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

Tubes for bringing air in and out

Sacs for exchanging Oxygen and Carbon dioxide
Two types of cells in the air sacs

#1  Very thin barrier

#2  Detergent

Blood flow  C02

Oxygen
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-transplantation

Airway stem cells
Cells from an IPF patient’s lungs grown in lab!
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!