Regenerative medicine – the new paradigm
- In vitro evidence of efficacy
- Laboratory animal studies
- Canine / Feline / Equine Clinical Data

Regenerative Medicine
The New Paradigm
- Pain Reduction
- Inflammation Reduction
- Tissue Regeneration
- Quality of Life Extension
Evidence Pyramids

Evidence Based Medicine

U.S. Preventative Services Task Force

Level I: at least one randomized controlled trial
Level IIa: controlled trials without randomization
Level IIb: cohort or case-control studies
Level IIc: uncontrolled trials – multiple time points
Level III: expert opinions


EBM for Clinical Solutions
Regeneration Via Differentiation

Isolation, Characterization, and Differentiation Potential of Canine Adipose-Derived Stem Cells

Adipogenic Osteogenic Chondrogenic


Regeneration Via Differentiation

Evaluation of the osteogenic and chondrogenic differentiation capacities of equine adipose tissue-derived mesenchymal stem cells

Clinical Relevance: "Equine AT-MSCs represent a suitable cellular source for regenerative treatment of bone or cartilage defects."


Joint Lubrication

Induction of chondrogenesis and expression of superficial zone protein (SZP) lubricin by mesenchymal progenitors in the infrapatellar fat pad of the knee joint treated with TGF-β1 and BMP-7

Rabbit Cartilage Regeneration

At 8 weeks, 12/12 (100%) of defects in treated group healing with hyaline-like cartilage. Only 1/12 (8%) of controls healed.


Canine Elbow Coronoid Disease Cartilage Regeneration

Arthroscopy Timeline
Initial — surgical cleanup only
Day 90 — no change, lame,
Add adipose stem cell Rx
Day 180 — cartilage regeneration

Pre – Stem Cell – Day 90
Day 180 (90 Days Post – Stem Cell)

Sherman Canapp, DVM, Dipl. ACVS; Presented AVMA 2009

Canine Medial Shoulder Instability Repair

a. Glenoid
b. Glenohumeral lig.
c. Subscapularis ten.
d. Humeral head

Pre – Stem Cell
90 Days Post – Stem Cell

Sherman Canapp, DVM, Dipl. ACVS; Presented AVMA 2009
"Adipose derived stem cell therapy demonstrated promising results in five cases of muscle injury in working German shepherd dogs (semitendinosus). All dogs were able to return to their previous training and occupations as police and Schutzhund dogs with a functional gait.

In contrast, the surgeon’s previous experience was that the dog’s careers were typically shortened due to apparent fibrosis/muscle contracture, and continuing muscle disease.”

Severe Muscle Tear – 5 Cases

<table>
<thead>
<tr>
<th>Name</th>
<th>Cell P</th>
<th>Pre-Grade</th>
<th>Post-Grade</th>
<th>Weeks</th>
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<tbody>
<tr>
<td>Gia</td>
<td>L7.8</td>
<td>3</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>jack</td>
<td>4.9M</td>
<td>2+</td>
<td>0</td>
<td>10</td>
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<tr>
<td>Sam</td>
<td>9.0</td>
<td>2</td>
<td>0</td>
<td>16</td>
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<tr>
<td>Hunter</td>
<td>9.7M</td>
<td>2</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>Jago</td>
<td>4.5W(1d)</td>
<td>2.5/4.0L</td>
<td>14/91</td>
<td>14</td>
</tr>
</tbody>
</table>

Marty Gardner, DVM  
116 cases proximal susp desmitis  
Adipose SVF – ultrasounded guided  
>90% return to full work, approx 6 months

Wes Sutter, DVM, dACVS  
Plantar tendinitis  
PRP+ Fresh BM or PRP + Adipose SVF  
Both better than PRP alone – Early better

Chris Johnson, DVM, dACVS  
Fresh BM or Fresh adipose SVF  
Do not wait 30 days – too much scar  
Most cases improve over conservative

Larry Galuppo, DVM – UCD  
DDF Lesions - 40 horses – minimum 6 month  
BMAC, BM cultured, Adipose SVF  
“Reasonable” success for all treatments  
Adipose SVF better for severe lesions

Sport Horse Study

Sport Horse Suspensory Study

- 84 horses with SL desmitis tx with ASCs
- All horses tx at single referral center
- All dx with diagnostic anesthesia, u/s and/or MRI
- Consistent rehab protocol
- Stringent outcome measure
  - in full work for minimum of 1 year


85.7% returned to prior level or higher  
13.1% returned to lower level  
1.2% did not return to work


All treated with Vet-Stem adipose-derived stem cells. Dr. Rich has now treated more than 500 horses with this therapy
Chronic Stifle Osteoarthritis Study

- 365 Day Pilot Study, 9 dogs
- Chronic Post-Surgical OA (>3 Mo)
- Single Surgeon all cases
- Intrarticular stem cells – 1X
- Vet and Owner assessments at pre, 30, 90, 180, 365
- N=9 for 180 day data

Chronic Stifle Osteoarthritis Study

- Vet and owner total scores statistically improved at 30 and 90 days over baselines (P<0.001)

Clinical Case Example - Knee
Prospective Elbow OA Trial

Effect of Intraarticular Injection of Autologous Adipose-Derived Mesenchymal Stem and Regenerative Cells on Clinical Signs of Chronic Osteoarthritis of the Elbow Joint in Dogs*

Linda L. Black, DVM, PhD
James Carusò, DVM, MS, DACVLA, DAAAPM*  
Cheryl Adams, DVA, CVA, CCRIT  
Sara Dhople, BVSc, DAVSM*  
Andrew E. Sams, DVM, MS, DACVS*

Figure 1. Degree of improvement in orthopedic examination score in dogs with osteoarthritis of the elbow after intraarticular injection of autologous adipose-derived mesenchymal stem cells (% change; mean ± SEM; N = 6).

Randomized Controlled Trial

Effect of Adipose-Derived Mesenchymal Stem and Regenerative Cells on Lameness in Dogs with Chronic Osteoarthritis of the Coxofemoral Joints: A Randomized, Double-Blinded, Multicenter, Controlled Trial*

Linda L. Black, DVM, PhD
James Caruso, DVM, MS, DACVLA, DAAAPM*  
Susan Harman, AHT, BS  
Daniel A. Gingerich, DVM, MS  
Robert Harman, DVM, MPVM*
Blinded Hip OA Trial Design

18 DOGS-4 Clinics

A: TREATMENT  B: CONTROL

BASELINE VETERINARY/OWNER EVALUATIONS

Fat Collection Both Groups

IA SVF INJECTIONS  IA SALINE INJECTIONS

Veterinary and Owner Evaluations 30, 60, 90 Days

Black et al. Veterinary Therapeutics Vol.8, No. 4, Winter 2007

Study Parameters Evaluated

VETERINARY
- Lameness walk and trot
- Pain on manipulation
- Range of motion
- Functional disability (stiffness)

STATISTICAL
- Two-way repeated measures ANOVA
- 0.05 level of significance
- Two-way RM-ANOVA
- Data was pooled for further analysis

Black et al. Veterinary Therapeutics Vol.8, No. 4, Winter 2007

Bilateral Coxofemoral OA Study
Randomized Controlled Trial

**Effect of adipose-derived nucleated cell fractions on tendon repair in horses with collagenase-induced tendinitis**

Alan J. Nixon, BVSc, MS; Linda A. Dooly, DVM, PhD; Jennifer L. Hagg, BS; Amy E. Yang, DVM; Daniel L. Ward, PhD

Design:
- 8 Horses – 4 treated / 4 controls
- Collagenase induced injury – Rx 10 days later
- Fully blinded histology
- Controls were treated with same volume of saline


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**Cornell/Nixon Tendon Study**

**Saline Control**

**Stem Cell Treated**

H&E Stain

- Reduce infiltrate (P<0.015)
- Imp collagen fiber uniformity (P<0.040)
- Imp overall healing score (P<0.028)

Polarized Light
1. In-vitro and laboratory animal data support the mechanisms and the theory of using stem cells in orthopedics.

2. There are uncontrolled and also blinded placebo-control clinical trials that support the validity of use of adipose stem cells in canine and equine medicine.

3. The evidence rises to Level I in support of clinical use in the horse and the dog.

Summary - Regenerative Medicine