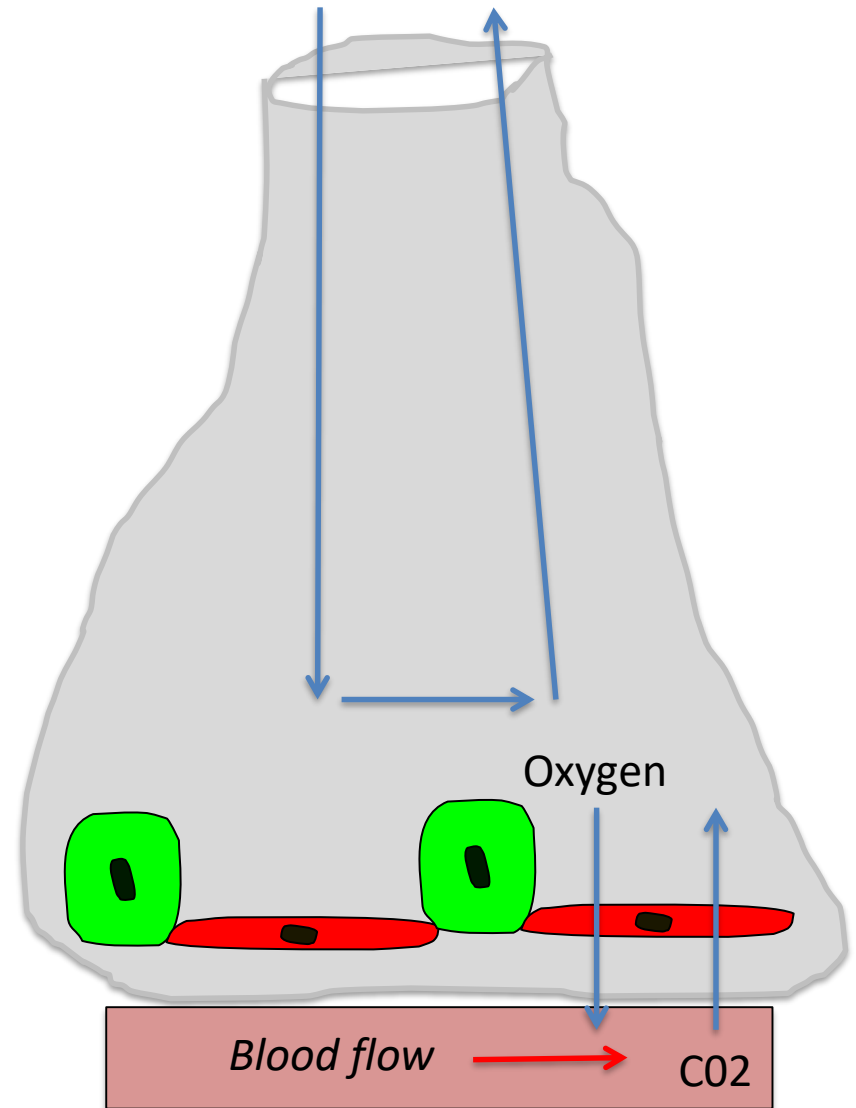
#1

Very thin barrier



#2

Detergent

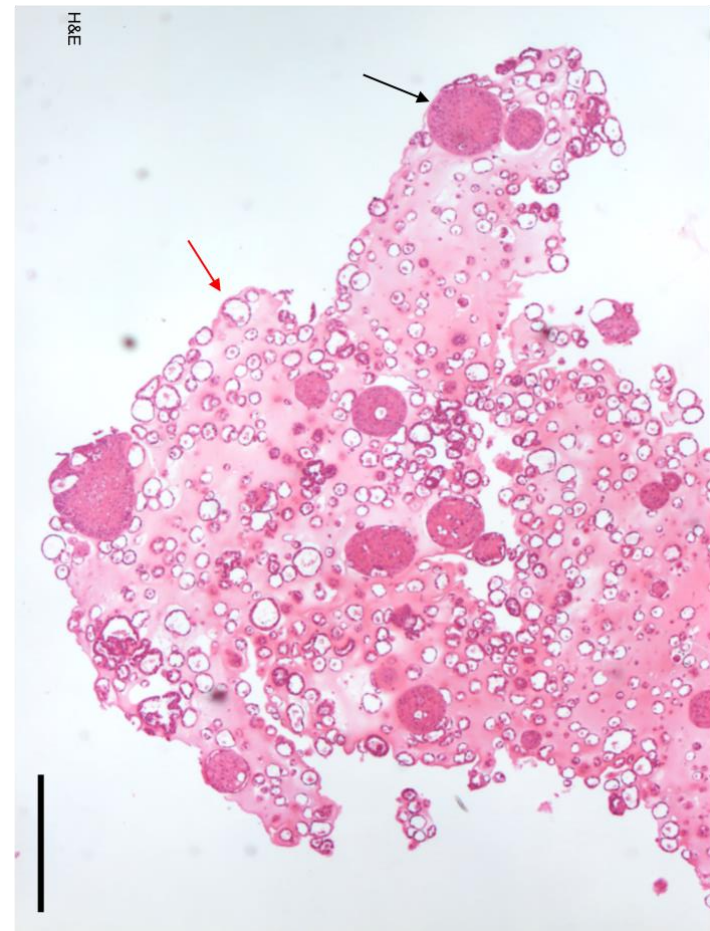
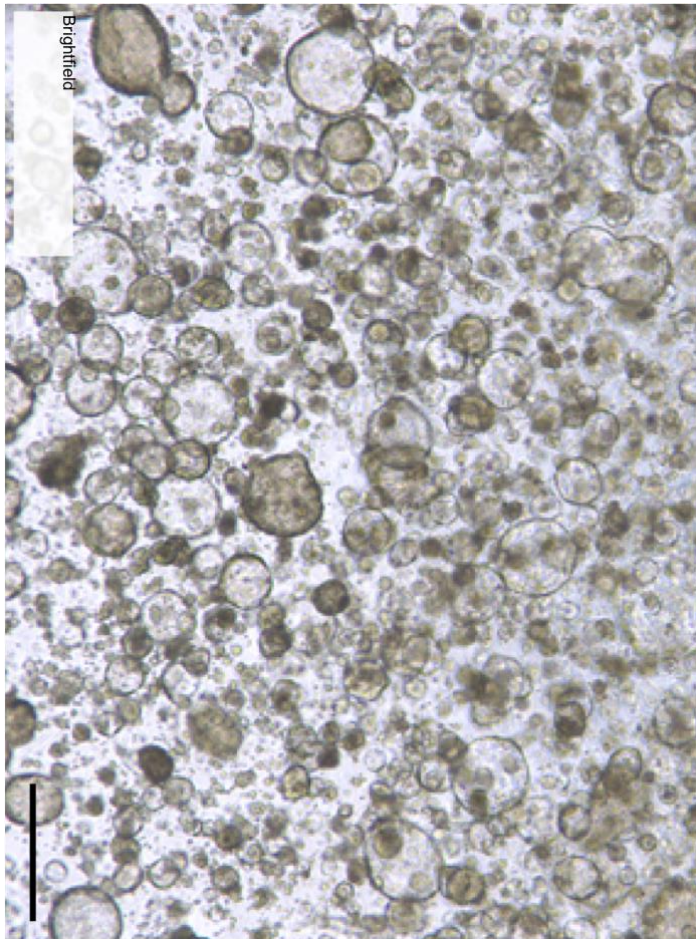
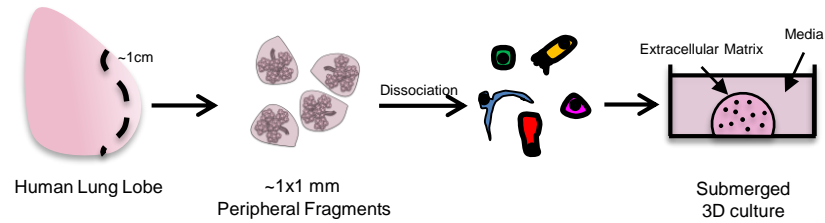


# IPF may be a stem cell disease!

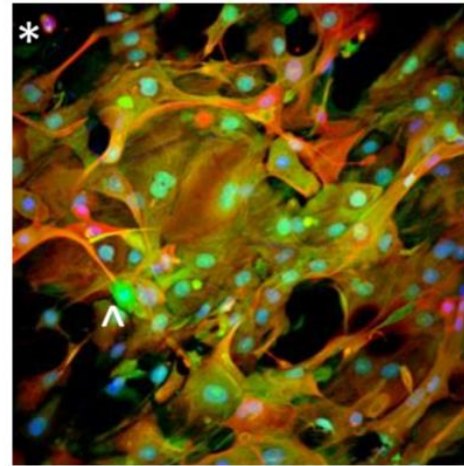
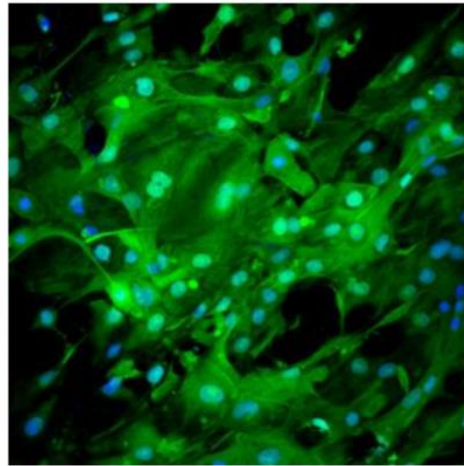
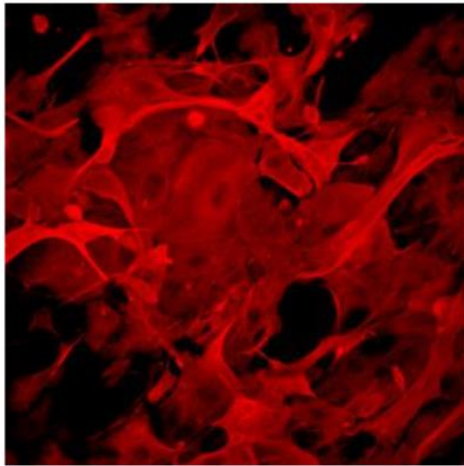
- The good:
  - Lung is easy to access (by bronchoscopy)
  - Disease is very active, so even halting progression may be very helpful
  - Stem cells could reduce severity of “flares”
- The bad:
  - How to get rid of defective stem cells without making patients sick?
- The unknown:
  - After engraftment, will they remain healthy and active?
  - Which is more feasible, adult versus pluripotent derived cells and self versus other?



# Human lung stem cells grown in the lab



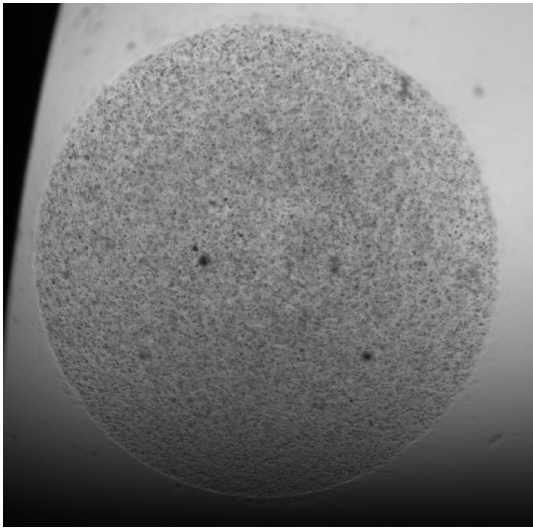
# Correcting cystic fibrosis airway stem cells for re-plantation



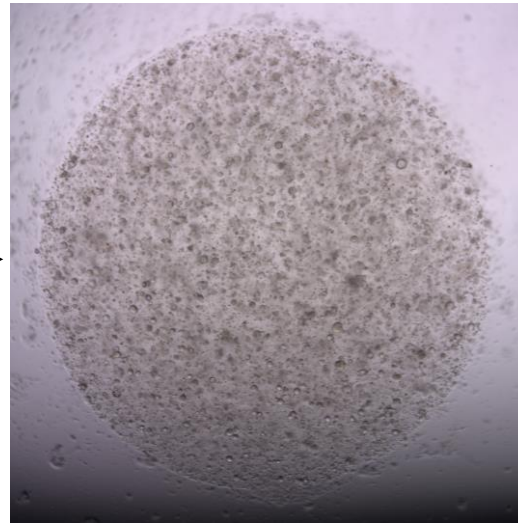
Krt5  
Calcein Green  
Hoescht

Airway stem cells

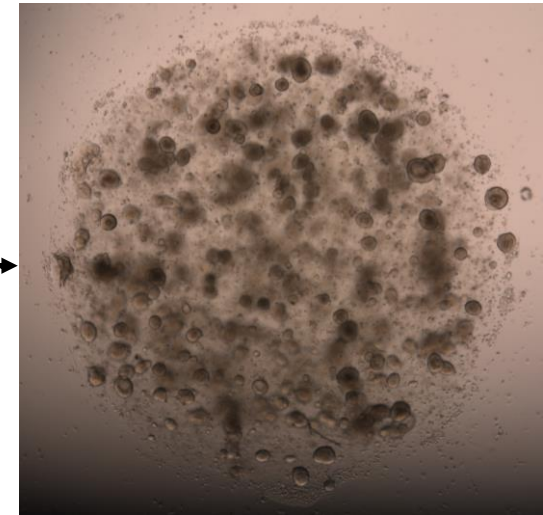
# Cells from an IPF patient's lungs grown in lab!



Day 2



Day 5



Day 8

# Summary

- IPF may be a bona fide lung stem cell disease
- Researchers are developing ways to collect and expand lung stem cells for transplantation
- The best source of stem cells (pluripotent versus adult) is not clear
- Hopefully coming down the pike!