



Dr Rob Young

General Physician
Auckland City Hospital

Stem Cells and The Lung - Main Session

Friday, 21 June 2013

Start 5:30pm

Duration: 20mins

Baytrust



Rotorua GP CME 2013

NZMA
New Zealand Medical Association

General Practice Conference & Medical Exhibition

20-23 June 2013 | Energy Events Centre | Rotorua

Stem Cell therapy in COPD

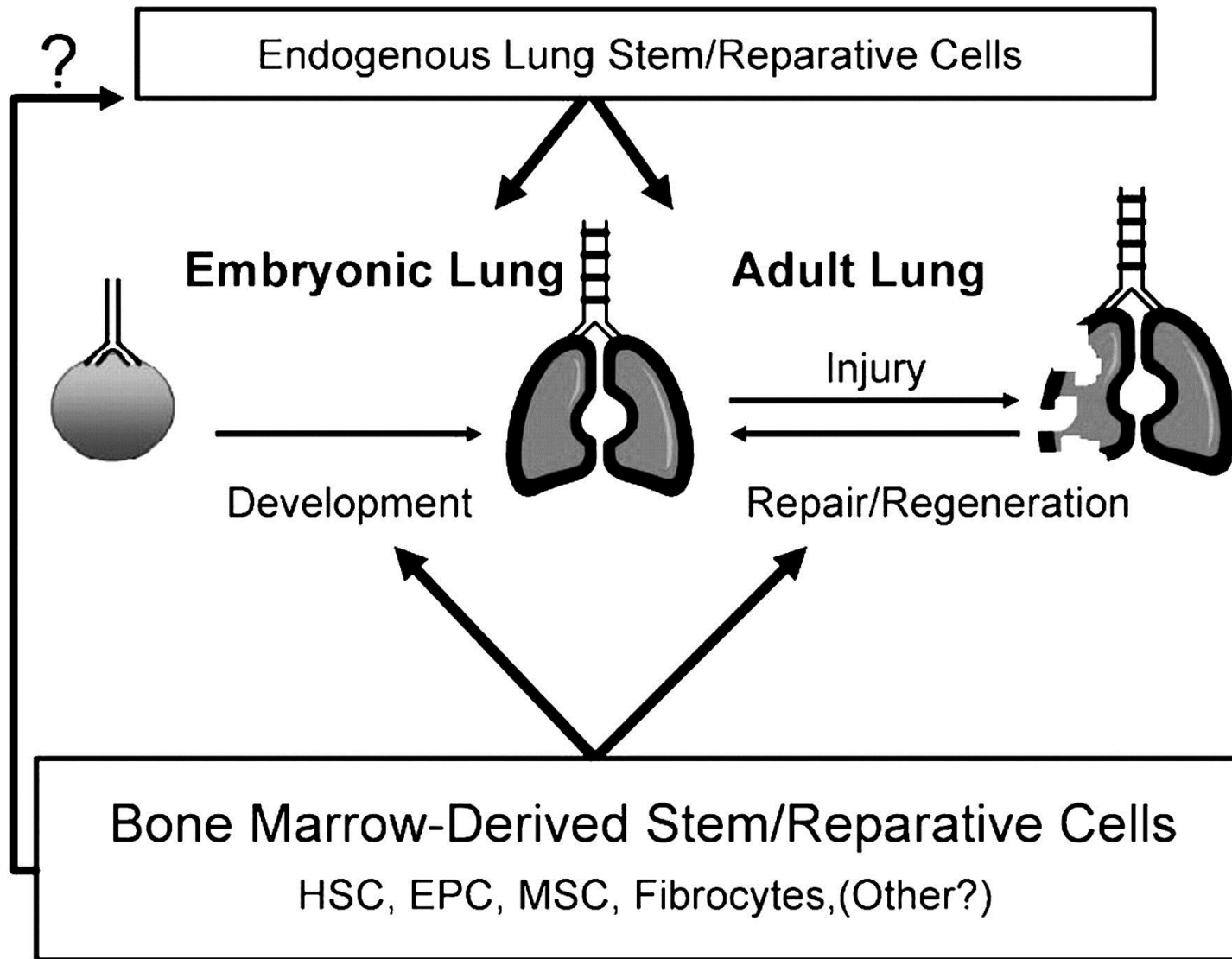
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THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

Stem Cells and the lung



NEJM 2011

Endogenous Lung stem cells described for the 1st time

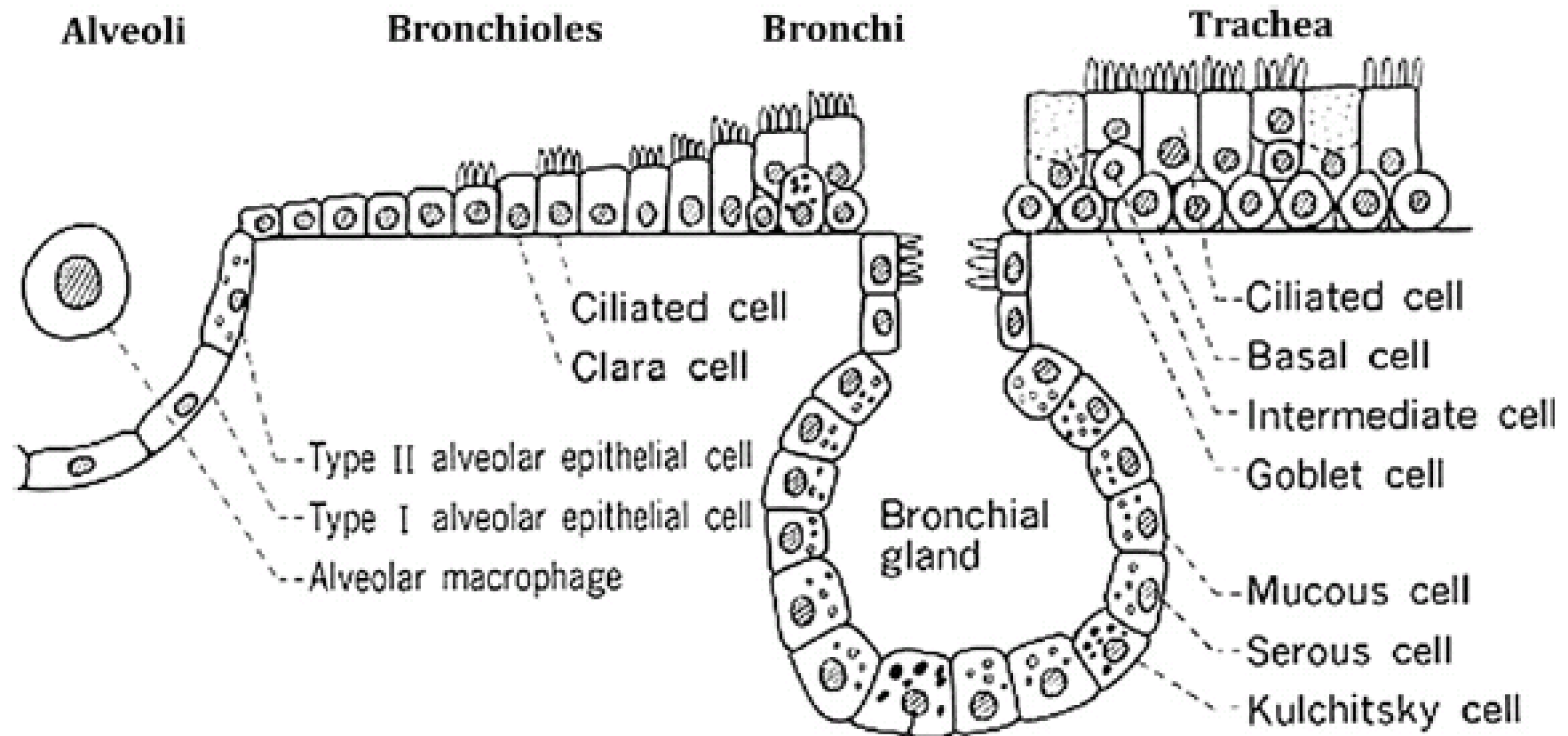
Cells could regenerate into epithelial, structural and vascular tissues

Self Renewal

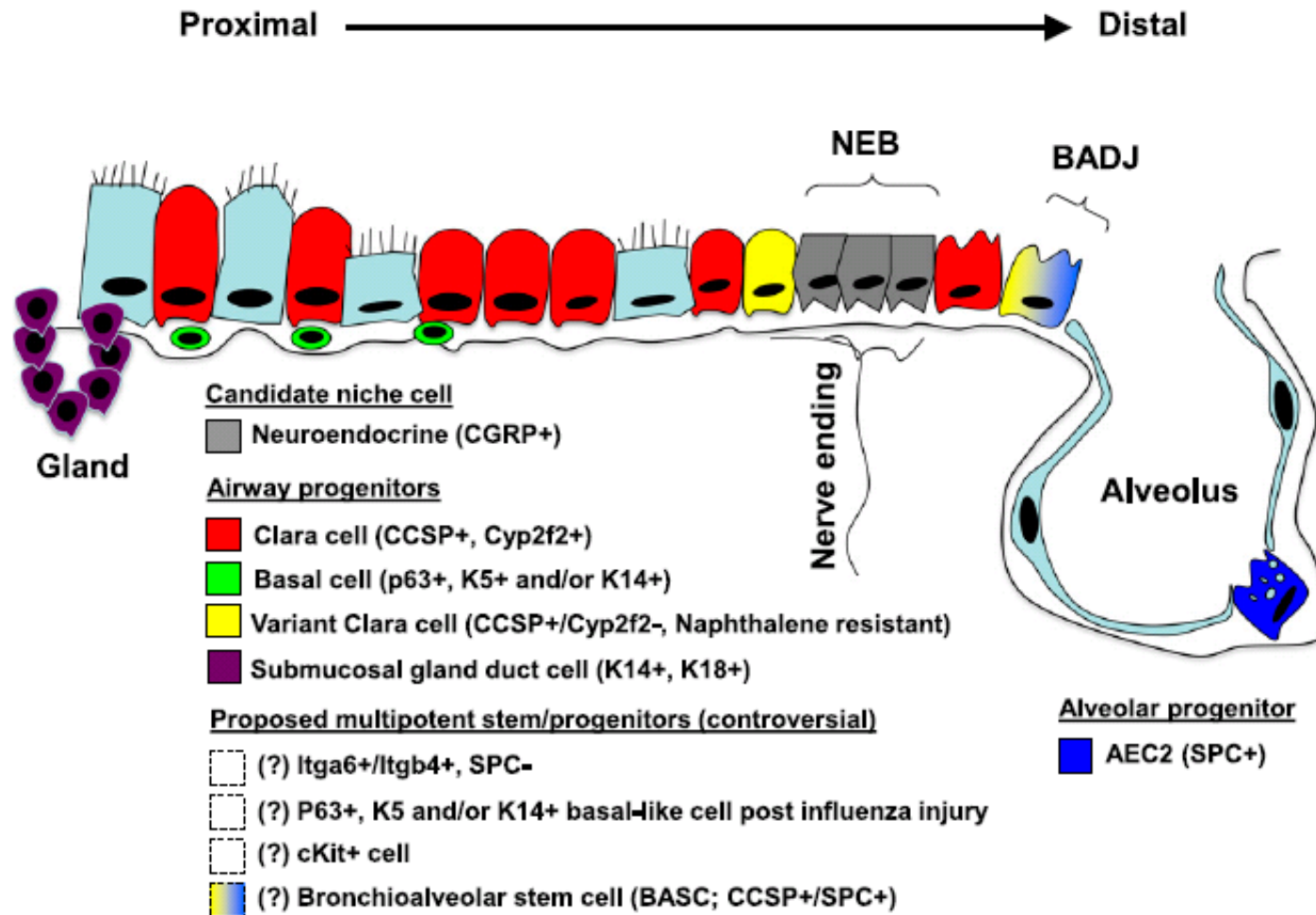
Clonogenicity

Multipotentiality

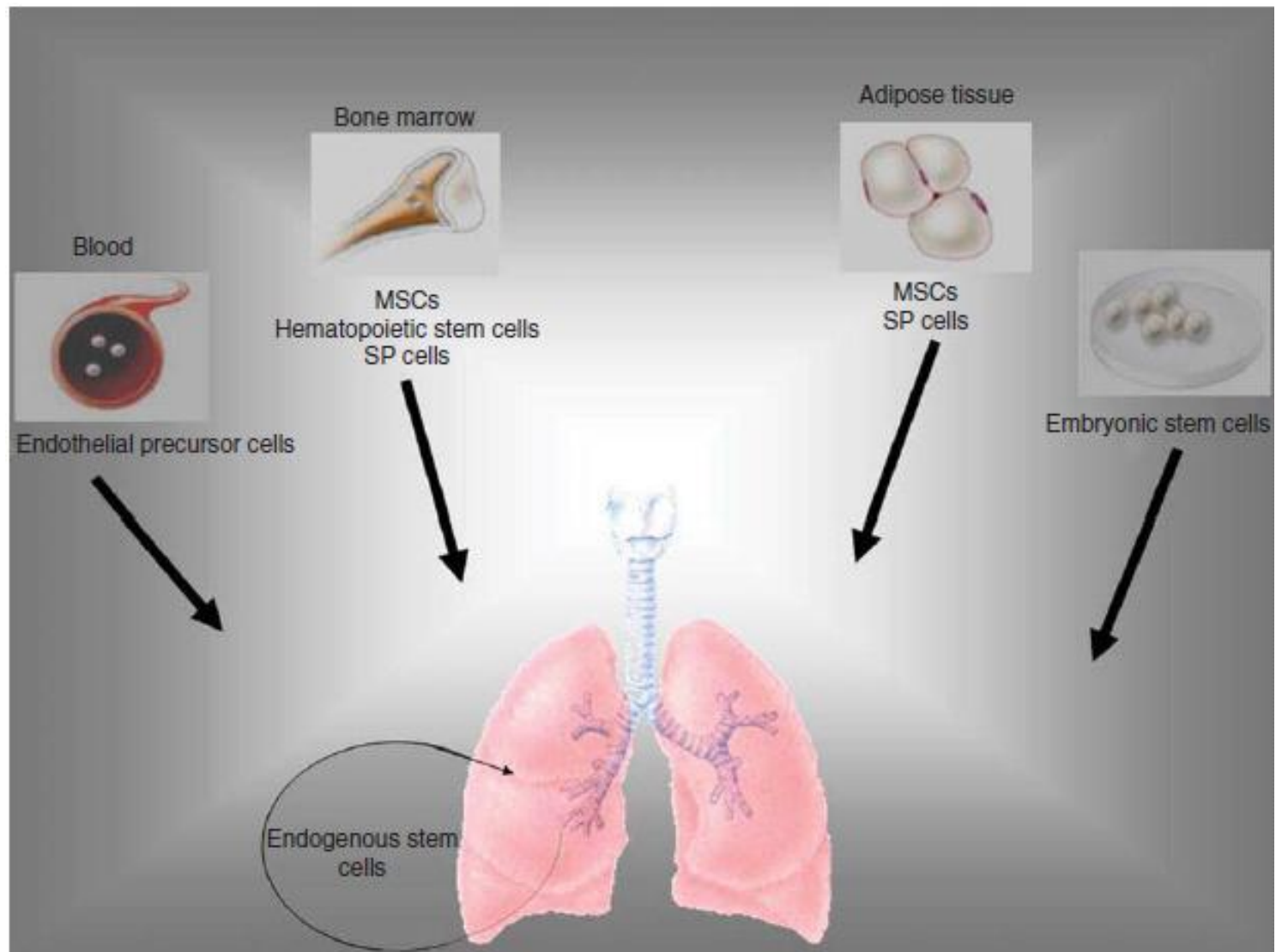
The lung is complex – 40 different cell types



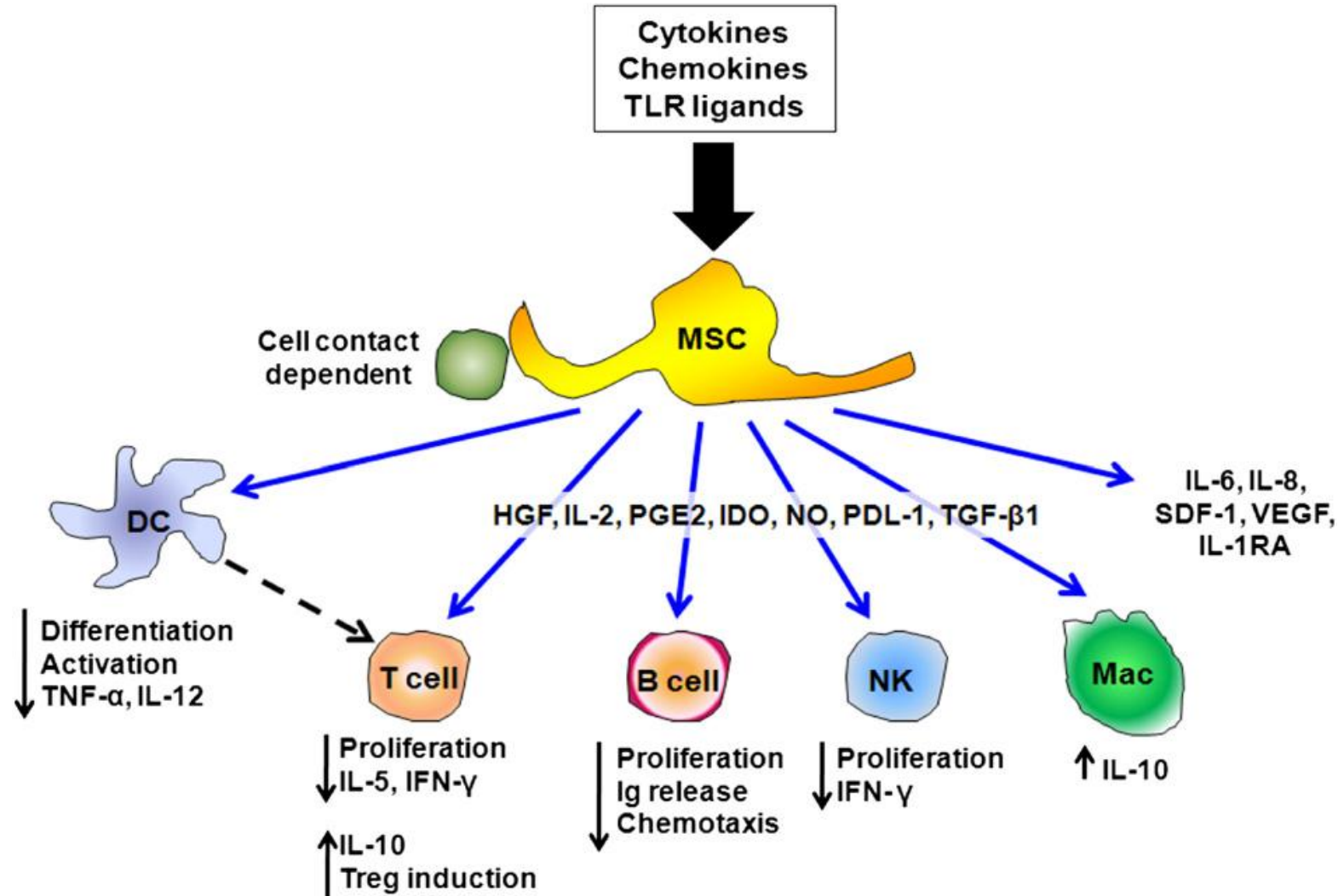
Endogenous Stem Cells in the Lungs

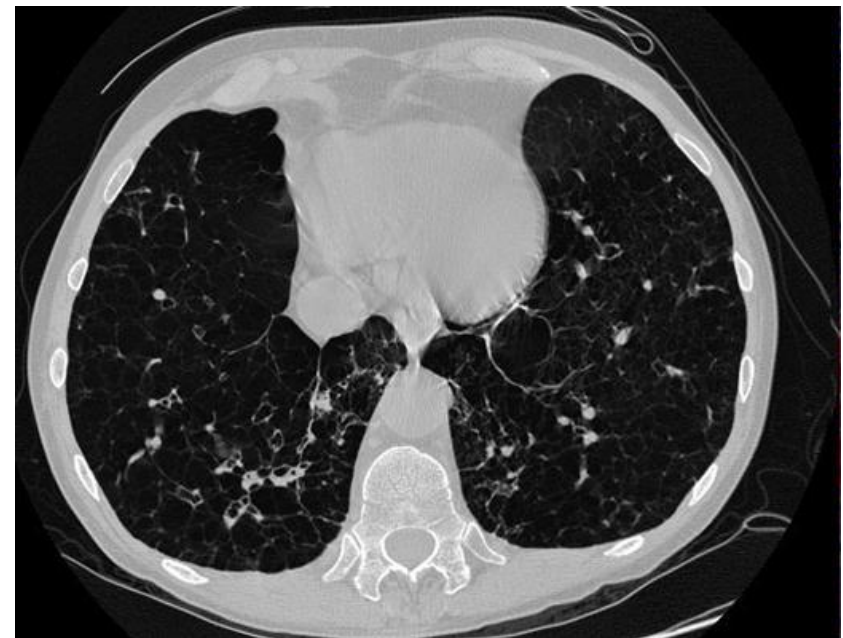
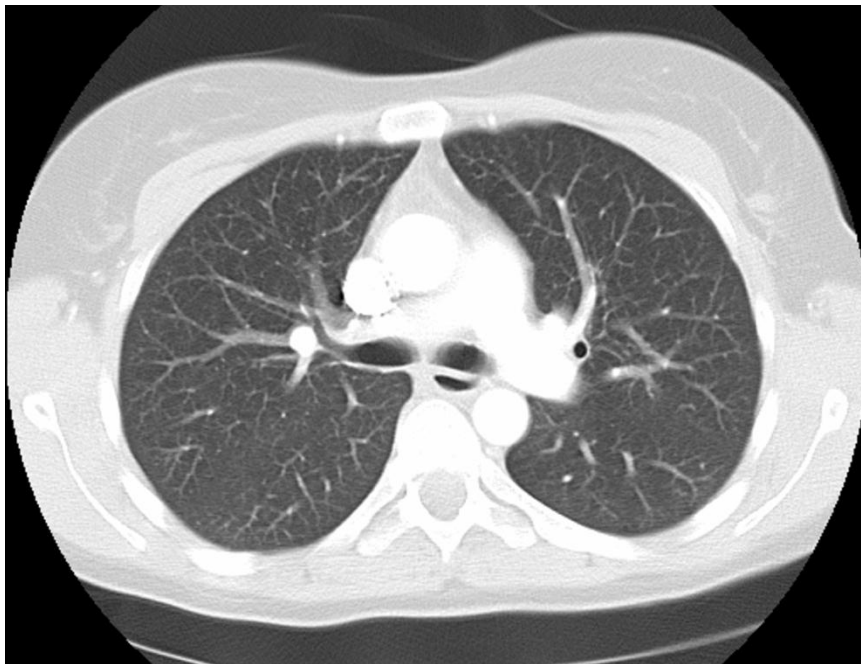
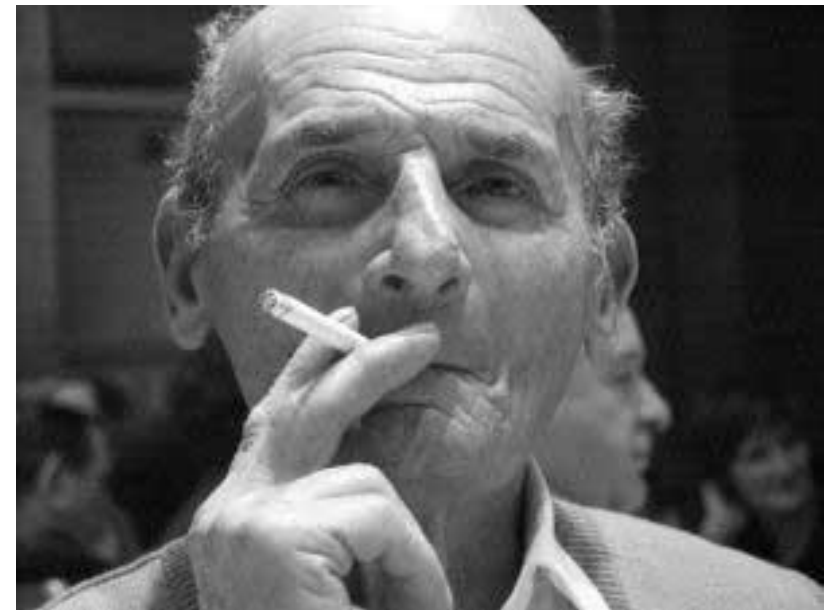
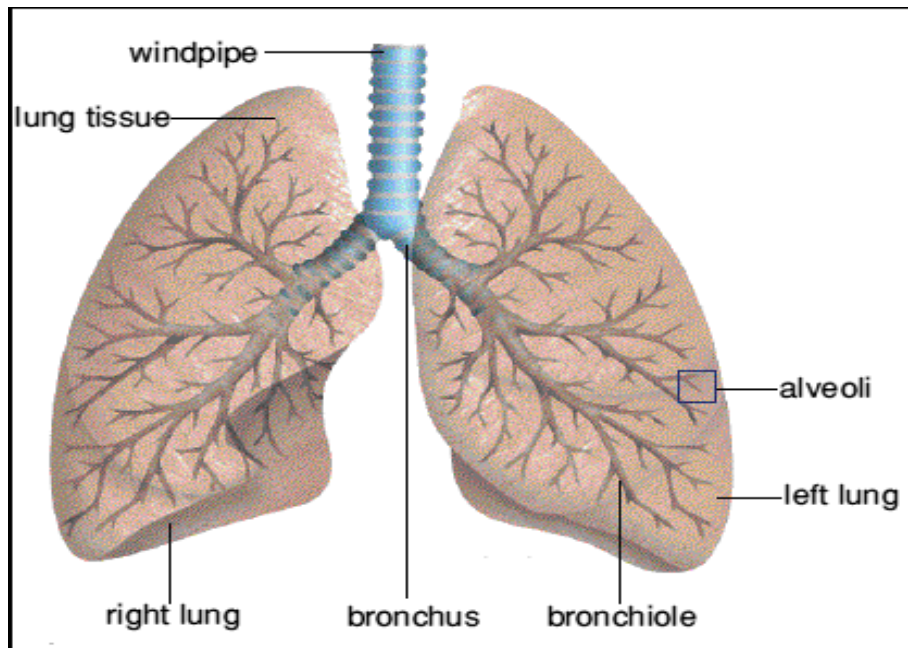


Stem Cell therapy and the Lungs



Pluripotent Mesenchymal Stem Cell





Stem Cell therapy in animal models of COPD



Stem Cell therapy in animal models of COPD

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Stem Cell therapy in animal models of COPD



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Stem Cell therapy in animal models of COPD



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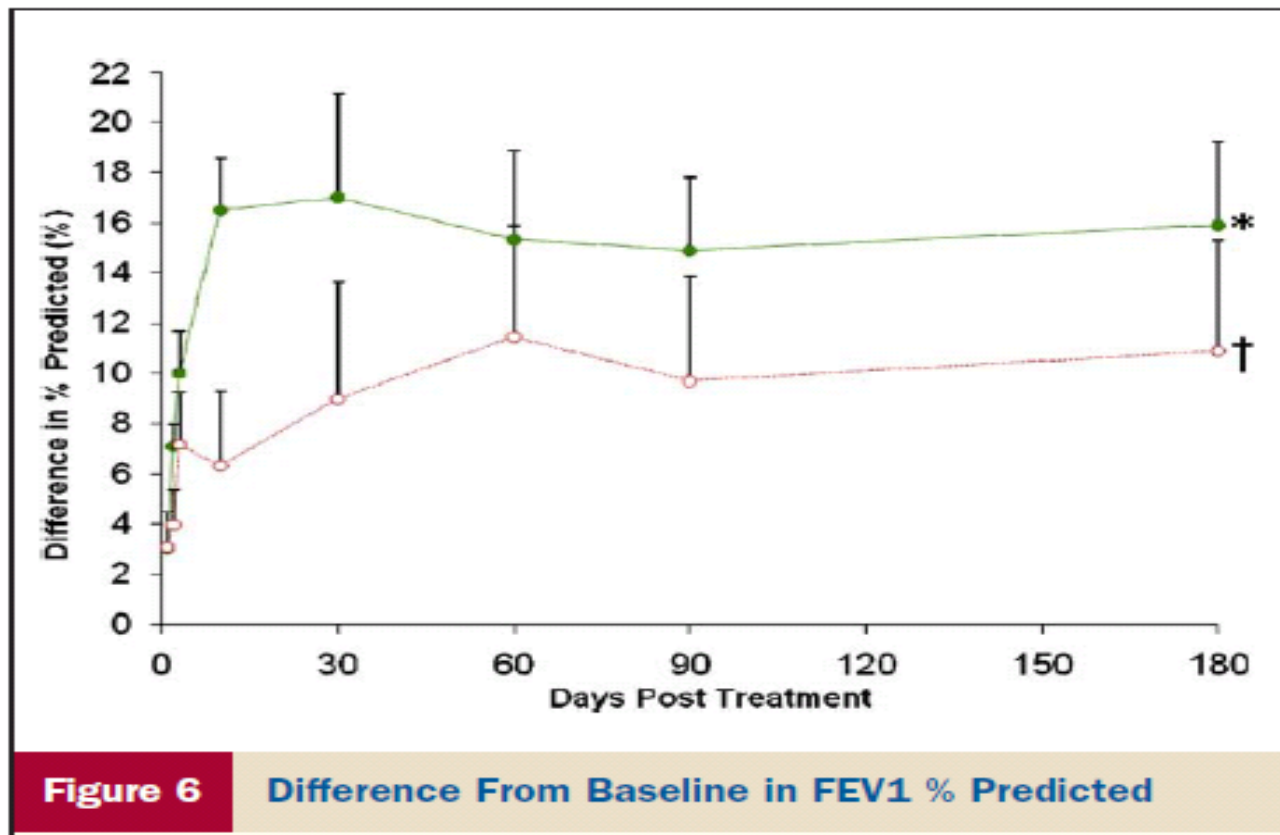
MSC have low immunogenicity (low expression of HLA class molecules) and anti-inflammatory immune-modulatory effects.

Stem Cell therapy and limitations of animal studies

- They're in animals (not humans)
- The exposure is often short and intense and not representative of the chronic smoking effect
- The lung injury model is generally acute lung injury rather than long term inflammation with remodeling and acute exacerbations

Stem Cell therapy in human studies

- 2009: MSC were infused into humans within 10 days of a myocardial infarction and FEV₁ improved up to 6 months later compared to the control group (JACC 2009, Hare et al. N=53)



Rationale for Stem cells in COPD

- Multipotent Cells isolated from bone marrow and adipose tissue (allogeneic with low immunogenicity)
- Known anti-inflammatory and immune-modulatory effects by secreting epithelial and endothelial growth factors
- Rodent models of acute lung injury from smoking showed stem cells blocked the development of emphysema

Mechanisms leading to SC benefit in COPD

1. Transplants of the cells may build healthy lung tissue that is diseased or has been destroyed in COPD patients.
2. Stem cells could in theory reduce inflammation in the airway alveoli (where respiration occurs) preventing further damage and perhaps tipping the balance toward natural repair. Stem cells may do this through so-called “immunomodulation” functions, perhaps via growth factors.
3. Stem cells may stimulate the formation of new capillaries in the lung leading to tissue repair and better function.

RCT of Stem Cells in COPD



CHEST

Original Research

COPD

A Placebo-Controlled, Randomized Trial of Mesenchymal Stem Cells in COPD

Daniel J. Weiss, MD, PhD; Richard Casaburi, PhD, MD, FCCP; Robin Flannery; Michelle LeRoux-Williams, PhD; and Donald P. Tashkin, MD, FCCP

June 2013

RCT of Stem Cells in COPD

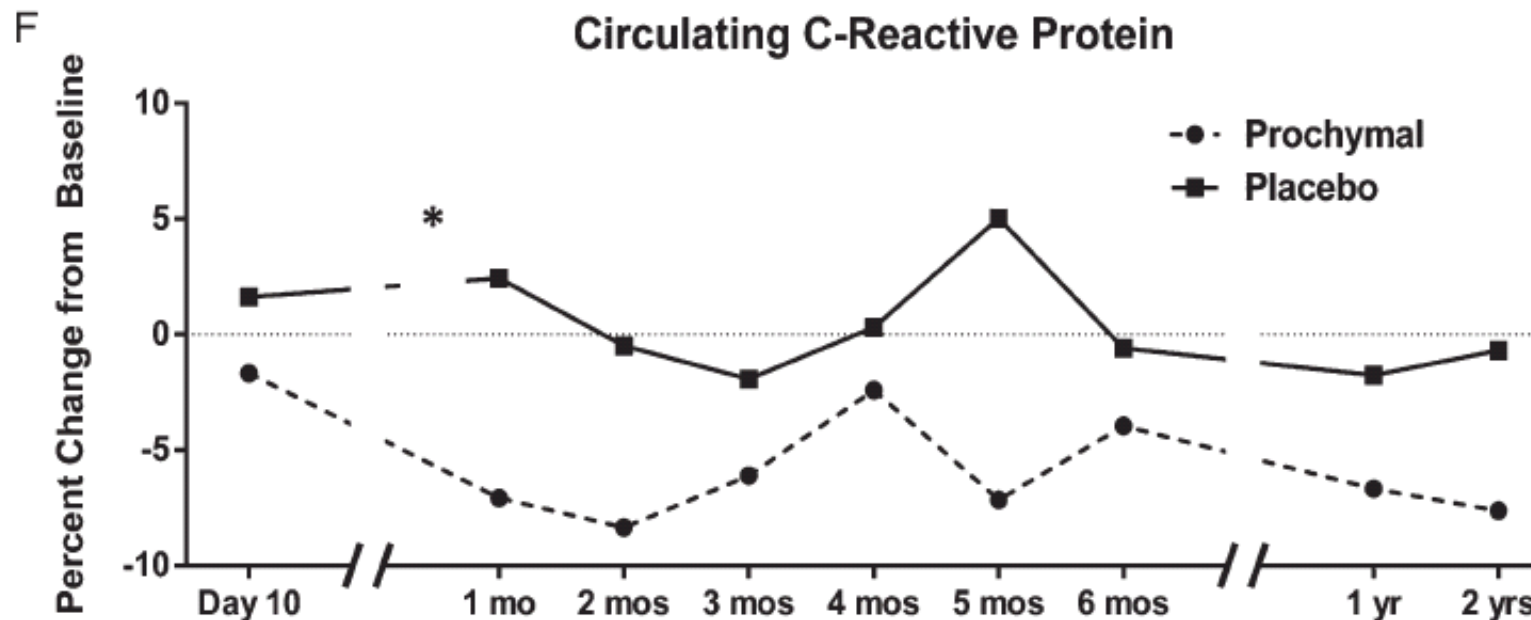
- Multicentre study of 62 patients with moderate (GOLD 2-3) COPD based on spirometry
- Monthly infusions of allogeneic mesenchymal stem cells (MSC) or vehicle control for 4 months
- Followed for 2 years with assessment of symptoms, serum markers and physiological testing (spirometry and 6 minute walk tests)

RCT of Stem Cells in COPD - results

- No toxicity issues, deaths or adverse reactions
- Protocol completion was 100% in treatment group and 74% in placebo group.
- No increase in adverse events, infective exacerbations or disease progression in the MSC treatment group
- Compared to placebo, no difference in symptoms (QOL) and pulmonary function tests

RCT of Stem Cells in COPD - results

- In patients with elevated CRP at baseline (N=29/62), there was a sustained reduction in CRP level in the MSC group of about 5-10%



Stem Cell therapy and long term safety data

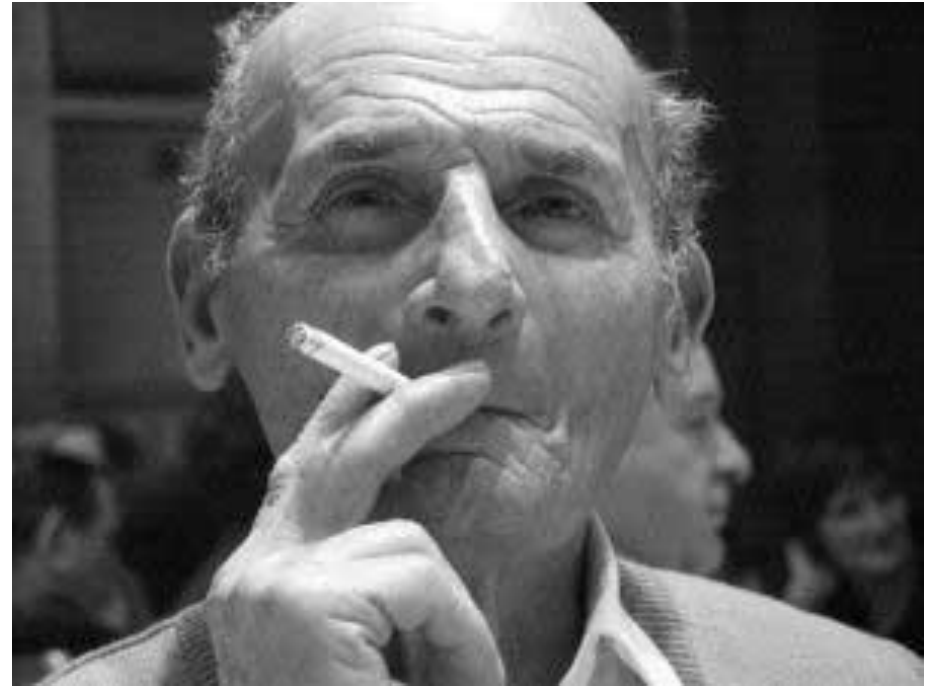
- Stem Cell efficacy uncertain with respect to dosing, dosing frequency and disease modifying effect
- Theoretical concerns relate to
 - Neoplasia
 - Infections
 - Zo-onoses (Prion disease from the cell culture reagents)
 - Cell rejection/inflammation
 - Pulmonary thromboembolism
- Studies to date suggest MSC infusions are well tolerated (transient fever sometimes noted)

Stem Cell Therapy in Acute Lung Injury

Mesenchymal Stem Cell function....

- anti-inflammatory and immune-modulatory effect lowering inflammatory cytokines
- increase bacterial clearance through more efficient macrophage activity
- improved lung repair and ability of MSC to differentiate into mature cells.

?Benefit from MSC paracrine factors and not engraftment with regeneration of tissue as such.



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