



Development of Adult Stem Cell Therapies

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Overview

- Introduction
- Background on stem cells
- Mesoblast's MPCs – the story so far
- Australia as a centre for stem cell development



Introduction: Mesoblast



Overview of Mesoblast

- Founded in 2004
- Australian, ASX-listed company
- Global HQ in Melbourne
- Subsidiary (Angioblast) based in New York
- Now 4th largest biotech company in Australia
- Main focus is development of adult stem cells (Mesenchymal Precursor Cells; MPCs) for a wide range of indications



Background: Stem Cells



Embryonic vs Adult

Embryonic Stem Cells

Ethical concerns

Limited supply/restrictions on use

No near-term clinical products

Adult Stem Cells

No ethical concerns

Limitless supply

Clinical development is at an advanced stage



Types of Adult Stem Cells

Haematopoietic Stem Cells

- Give rise to bone marrow and blood cells
- Readily obtained from bone marrow/umbilical cord blood
- Already used clinically in cancer patients (but with limitations)

Mesenchymal Stem Cells

- Give rise to cells that form solid organs and tissues
- Much more difficult to obtain substantial numbers of cells – isolation and culture expansion required



Autologous vs Allogeneic

Autologous:

(Patient's own cells)

- ◆ High cost
- ◆ Variability of source material
- ◆ Not suitable for emergency use (unless banked in advance)

Allogeneic:

(Cells from a donor;

“Off the shelf”)

- ◆ Lower cost (economy of scale)
- ◆ Uniform source material
- ◆ Ideal for emergency use
- ◆ Immunogenicity concerns? Not necessarily!



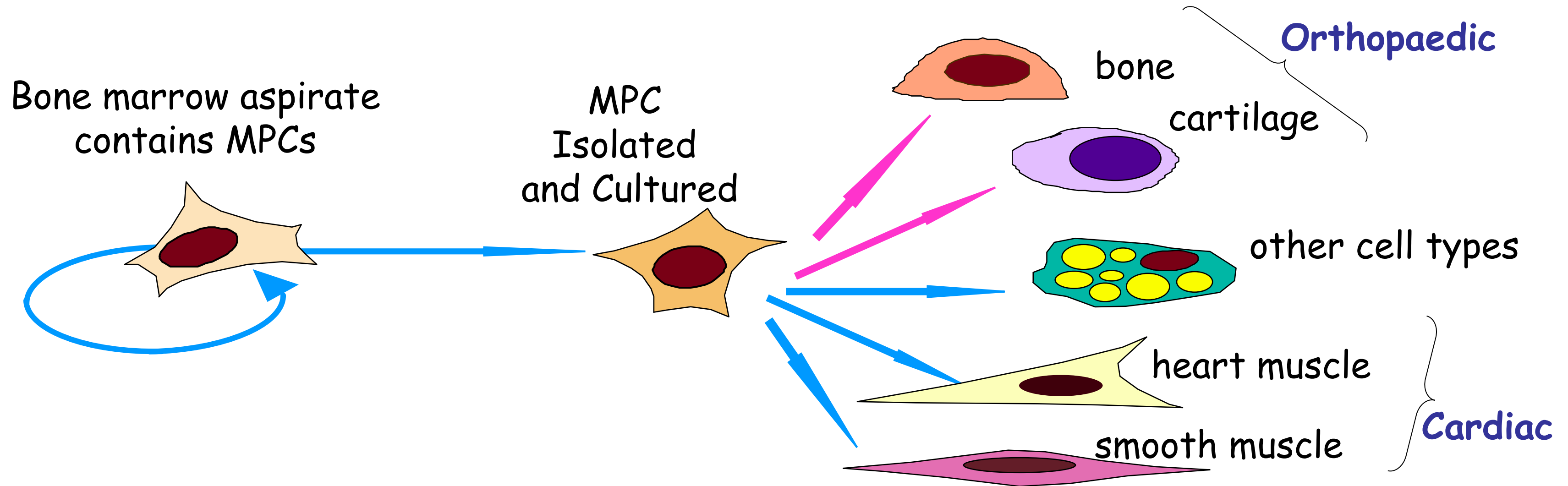
Mesoblast's MPCs



Mesenchymal Precursor Cells

- MPCs are precursors to mesenchymal stem cells, primarily found in bone marrow, dental pulp, fat and skin
- MPCs from a donor do not elicit immune responses even when administered to unrelated recipients – therefore they can be used in an allogeneic (off the shelf) manner
- Mesoblast's proprietary manufacturing process involves isolation of MPCs from bone marrow using monoclonal antibodies that bind to unique markers on MPCs, followed by culture expansion
- Mesoblast is developing allogeneic (main focus) and autologous MPCs

Mesenchymal Precursor Cells

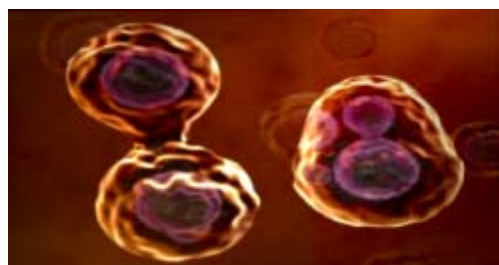
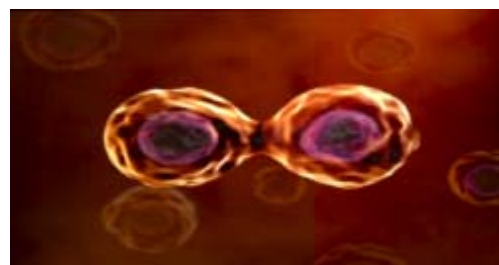
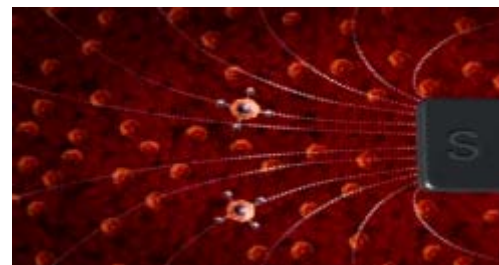
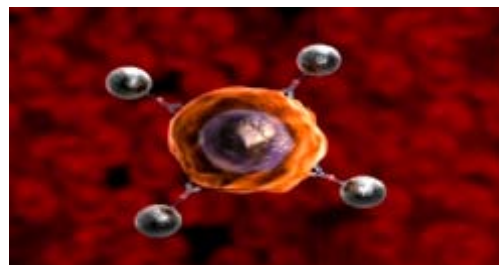
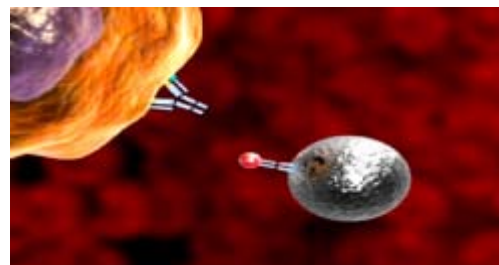
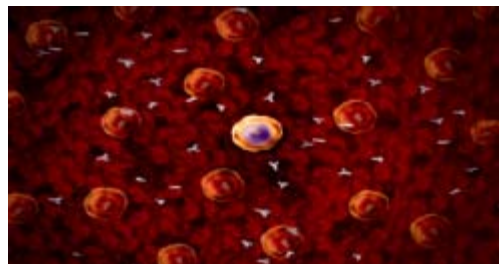
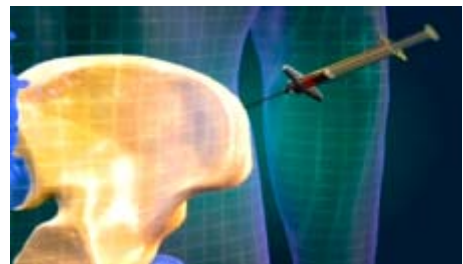


Proprietary Isolation/Expansion For Allogeneic MPC



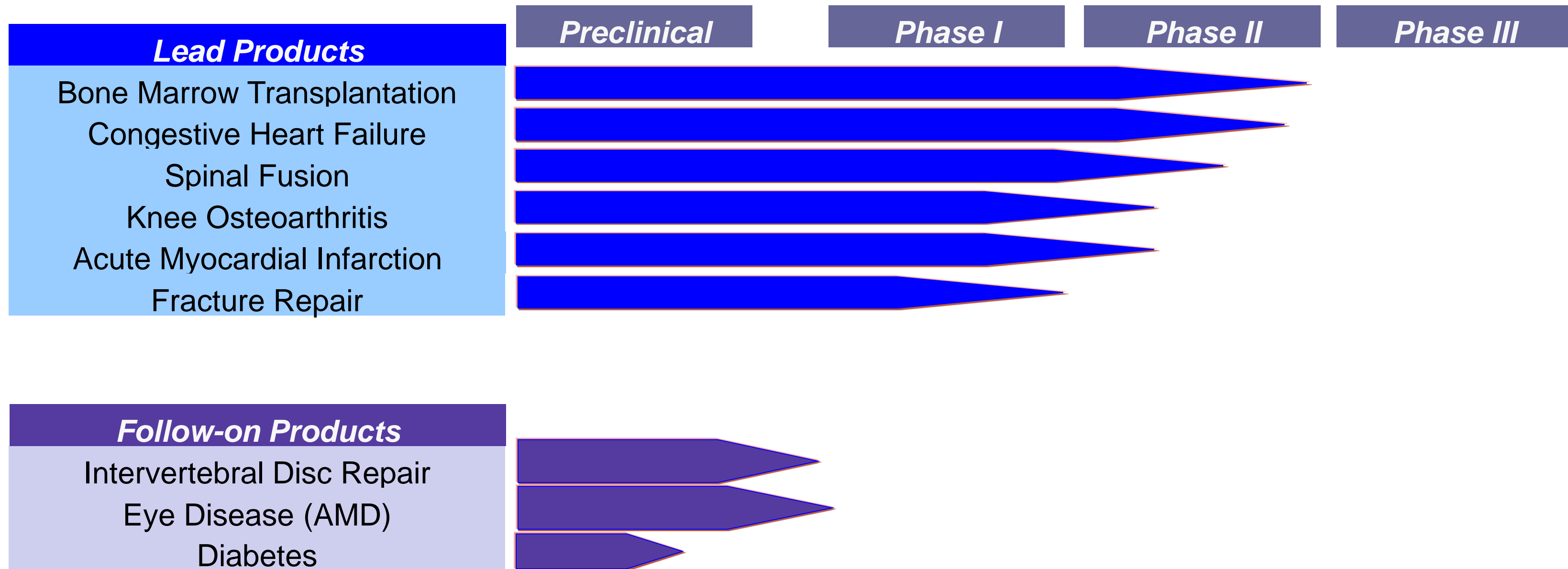
Advantages

- Precise identification
- Ease of isolation and scale-up
- Purer initial stem cell pool
- Homogeneous population
- Efficient large-scale expansion
- Lower costs of cell culture process
- Batch-to-batch consistency
- Stringent release criteria
- Greater potency of expanded product





“Off-the-Shelf” Product Pipeline





Clinical experience with autologous MPCs

- First MPC trial took place at Royal Melbourne Hospital:
 - Treatment of severe tibia/femur fractures in 10 patients
 - Prior to enrolment, patients had gone 5-32 months without healing, despite 1 or more surgical interventions
 - All 10 showed significant new bone growth at 6 and 12 months post MPC treatment
 - 82% (9 of 11) of the treated fractures successfully healed (radiographic and clinical assessment)



TGA Manufacturing Approval Granted

- TGA granted Mesoblast a licence to manufacture and supply autologous MPCs in July 2010
- Contract manufacture at Cell Therapies, Melbourne
- Current focus is use of autologous MPCs for bone repair



Clinical experience with allogeneic MPCs

- 7 clinical trials ongoing using allogeneic MPCs for:
 - Prevention of osteoarthritis
 - (Lumbar/cervical) spinal fusion
 - Heart failure
 - Acute myocardial infarction
- Also, 1 trial ongoing using umbilical cord blood expanded ex vivo using MPCs in patients with haematological malignancy
- Trials are taking place in Australia and/or US



Clinical experience with allogeneic MPCs

- Over 60 patients treated with allogeneic MPCs
- 25 patients treated with umbilical cord blood expanded *ex vivo* using allogeneic MPCs
- No significant immunological response or cell-related safety concerns observed to date



Allogeneic MPCs: Very Promising Efficacy Data

- Significantly improved cardiac function in patients with heart failure (22% mean **increase** in ejection fraction in MPC group at 6 months, c.f. 18% mean **decrease** in controls)
- In first 25 patients who received MPC-expanded cord blood, **80%** met composite efficacy endpoint (100 day survival & sustained platelet and neutrophil engraftment), c.f. **38%** in controls. Incidence of severe graft-versus-host disease also seems to be lower.



Australia as a base for cell therapy development

World leading academic research

- Mesoblast's MPC technology was originally developed at Hanson Institute/Institute of Medical and Veterinary Science in Adelaide
- Continue to work with IMVS, and other centres of excellence in Australia, including:
 - Melbourne Uni, Monash Uni, Monash Medical Centre, Royal Melbourne Hospital (Victoria)
 - Flinders Uni, Queen Elizabeth Hospital (SA)
 - Murdoch Uni (WA)
 - John Hunter Hospital (NSW)



Australian regulatory environment

- Regulation of cell based therapies is not clearly addressed in current Australian regulations
- However, New Biologicals Framework to be implemented in 2011 will address that
- A separate unit will be established within TGA to assess biologicals
- Biologicals will be classified according to level of manipulation and risk

Australian regulatory environment

- New framework recognises unique nature of these treatments – they are neither drugs nor devices
- Level of regulation tailored to level of risk
- This contrasts with reg environment elsewhere:
 - US: no regs specifically aimed at cell therapies
 - EU: just adapted pre-existing medicinal product regs to include cell therapies



Conclusion

- Australia is already a world-leading centre for cell based therapy development
- Expect profile and impact of this sector to continue to grow over coming years



Thank you, any questions?