IN VIVO EVALUATION OF THE SYNTHETIC THROMBIN PEPTIDE, TP508, IN ARTICULAR CARTILAGE REPAIR

*Karnaugh, R D. (A-North Shore University Hospital/ Long Island Jewish Medical Center); **Ryaby, J T (E-Orthologic Inc.); *Razzano, P (A-North Shore University Hospital/ Long Island Jewish Medical Center); ***Crowther, R A. (E-Chrysalis); **Carney, D H. (E-Chrysalis); *Wu, D; *Dines, D M. (A-North Shore University Hospital/ Long Island Jewish Medical Center); +*Grande, D

**North Shore University Hospital/ Long Island Jewish Medical Center, Manhasset, New York. (516) 562-1138, Fax: (516) 562-1022, dgrande@nshs.edu

Introduction: Degeneration of articular cartilage related to trauma and osteoarthritis remains a major problem in orthopaedics. This study was designed to evaluate the in vivo effect of the synthetic thrombin peptide, TP508, in the repair of full-thickness articular cartilage defects. Thrombin is an essential factor in hemostasis, inflammation, and tissue repair. TP508 binds to high-affinity receptors and mimics cellular effects of thrombin at sites of tissue injury.

Methods: Twenty-four adult male New Zealand White rabbits underwent unilateral knee arthrotomies. Three-millimeter full-thickness articular cartilage defects were made in the femoropatellar groove. TP508 within a poly-lactglycolide (PLGA 85:15) 20um microspheres at two different concentrations were mixed with a type I collagen gel (Vitrogen, Cohesion Technologies) and implanted into the osteochondral defect sites (Fig 1.). Two control (PLGA 85:15 -collagen gel alone or untreated defect) groups and two experimental groups consisting of eight NZW rabbits each were treated with TP508 at dosages of 10 and 50ug/ml, respectively. Animals were allowed free activity postoperatively and were sacrificed at two, four, and eight weeks postoperatively. Defect areas were harvested and macroscopically evaluated. Histologic sections were cut at 5-um thickness and stained with hematoxylin and eosin, and Safranin-O/fast green.

Results: The control defects healed with a less congruent articular surface and a uniformly opaque appearing repair tissue. In contrast, specimens containing TP508 healed with a generally smooth articular surface and a translucent repair tissue more closely resembling the native articular cartilage. The degree as well as quality of healing was assessed and scored with a grading system modified from O’Driscoll et al for cartilage repair. (Maximum score was 24 points.) Safranin-O staining as well as polarized light examination of representative sections was undertaken to assess the proteoglycan content and structural characteristics of the repair matrix. Control specimens healed with a primarily fibrous or fibrocartilagenous matrix. Defects treated with TP508-collagen gel demonstrated enhanced healing when compared to controls. Furthermore, there was a strong tendency toward a hyaline appearing matrix with increased Safranin-O staining and birefringence under polarized light more closely resembling the normal native cartilage. Mean histologic scores for PLLA-collagen gel alone and untreated defects at eight weeks were 6.8 (+0.8) and 9.3 (+4.0) (p<0.01), respectively. Interestingly, there was no apparent incremental benefit noted in using a higher TP508 dosage.

Discussion: Implantation of the synthetic thrombin peptide, TP508 into osteochondral defects enhanced repair of articular cartilage. The resultant repair was equal to or superior to prior studies using more complicated strategies of repair, such as cell transplantation. An advantage of TP508 would be its ready availability in the operating room and technical feasibility. Studies are ongoing to further characterize the use of TP508 for cartilage repair.

Table 1: Summary of histological scores for repair of cartilage defects at eight weeks postop. TP508 treated defects scored significantly (p < .01) higher than controls.

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**Orthologic, Inc., Tempe, Arizona.
***Chrysalis, Galveston, Texas.