

## Topics to consider when choosing mesenchymal stem cell (MSC) therapeutics:

1. **Characterization:** Of the stem cell populations that are under consideration for applications to regenerative medicine, bone marrow derived mesenchymal stem cells (BMMSC) are the most studied and best characterized (Smith 2008).
2. **Multipotent differentiation:** In laboratory studies, stem cells from several tissues have been shown to be capable of differentiation along numerous lineages. BMMSCs have demonstrated the ability to differentiate into bone, cartilage, tendon, ligament, meniscus, intervertebral disc, fat, muscle and nerve cells (Muschler et al 2004).
3. **Musculoskeletal tissue differentiation:** When compared in laboratory studies, BMMSC clearly outperformed adipose derived mesenchymal stem cells in models of cartilage (Winter et al, 2003; Im et al, 2005; Kisiday et al, 2008; Noel et al, 2008; Vidal et al, 2008) and bone (Im et al, 2005; Noel et al, 2008) differentiation.
4. **Cell numbers:** Bone marrow is known to contain fewer stem cells per volume of tissue relative to adipose tissue (Muschler et al, 2004), although the practice of culture expansion of BMMSCs for clinical applications yields a highly homogenous population numbering in the millions. Estimated yields for current adipose derived practices in which culture expansion is not conducted are hundreds of thousands of stem cells (Frisbie and Smith 2010).
5. **Long-term follow-up:** Multicenter, long term clinical follow-up data is available for bone marrow derived stem cell therapies (Ferris et al, 2009; Godwin et al, 2011).
6. **Rates of re-injury:** The following has been reported for BMMSC treatments:
  - A. Relative to standard treatment methods for superficial digital flexor tendon (SDFT) tendinopathy, the rate of reinjury was significantly lowered (18% (n=71) vs. 54% (n=208) ) in BMMSC treated National Hunt Horses after two years (Fortier and Smith 2008; Dyson 2004; Godwin et al, 2011).
  - B. In a 2007 study following race horses that were treated for superficial digital flexor tendon (SDFT) injuries, those that were given conventional treatments resulted in a reinjury rate of 100% within 12 months (n=15). Horses treated with BMMSCs resulted in a reinjury rate of 18% (n=11) after 12 months. Of the 9 horses that received BMMSCs and returned to racing, all had improved ultrasound images at 6 months and produced good-optimal racing performances within one year (Pacini et al, 2007).

## References

- Smith, R.K. (2008) Mesenchymal stem cell therapy for equine tendinopathy. *Disabil. Rehabil.* **30**, 1752-1758.
- Muschler, G.F., Nakamoto, C., Griffith, L.G. (2004) Engineering principles of clinical cell-based tissue engineering. *J. Bone Joint Surg. Am.* **86-A**, 1541-1558.
- Winter, A., Breit, S., Parsch, D., Benz, K., Steck, E., Hauner, H., Weber, R.M., Ewerbeck, V., Richter, W. (2003) Cartilage-like gene expression in differentiated human stem cell spheroids: a comparison of bone marrow-derived and adipose tissue-derived stromal cells. *Arthritis Rheum.* **48**, 418-429.
- Im, G.I., Shin, Y.W., Lee, K.B. (2005) Do adipose tissue-derived mesenchymal stem cells have the same osteogenic and chondrogenic potential as bone marrow derived cells? *Osteoarthritis Cartilage* **13**, 845-853.
- Kisiday, J.D., Kopesky, P.W., Evans, C.H., Grodzinsky, A.J., Mcllwraith, C.W., Frisbie, D.D. (2008) Evaluation of adult equine bone marrow- and adipose derived progenitor cell chondrogenesis in hydrogel cultures. *J. Orthop. Res.* **26**, 322-331.
- Noel, D., Caton, D., Roche, S., Bony, C., Lehmann, S., Casteilla, L., Jorgensen, C., Cousin, B. (2008) Cell specific differences between human adipose-derived and mesenchymal-stromal cells despite similar differentiation potentials. *Expt. Cell Res.* **314**, 1575-1584.
- Vidal, M.A., Robinson, S.O., Lopez, M.J., Paulsen, D.B., Borkhsenius, O., Johnson, J.R., Moore, R.M., Gimble, J.M. (2008) Comparison of chondrogenic potential in equine mesenchymal stromal cells derived from adipose tissue and bone marrow. *Vet. Surg.* **37**, 713-724.
- Frisbie, D.D., Kisiday, J.D., Kawcak, C.E., Werpy, N.M., Mcllwraith, C.W. (2009). Evaluation of adipose-derived stromal vascular fraction or bone marrow-derived mesenchymal stem cells for treatment of osteoarthritis. *J. Orthop. Res.* **27 (12)**, 1675-1680.
- Frisbie, D.D., Smith, R.K. (2010) Clinical update on the use of mesenchymal stem cells in equine orthopaedics *Equine Vet. J.* **42 (1)**, 86-89.
- Ferris, D.J., Frisbie, D.D., Kisiday, J.D., Mcllwraith, C.W., Hague, B.A., Major, M.D., Schneider, R.K., Zubrod, C.J., Watkins, J.J., Kawcak, C.E., Goodrich, L.R. (2009) Clinical follow-up of horses treated with bone marrow derived mesenchymal stem cells for musculoskeletal lesions. *Proc. Am. Ass. Equine Practns.* **55**, 59-60.
- Godwin, E.E., Young, N.J., Dudhia, J., Beamish, I.C., Smith, R.K. (2011) Implantation of bone marrow-derived mesenchymal stem cells demonstrates improved outcome in horses with overstrain injury of the superficial digital flexor tendon. *Equine Vet. J.* doi: 10.1111/j.2042-3306.2011.00363.x.
- Fortier, L.A. and Smith, R.K. (2008) Regenerative medicine for tendinous and ligamentous injuries of sport horses. *Vet. Clin. N. Am.: Equine Pract.* **24**, 191-201.
- Dyson, S.J. (2004) Medical management of superficial digital flexor tendonitis: a comparative study in 219 horses (1992-2000). *Equine Vet. J.* **36**, 415-419.
- Pacini, S., Spinabella, S., Trombi, L., Fazzi, R., Galimberti, S., Dini, F., Carlucci, F., Petrini, M. (2007) Suspension of bone marrow-derived undifferentiated mesenchymal stromal cells for repair of superficial digital flexor tendon in race horses. *Tissue Eng.* **13**, 2949-2955.