

## Stem Cell Populations for Fracture Healing: Which Ones are Most Useful?

Stem Cell Symposium, Orthopaedic Trauma Association Basic Science Focus Forum 2013

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### STEM CELL POPULATIONS IN FRACTURE REPAIR

- Mesenchymal Stem Cells (MSCs)
- Endothelial Progenitor Cells (EPCs)
- Muscle Derived Stem Cells
- Adipose-Derived Stem Cells
- Perivascular Stem Cells

### MESENCHYMAL STEM CELLS (MSCs)

- Traditional stem cell population used in fracture repair
- Due to their known ability to differentiate into cartilage and bone *in vitro*
- Universal Definition (International Society for Cellular Therapy)
  - Plastic Adherent
  - Express CD105, CD73, CD90
  - Lack expression CD45, CD34, CD14, CD11b, CD79a, CD19, HLA-DR
  - Differentiate into osteoblasts, adipocytes, chondroblasts
- Multiple preclinical investigations have demonstrated the ability of ex vivo cultured MSCs to accelerate fracture healing<sup>1</sup>, and heal bone defects when combined with osteoconductive scaffolds<sup>2</sup> or osteoinductive proteins<sup>3</sup>
- Some authors have reported ineffectiveness when using MSCs to heal bone defects in preclinical models<sup>4</sup>
- There have been several case series reported in the literature of MSC therapy in humans but no comparative studies with AICBG<sup>5,6</sup>

### ENDOTHELIAL PROGENITOR CELLS (EPCs)

- Precursor cells which reside in the bone marrow and peripheral blood
- Form vascular networks in vitro
- Mobilize and home to areas of tissue ischemia
- Contribute to post natal neovascularization
- Highly effective angiogenesis in animal models of MI, limb ischemia, and stroke
- Accepted Markers:
  - CD133, CD34, VEGFR-2
  - Uptake of AcLDL and Leptin
  - Tube formation on Matrigel
- Multiple authors have demonstrated effectiveness with EPC therapy for healing bone defects in preclinical models<sup>7-9</sup>

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### EPCs VERSUS MSCs

- Recent preclinical investigation has demonstrated increased effectiveness of EPC therapy over MSC therapy in a bone defect model<sup>10</sup>
- Other authors have reported synergistic effects on angiogenesis and osteogenesis when EPCs and MSCs are combined in preclinical models<sup>11</sup>
- Recent basic science investigation has demonstrated that both AICBG and RIA contain viable populations of MSCs and EPCs<sup>12</sup>

### CONCLUSIONS

- Both MSCs and EPCs have demonstrated effectiveness in preclinical models of fracture healing
- There is emerging evidence to suggest that EPCs may be superior to MSCs, due to their combined effects on osteogenesis and angiogenesis
- The best strategy may be combined administration of both cell populations

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