

Cartilage Repair Models

Injury of articular cartilage due to trauma or pathological conditions is the major cause of disability worldwide, especially in North America. The increasing number of patients suffering from joint-related conditions leads to a concomitant increase in the economic burden. Several strategies to repair and replace knee joint cartilage are needed since knee-associated disabilities are more prevalent than any other joint. Because of inadequacies associated with widely used approaches, the orthopedic community has an increasing tendency to develop biological strategies, which include transplantation of autologous (i.e., mosaicplasty) or allogeneic osteochondral grafts, autologous chondrocytes (chondrocyte transplantation), tissue-engineered cartilage substitutes or the local application of a compound.

Aginko's vast experience in the study of human and animal bone and cartilage biology allows Aginko to provide a wide range of services tailored to individual needs that support product development intended for clinical human applications.

Cartilage Repair Preclinical Strategies

The FDA recognizes that choosing and determining the suitability of an animal model(s) for evaluation of any specific product is difficult because there is no perfect animal model of articular cartilage injury. As discussed at the March 2005 CTGTAC meeting (*):

- the scientific literature contains descriptions of numerous methods for evaluating the nonclinical behavior of native cartilage and, consequently, articular cartilage repair or replacement products;
- not all of these methods may apply to a specific articular cartilage repair or replacement product; and goats, sheep and horses are the most frequently used large animal models for cartilage repair.

Chondral and Osteochondral Defect Models

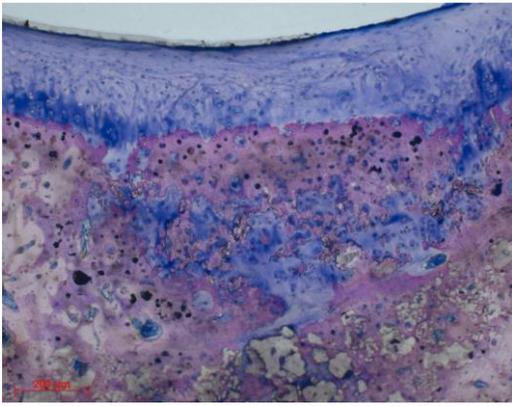
Species available include: rabbit, dog, goat, sheep, and horse.

Rabbit models are well described in the literature and are recommended by the FDA for preliminary, short-term, and proof – of – concept studies. These rabbit model permit an easy screening of compounds.

(*) Cellular, Tissue and Gene Therapies Advisory meeting, May 14-15, 2009

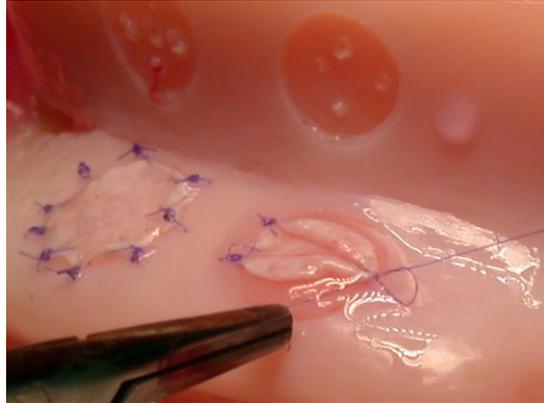
(*) Cellular, Tissue, and Gene Therapies Advisory Committee meeting, March 3, 2005
(<http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4093T1.htm>); March 4, 2005
(http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4093T2_01.htm).





Osteochondral defect model in the rabbit repaired with a tissue engineered implant.

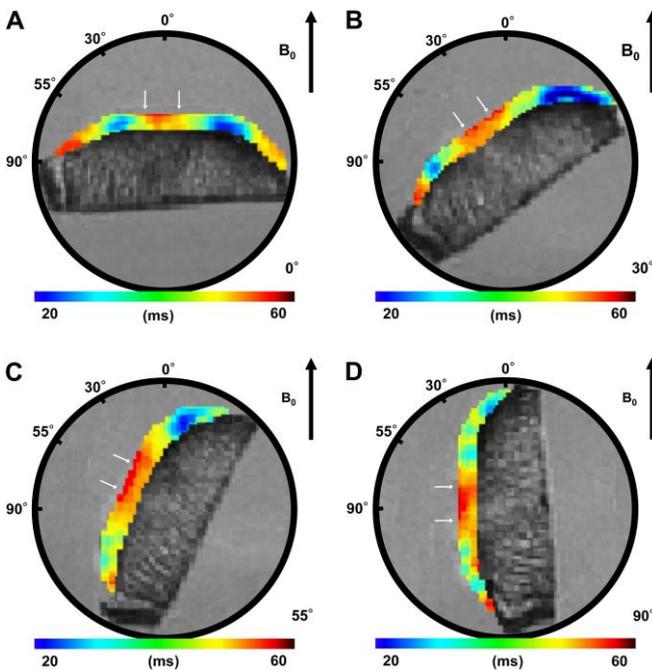
Large animal models, recommended for long-term studies, can incorporate multiple defects and are amenable to arthroscopy and MR imaging.



Osteochondral defect superficial (Full thickness defect) covered with the application of a membrane.

Outcome Measures

- Histology: morphology, proteoglycan and cell loss, cartilage damage, osteophyte formation. Aginko has developed special protocols to samples cartilage defects. All slides are graded by expert histopathologists.
- Radiology: X-ray, micro-CT
- Serum, joint fluid, and urine biomarkers
- Cartilage biochemistry
- Chondrocyte metabolism
- Arthroscopy
- MRI (morphology, quantitative analysis)



Courtesy of Osteoarthritis and Cartilage
Volume 17, Issue 10, October 2009, Pages 1341-1349 A. Watanabe, C. Boesch, S.E. Anderson, W. Brehm and P. Mainil Varlet

