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# Agili-CTM Induced Cartilage Regeneration: Insights in to the Mode of Action, In Vitro And In Vivo Data

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**Summary**:
Agili-C™ is a first-of-a-kind acellular scaffold capable of inducing regeneration of cartilage and subchondral bone

**Abstract**:
INTRODUCTION Regeneration of hyaline cartilage is the ultimate goal of orthopedics. Current approaches for treating focal cartilage defects each present several drawbacks. Acellular scaffold, capable of attracting stem cells, that guides a regenerative process culminating in the formation of a hyaline-like cartilage could be an ideal solution. The Agili-CTM is a first-in-class acellular implant that has been designed to allow regeneration of hyaline cartilage and subchondral bone. METHODS In-vitro experimentation: Response of normal human adult articular chondrocytes to the Agili-CTM implant was studied in a model, in which the chondral phase of the Agili-CTM implant was placed inside cartilage plugs and cultured for up to 120 days. Chondrocyte survival, migration, proteoglycan (PG) synthesis, gene expression of collagen type II and aggrecan, histology, and immunohistochemistry were performed to characterize cellular responses. In-vivo experimentation: A long-term study was conducted on 24 mature female, 55-60 kg, Saanen goats. A critical size focal osteochondral defect (6mmx10mm) was created in the medial femoral condyle. In 16 of the goats Agili-C™ implants were inserted into the defect. Eight goats served as empty defect control. The goats were followed for up to 12 mo. Following sacrifice macroscopic evaluation by independent blinded experts, micro CT, synovial fluid analysis, 7 Tesla MRI utilizing T2 mapping and blinded histology and immunohistochemistry with modified ICRS II and O'Driscoll scores were performed. RESULTS In-vitro data: Chondrocytes migrated into the implant either when cultured as monolayers in the presence of Agili-CTM construct or as tissue explants implanted with Agili-CTM construct. The migrating cells remained viable within and around the construct for the entire duration of the experiment evidenced by live/dead assay. Signs of the extracellular matrix formation were evidenced inside 3D structure of the scaffold. PG synthesis and gene expression of collagen type II and aggrecan were elevated by more than 2.5 fold in cartilage with the scaffold vs corresponding controls. In-vivo data: Hyaline cartilage and bone regeneration were found in the Agili-CTM implanted goats but not in the controls. Results of Gross Appearance Macroscopic Evaluation (Max=15) at 12 mo after implantation (n=7) were 13±1 vs. 9±1 in the control group (n=3, $p<0.01$). Agili-CTM histological result scored 33/38 at 12 mo, while control group was 18. New MOCART score average of the Agili-CTM treated animals was 32±1 (max= 34) vs. 17±1 in the untreated control group. DISCUSSION & CONCLUSIONS The Agili-CTM implant is capable of inducing articular cartilage regeneration. The regenerated tissue resembles hyaline-like cartilage evidenced by the expression of specific markers, PG aggregation with typical zonal distribution as well as subchondral bone plate regeneration, lack of intra-cartilaginous osteophyte formation and self-reconstructing of the articular contour. In summary, the Agili-C™ is a first-of-a-kind acellular scaffold capable of inducing regeneration of cartilage and subchondral bone. It appears to be useful in the treatment of focal articular cartilage defects and might also prevent deterioration of the surrounding articular

surface acting to prevent progression to osteoarthritis.