Adult stem cells in veterinary medicine can be derived from adipose tissue or from bone marrow. In small animal veterinary medicine stem cells are more commonly collected from adipose tissue but my opinion is that bone marrow-derived cells remain a perfectly reasonable option. There are key species differences and this is one difference between the canine and equine world. In horses, adult stem cells are usually collected from bone marrow because it can be performed in the standing horse and the BM provides a better source of cells than fat. In dogs, adipose-derived stem cells (ASC) are usually collected from the falciform ligament but can also be collected from any fat deposit such as just caudal to the shoulder or from the inguinal region. Although the data is not definitive; recent investigations have suggested that cell harvest from the falciform ligament generally yields the largest, most predictable amount of cells. Adipose-derived cells appear to have a similar potential for differentiation into bone, cartilage, adipose, and fibrous tissues as bone marrow derived cells. This multipotency is a key component to calling a cell a “stem cell” and is something we, and others, have been able to demonstrate from fat and BM derived cells in the dog and horse.

Adipose-derived stem cells hold great potential for the treatment of many conditions in the dog because of their trophic and anti-inflammatory properties and because they can differentiate into several other cell lines. The most notable tissues that adult stem cells can form is bone and cartilage. Because of this the main focus in the veterinary literature has been the treatment of osteoarthritis (OA). In two, prospective, randomized, placebo-controlled studies, dogs with lameness from osteoarthritis improved as compared to dogs treated with placebo. However, the strength of this evidence should be considered as the number of dogs evaluated was small and only subjective outcome measures (owner and veterinarian opinion) were used. Data in other species would suggest that ASCs could be used for bone and ligament injuries, spinal cord injury, cardiomyopathies, and inflammatory conditions of the gastrointestinal tract and skin. Certainly, many empirical stories are available for these types of conditions. In addition, the potential to gain valuable information from naturally occurring animal diseases in order to translate it to the human field is immeasurable.

Currently, for veterinary use, ASCs are isolated by collagenase digestion of adipose tissue that yields an initial stromal vascular fraction (SVF) that can be further processed by cell culture. Historically, stem cell therapy in dogs has been limited to commercial operations (e.g. Vet Stem) that will process fat obtained from a patient, and return a stromal vascular fraction (SVF) preparation of stem cells to the veterinarian for injection. Stem cells are not specifically isolated or cultured. This process is time intensive, requiring a veterinarian specifically trained (this is an online training process via Vet Stem) in proper handling of the care and acquirement of tissue. However, systems are now available that allow this processing to be performed directly in the veterinary clinic with little training. While this adds convenience and reduces time and cost it introduces error and variability in the product (SVF). Thus the patient, with systemic illness, must undergo a general anesthetic episode for surgical collection of fat. Significant cost can be incurred by the owner for the surgical procedure and the process of preparing the SVF from the fat. Although this process is far from perfect it is what is currently available. The SVF has many limitations. First, it is important to understand that this “treatment” includes all
nucleated cells harvested from the fat collection. It has been estimated that approximately 1% of these cells are stem cells. Second, the variability in the product is exceptionally high. For example, would you expect the cells from a 10 year old, obese, Labrador retriever that has had OA for its entire life to be similar to a 1 year old Greyhound that will likely never develop OA? Third, since there is no quality control of the product it may have undesirable effects. For example, cells from donors express high levels of anti-inflammatory cytokines while others express high levels of inflammatory cytokines.

The potential of allogeneic stem cells for treatment is apparent when evaluating differences in cost, time, patient morbidity and efficacy. The established technical aspects of culturing and storing ASCs will aid in the genesis of a large store of treatments because the culture process expands the cell number exponentially; allowing multiple doses to be generated from a single donor. Cells can be harvested from tissue that is normally discarded from normal patients undergoing elective surgery (e.g. ovariohysterectomy) eliminating patient morbidity. SVF preparations are limited in cell number and individual variations; allogeneic ASCs samples could be selected to optimize treatment potential. However, all of this is dependent upon an assumption that there will be no host adverse immune response because the donor allogeneic cell immune recognition is lost with passage of the cells in culture. Immunophenotypic changes in harvested cells have been documented after culture in several species, and the ability of stem cells to stimulate T helper cells has been shown to be dramatically diminished or lost completely in people and in baboons. Our in vitro and in vivo data in dogs support this, as cell surface markers on the stem cells are lost with cell passage and after intra-articular injection in normal dogs we found no clinical or histopathologic evidence of inflammation. Allogeneic canine stem cells have been studied before and appear to cause no adverse reactions and have been shown to be osteogenic in bone healing studies. Similarly, in limited clinical investigations, we have found no adverse reactions when giving allogeneic stem cells intra-articular or intravenous.

Preliminary data from two investigations we are performing may have immediate clinical impact. In a study were we investigated the viability of stem cells when exposed to synovial fluid we found that cell viability was not affected when they were exposed to synovial fluid from normal joints. However, when the same cell lines were exposed to synovial fluid from joints with OA we found diminished viability and cell viability improved as the synovial fluid was diluted. This data suggests that injecting stem cells directly into inflamed joints with OA may limit the viability, and therefore the usefulness, of the cells being injected. In a randomized clinical investigation of the effect of SVF or allogeneic cells for the treatment of FCP after arthroscopy and proximal ulnar osteotomy we found that patients that did not receive cells had a successful outcome (at 6-months) only 25% of the time. Patients that did receive cells had a successful outcome 70% of the time.

Stem cell therapy shows promise as a therapeutic option for many diseases however, the current limitations of autogenous ASC in veterinary medicine dramatically curb their clinical applications. If an allogeneic stem cell treatment proved to be safe, effective, affordable and available, veterinary patients would benefit.


