Stem Cell Therapy for *"Permanent"* Stroke

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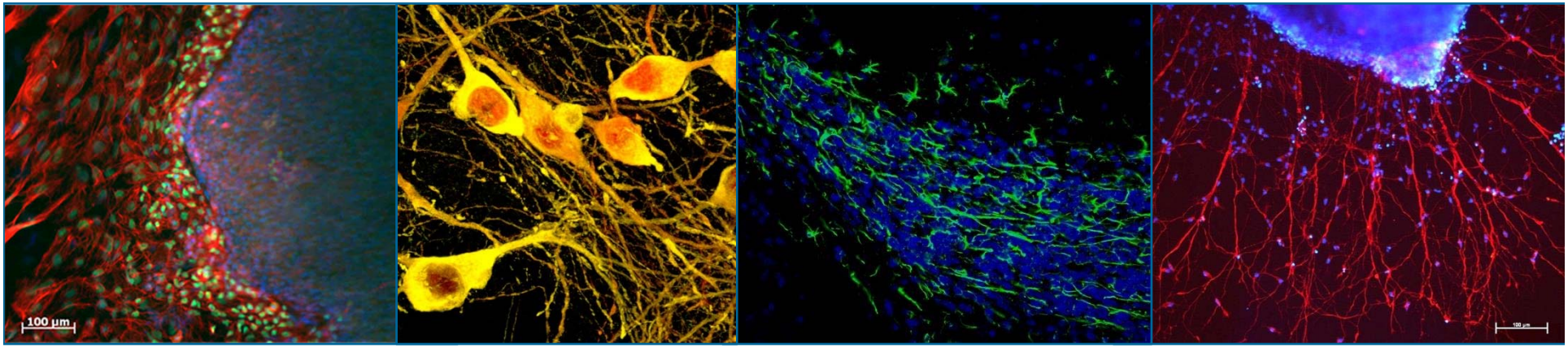
Outline

- Stem cell overview
- Review of stem cell therapies
- Stem cell therapies in stroke



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What is a stem cell?

A stem cell is a primitive cell capable of:

- self-renewal
- conversion to more differentiated cells
- proliferation
- leading to regeneration of tissues

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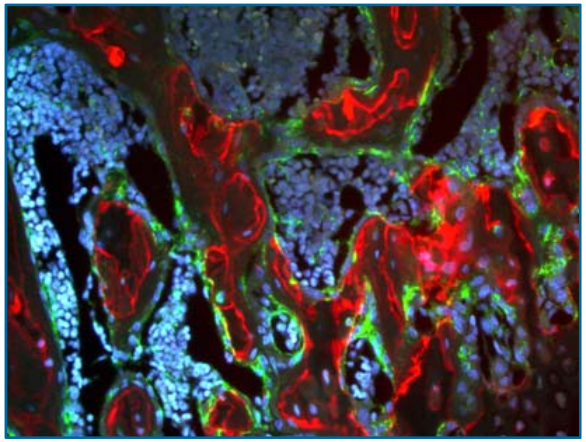
Tissue specific stem cells

often called “adult” or somatic stem cells but also includes stem cells isolated from fetal tissues and umbilical cord blood
involved in tissue homeostasis and repair
generally multipotent
difficult to isolate and grow in large numbers in the laboratory



Bone marrow

HSCs CD34+

MSCs CD34-

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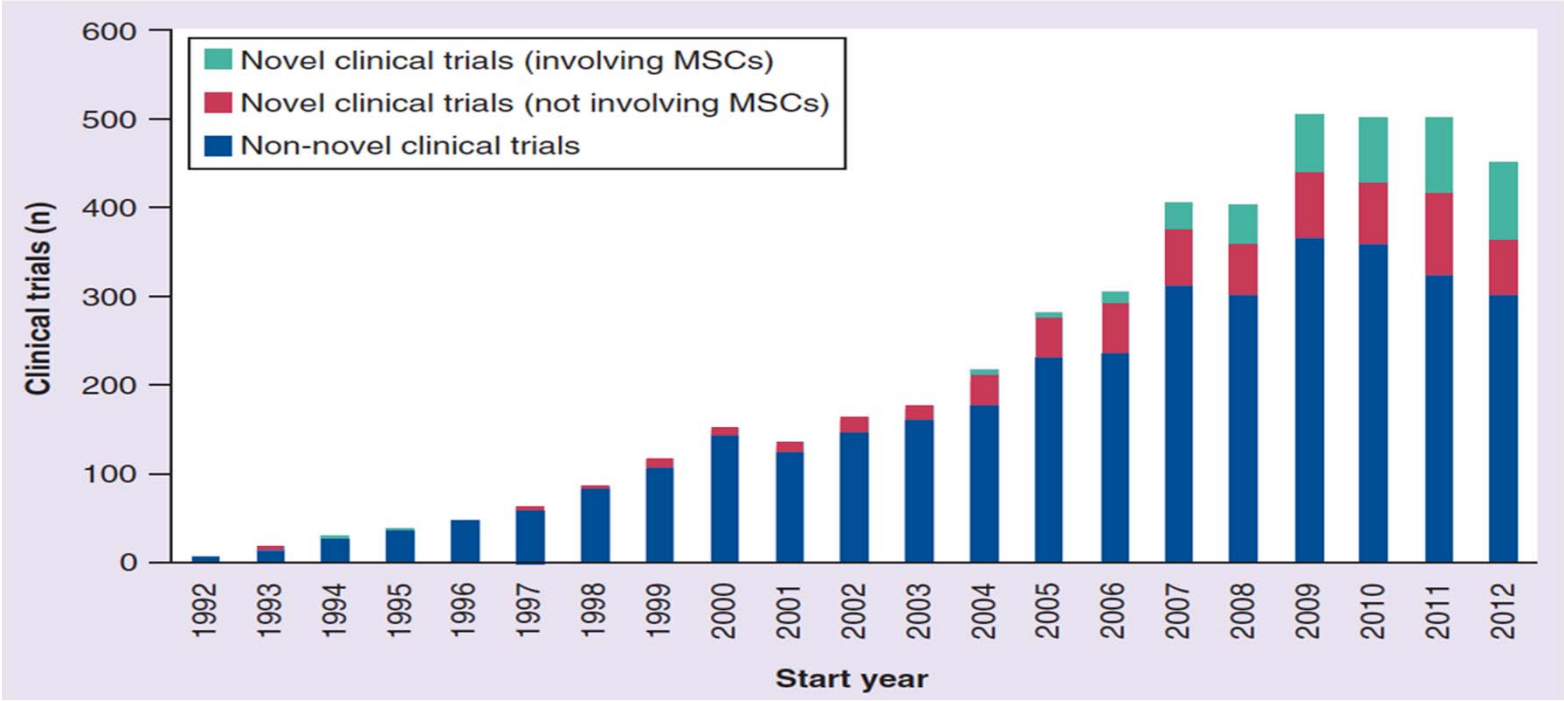
Growth in ‘novel’ applications of stem cells



Li et al. *Regen Med* 2014; 9(1):27-39 (colours modified). *Original data from* www.clinicaltrials.gov
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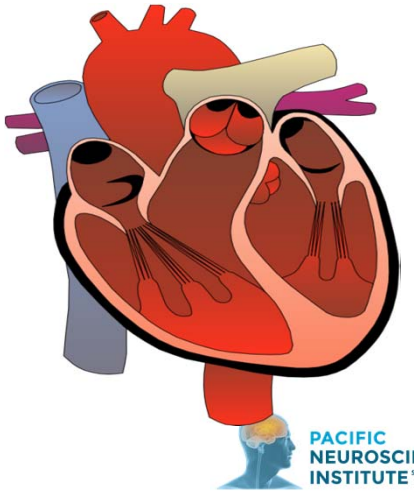
Stem cell trials for cardiac disease: 1

Congestive cardiac failure and refractory angina

- large number of trials over last 15 years using autologous or allogeneic bone marrow derived cells (MSCs and HSCs)
- demonstrated to be safe but minor or no clinical benefit
- likely to be delivering paracrine effects on endogenous cardiac progenitor cells
- allogeneic trials being undertaken in Australia by Mesoblast, an ASX listed company
- cardiac progenitors derived from hESC implanted for 1st time in October 2014 (France)



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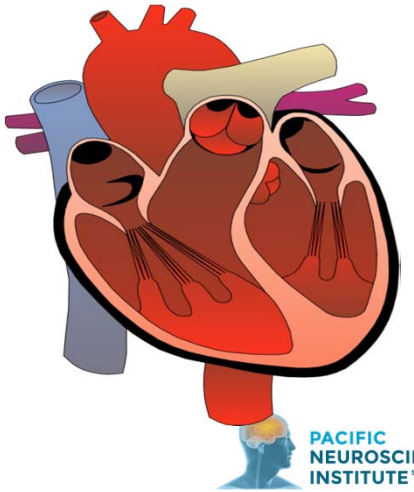
Stem cell trials for cardiac disease: 2

Acute myocardial infarction

- number of trials underway involving bone marrow and adipose derived stem cells
- one randomised double blind trial showed ongoing benefit up to 18 months
  - better mean reduction in infarct size
  - better improvement in LV perfusion
  - no major adverse events
- larger, randomised trial now underway in Europe



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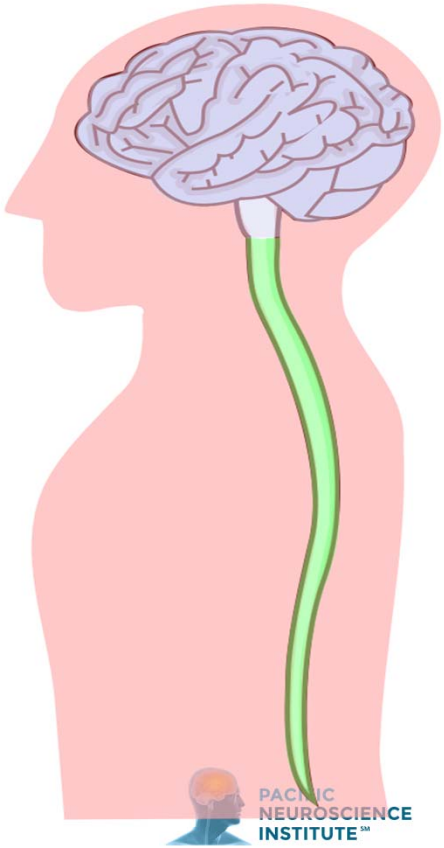
Stem cell trials for spinal cord injury: 1

Acute thoracic spinal cord injury

- Geron trial (US) involving oligodendrocyte progenitor cells from human ESC
- Phase I commenced October 2010 (FDA approved first in human) but discontinued in 2011:
  5 people treated within 7-14 days of injury
- Delivered directly into lesion
- No serious adverse events
- Geron's stem cell assets taken over by Axterias Biotherapeutics in 2013 and plan to continue with clinical trial

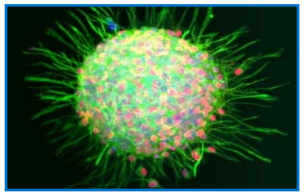


Stem cell trials for spinal cord injury: 2

Chronic thoracic spinal cord injury

- Numerous trials using MSCs and olfactory ensheathing cells from nose
  - Limited benefit, with one report of tumour formation from olfactory cells

- StemCells Inc are conducting Phase I/II trial in Switzerland
  - fetal-derived neural stem cells
  - 12 patients (both complete & incomplete) enrolled
  - monitoring for safety and have demonstrated improvements in neurological function below injury site
  - Results were expected to be announced in mid-2015
  - 1st patient enrolled in phase II trial to study cervical SCI



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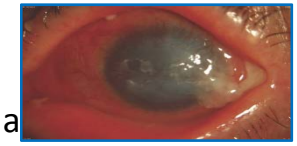
Stem cell trials for blindness: 1

Corneal disease

- Numerous trials using autologous limbal stem cells to replace damaged or diseased cornea
  - majority of patients treated in large Italian trial had permanent corneal restoration

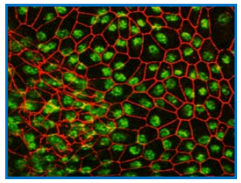


- Trial undertaken at UNSW, Sydney Eye Hospital a Save Sight Foundation
  - biopsy expanded *in vivo* on therapeutic grade contact lens
  - autologous limbal cells or conjunctival epithelial cells then transferred to eye via contact lens
  - 16 people treated, with 10 achieving a clinically stable corneal epithelium at a median of 2.5 year follow up. Half of these had some improvement in visual acuity

Stem cell trials for blindness: 2

Macular degeneration

- Several trials underway or about to begin; one completed
- US company Advanced Cell Technology (now trading as Ocata Therapeutics) started two clinical trials in 2011
  - Dry age related macular degeneration
  - Stargardt's macular degeneration
  - Phase I/II trials use retinal pigment epithelial (RPE) cells derived from human ESC



- Stem Cells Inc has completed phase 1 study in Stargardt's macular degeneration using allogeneic human neural stem cells
- London Project to Cure Blindness with Pfizer planning trial using sheets of RPE for acute macular degeneration
- RPE derived from iPSC transplanted in Japan, October 2014

Stem cell trials for cerebral palsy

- Substantial speculation about use of umbilical cord blood
- Phase II clinical trial at Duke University
  - re-infuse autologous cord blood in children <6yrs and seeking to treat 120 children
  - assumes infused cells will home to areas of ischaemic damage
  - results yet to be published but has attracted a lot of attention based on anecdotal reports
- Korean study
  - 96 treated (31 with erythropoietin & donor cord blood)
  - Improvement in motor skills and cognitive function

Stem cell trials for stroke

- Although improvement demonstrated in animal models, not yet shown in patients
- UK based company ReNeuron have commenced a trial
  - Phase I study – 12 patients using genetically engineered fetal neural stem cells
  - involves intracerebral injection into patients with significant disability 6 to 24 months after stroke
  - proposed action though known anti-inflammatory, trophic and pro-angiogenic properties
  - Interim data (9 patients) no ac

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Stem cell trials for stroke

- Stanford Phase 1 study, Sunovion trial (video)

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