

### ***Healing of Full-Thickness Chondral Defects Using IRAP and IGF1 Delivered by Gene Transfer to Articular Defects***

Having achieved a certain level of improved healing with the technique of subchondral microfracture (see 1996-1998 Laboratory Report), the Orthopaedic Research Center scientists are now trying to improve the quality of the repair tissue, particularly in terms of aggrecan content, as well as biomechanical function. This project is being done by Drs. Sophie Morriset, David Frisbie and Wayne McIlwraith. Using the equine gene sequence of interleukin-1 receptor antagonist (IRAP) that has been sequenced in the CSU Orthopaedic Lab, as well as the equine

IGF1 sequence from Dr. Alan Nixon's lab, both genes are being transferred with an adenoviral vector into full-thickness articular cartilage defects on the medial condyle of the femur. The results with this gene therapy technique will be compared to defects treated with subchondral microfracture alone.

**Acknowledgements:** This work is being funded by the Steadman-Hawkins Sports Medicine Foundation for the research costs and by a Medical Research Council of Canada grant to Dr. Morriset for three years' salary funding.

### ***Serum Markers for the Early Detection of Incipient Musculoskeletal Injury in the Racing Thoroughbred***

This project is being carried out by Drs. Clark Billingham, David Frisbie and Wayne McIlwraith in conjunction with Drs. Rick Arthur, Vince Baker and Jeff Blea, racetrack veterinarians in Southern California. Regular clinical examinations and monthly blood samples are being taken on a population of 200 racing Thoroughbreds. The hypothesis of the research is that, if a horse suffers a musculoskeletal injury, we will find a change in the

serum markers that could predict this injury. Samples have been taken from this population of Thoroughbreds during the past year, and these samples are currently being analyzed. The ultimate realization in this project would be an ability to predict a fracture before it occurs.

**Acknowledgements:** The Grayson-Jockey Club Research Foundation is funding this project.

### ***Articular Cartilage Resurfacing Using Implantation of Autologous Chondrocytes in a Collagenous Matrix***

In a project using novel tissue engineering techniques, being done by Drs. David Frisbie and Wayne McIlwraith, a small amount of articular cartilage (300mg) is taken from the non-articular portion of the lateral trochlear ridge of the femur in a horse. This cartilage undergoes digestion, and the isolated chondrocytes are then cultured on a collagen membrane. Three weeks later, the resulting cartilage construct is brought back to the same horse and

implanted in 15mm diameter defects using special PLA-PGA staples. These horses are being evaluated periodically with the arthroscope and specifically evaluated at four and twelve months to evaluate the quality of cartilage healing compared to control full-thickness defects.

**Acknowledgements:** This project is funded by Mitek (a division of Johnson and Johnson).

### ***Assessment of Bone Sialoprotein and COL2-3/4C as Markers of Bone and Cartilage Degradation in Equine Joint Disease***

This project is being done by Drs. Clark Billingham and Wayne McIlwraith. The COL2-3/4C have proven to be good markers of collagen degradation in the cartilage and bone (depending on whether we look at Type II or Type I collagen, which are specific for cartilage and bone respectively). Currently, we are working to develop an equine-specific antibody

for bone sialoprotein to combine with the collagen degradation markers that we presently have available for the horse.

**Acknowledgements:** This project is funded by the American Quarter Horse Association.

### ***Comparison of Imaging Modalities to Detect Suspected Bone Damage and Articular Cartilage Injury in the Equine Carpus***

This project, being carried out by Drs. Jim Becht, Richard Park, Chris Kawcak, Philip Steyn and Wayne McIlwraith, is a parallel study to the one looking at synovial and serum markers to distinguish osteoarthritis in exercised horses compared to the changes in markers with exercise alone. In this instance, the horses from both groups are being imaged with radiographs, CT (including 3-D

osteosorptiometry), nuclear scintigraphy, MRI, and thermography. Analysis will be done to compare the changes occurring in these imaging modalities with exercise versus when there is a chip fragment (osteoarthritis) present in the joint.

**Acknowledgements:** This project is funded by a CSU College Research Council Grant.

### ***Evaluation of the Ability of Prophylactic Administration of Intravenous Hyaluronan (Legend™) to Prevent Traumatic Arthritis in Training and Racing Thoroughbreds***

This project, done by Drs. Wayne McIlwraith, Clark Billinghamurst and David Frisbie, is monitoring, with clinical examination and synovial fluid and serum markers, the ability of IV-HA to prevent traumatic joint disease. The protocol is somewhat parallel to the experimental study reported by the Orthopaedic Research Laboratory in 1995 where three treatments with IV-HA one week apart were evaluated in an experimental model of OA. In this case, there is no

prior disease present. The animals have been regularly examined clinically, but it was felt that the changes or decrease in disease process due to IV-HA would be quite subtle, and perhaps markers could distinguish differences.

**Acknowledgements:** Bayer Animal Health is providing the funding for this work.

### ***Evaluation of an In-Shoe Pressure Sensor Compared to a Mat Sensor and Force Plate Analysis***

The Orthopaedic Research Center has already evaluated the use of Tekscan mats in obtaining an objective measure of weight-bearing and/or lameness (See summary on page 61). This present study, being done by Valerie Perino as part of her PhD research with Drs. David Frisbie, Chris Kawcak and Wayne McIlwraith, is evaluating an in-shoe pressure sensor made by the same company and also comparing it to a force plate, which is currently

considered the gold standard and has only recently been acquired by the Orthopaedic Research Laboratory. The overall goal is to find the most practical and efficient means of objectively evaluating lameness and gait.

**Acknowledgements:** This project is being funded by a grant from the CSU College Research Council.

### ***Evaluation of the Chemotactic Effects of Cytokines and Growth Factors on Stem Cells***

Stem cells are one of the strategies proposed to augment healing in musculoskeletal tissues including articular cartilage and tendon. This in-vitro study, being done by Drs. Sophie Morriset and David Frisbie, will evaluate various cytokines including growth factors and their effect on cellular chemotaxis. This could provide information on the best factor(s) to select in in-vivo stem cell

augmentation studies in order to find the optimal combination that could then be used in the clinical patient

**Acknowledgements:** Funding for this work has been provided by a CSU College Research Council grant.

### ***Evaluating the Reduction in Lameness and the Prevention of Pathologic Bone Change in the Navicular Bone (Navicular Disease)***

This study is evaluating the use of the Dynamix™ shoe, a novel polyurethane shoe, in treating navicular syndrome and will be compared to two other commonly used shoe treatments—regular egg bar shoes and ‘Natural Balance’ shoes. This project is being done by Drs. David Frisbie, Chris Kawcak, Wayne McIlwraith, Gayle Trotter, Dean Henderickson and surgical resident Dr. Jeff

Allredge. Previous work has been done on evaluating the Dynamix shoe for relieving hoof stress (see summary on page 91), and this is a clinical study using cases of navicular disease/palmar heel pain that block out with a palmar digital nerve block.

**Acknowledgements:** Hippodynamix AG, Switzerland has funded this project.

**Left: Natural Balance shoe;  
Center: Egg Bar shoe;  
Right: Dynamix shoe**



### ***Retrospective Study of the Value of Arthroscopic Surgery in the Treatment of Subchondral Cystic Lesions***

This study is being done by Dr. Emily Sandler (a student who worked as an undergraduate student in the Orthopaedic Research Laboratory and was then an intern at Rood and Riddle Equine Clinic), along with Drs. Larry Bramlage, Rolf Embertson and David Frisbie. In this study, Dr. Sandler reported on the follow-up results of 150 cases of subchondral

cystic lesions in the stifle operated by Drs. Bramlage and Embertson at Rood and Riddle Equine Hospital (Dr. Bramlage is a member of the Orthopaedic Research Advisory Board). Dr. Frisbie is doing statistical analysis on these data to clarify the exact prognosis following arthroscopic surgery to treat these cases.

### ***Evaluation of Pain-Relieving (Analgesic) Drugs in the Horse***

Using a model of acute synovitis (lipopolysaccharide injection) in the equine joint, Dr. Peter Hellyer, Dr. Kursheed Mama and Ann Wagner of the anesthesia section, along with Drs. Dean Hendrickson and David Frisbie, will test various pain-relieving medications for their potential value in joint injury and after joint surgery. The synovitis is a temporary, short-acting one that causes no permanent harm to the horse, and provides an effective way of

evaluating various analgesic drugs. The use of intra-articular analgesic drugs at the time of arthroscopic surgery is popular in human medicine, and this is a good way to evaluate the best candidate for clinical use in the horse.

**Acknowledgements:** The Hadley and Marion Stuart Foundation provided the funding for this work.

### ***Evaluation of Expression of Inflammatory Cytokines in Equine Clinical Joint Disease***

Using RealTime PCR, the expression of messenger RNA for a large number of purported mediators in joint disease will be evaluated in this project being done by Dr. Kirstie Timm, along with Drs. David Frisbie and Wayne McIlwraith. Mediators being evaluated include various interleukins, TNF, IGF, TIMPs and metalloproteinases. This project will

clarify which mediators are most important in clinical disease in the horse.

**Acknowledgements:** This work is being funded by the CSU College Research Council (Colorado Parimutuel Fund).

### ***Evaluation of Message Expression from Synovial Membrane and Articular Cartilage of Exercised versus Non-Exercised Horses with Osteoarthritic Change in the Joints***

This project is running in parallel to the project on markers with exercise versus disease (see summary on page 70). Samples of synovial membrane and articular cartilage have been taken, and these will be evaluated using RealTime PCR for messenger RNA expression. This study will allow us to evaluate changes in expression of various inflammatory

cytokines with exercise, as well as in joints with osteoarthritis that are currently undergoing exercise.

**Acknowledgements:** This work is being funded by the CSU Equine Orthopaedic Research Fund.

### ***Cloning of Equine BMP-2 and VEGF Sequences***

This study is being done by Dr. Singe Balch, a post-doctoral fellow who is just starting work in the Orthopaedic Research Laboratory and Dr. David Frisbie. It is part of the on-going work on evaluation of growth factors to augment healing in osteomyelitis in the horse. It follows on from the in-vivo work done in rabbits by Dr. Louise Southwood for her PhD (see summary on page 94). Development for

equine sequences BMP-2 and VEGF could potentially facilitate the treatment of equine osteomyelitis by promoting bone formation with BMP-2 and enhancing vascularization with VEGF.

**Acknowledgements:** This project is being funded by the CSU College Research Council and the CSU Equine Orthopaedic Research Fund.

### ***Evaluation of Diode Laser versus Drilling for Promotion of Fusion of the Distal Tarsal Joints***

It has been long realized that lameness due to osteoarthritis of the distal tarsal joints (where motion is not a significant component) can be effectively resolved if the joint becomes fused. Methods evaluated in the past for promotion of joint fusion include drilling and the use of sodium monooacetate. Drilling has been successful, but sodium monooacetate suffers from severe complications if any of the material gets into the articulating tibiotarsal joint that provides movement to the hock. More recently, the use of diode laser has

been described to promote fusion, and this study, which is being carried out by Dr. Colin Scruton, along with Drs. Gary Baxter and David Frisbie and with support from Heather Colhoun and Claire Wilson, is designed to evaluate the ability to perform arthrodesis using the diode laser versus the old technique of drilling.

**Acknowledgements:** A grant from the CSU College Research Council (Parimutuel Racing Fund) provided the funding for this project.