BMP 12 GENE TRANSFER AUGMENTATION OF INJURED TENDON REPAIR

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**Relevance to Musculoskeletal Condition**

The new member of Bone Morphogenetic Protein (BMP) family, BMP 12, has the potential to augment injured tendon repair.

**Introduction**

BMP-12 is a new member of the human BMP family. It is the human homologue of mouse growth/differentiation factor (GDF)-7 and belongs to a new subgroup in the TGF-β superfamily. Accumulated evidence indicates that BMP-12 appears less osteogenic compared to other BMP proteins. Our previous studies demonstrated that adeno-virus mediated BMP-12 gene transfer into chicken tendon cells in vitro increased 3H-thymidine incorporation, cell proliferation and Type I collagen synthesis. No alkaline phosphatase activity was induced by BMP-12 gene transfer in cell lines which also responded to BMP-2. Recently, we also showed that injection of BMP-12 gene transferred mesenchymal progenitor cells into nude mouse muscles induced tendon-like tissue formation(1). To further investigate the potential of BMP-12 to augment tendon healing, we developed a complete tendon laceration model in chickens. Using this model, the effect of BMP-12 gene transfer on the repair process of injured tendons was investigated. Our results indicate that adenovirus mediated BMP-12 gene transfer into an injured tendon can augment tendon repair.

**Materials and Methods**

A replication deficient adenovirus carrying human BMP-12 (Adv-BMP12) was constructed as previously described(1). Twenty five 12-18 week White Leghorn chickens were used in the animal model. Under intramuscular Ketamine (30mg/Kg), Xylazine (6mg/Kg), and Acepromazine (1mg/Kg) anesthesia, surgery was performed on the long toes of both feet. Using a tourniquet and sterile surgical technique, mid-line incisions were made on the plantar surface of the long toes in zone II. The flexor sheath was opened longitudinally between the proximal and distal pulleys (which were left intact), exposing the flexor profundus tendon. A complete transverse laceration was made across the mid-section of each flexor profundus tendon. Repair of the laceration was made by two simple suture with 6-0 nylon suture. The sheath was not repaired. The skin was closed with a continuous running 6-0 nylon suture. Immediately following surgery, recombinant adeno-viruses were injected into operated tendons as described previously(2). The right long toe flexor tendon received a single 300 ul injection containing 3 X 107 pfu Adv-BMP12 and the left long toe flexor tendon (control) received 3 X 107 pfu Adv-βgal. Operated toes were immobilized in a boxing glove fashioned fiberglass cast. All animals walked freely in their cages and had free access to food and water. The operated tendons were harvested at week 2, week 4 and week 6 post-surgery. Tensile strength of the harvested tendons was tested with an Instron tensile test(3). Sample (week 4) Ultimate Force (Newton) Stiffness (Newton/mm) Displacement to Max Force (mm)

<table>
<thead>
<tr>
<th>Sample (week 4)</th>
<th>Ultimate Force (Newton)</th>
<th>Stiffness (Newton/mm)</th>
<th>Displacement to Max Force (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adv-βgal</td>
<td>3.29 ∀ 1.2</td>
<td>4.15 ∀ 2.3</td>
<td>1.75 ∀ 0.4</td>
</tr>
<tr>
<td>Adv-BMP12</td>
<td>6.47 ∀ 0.9*</td>
<td>8.86 ∀ 2.2*</td>
<td>1.9 ∀ 0.3</td>
</tr>
</tbody>
</table>

* Paired t-test P<0.05

Table 1. Mean (+SD) value for tensile properties of repaired tendons.

**Discussion**

The purpose of our research is to develop a gene therapy protocol to improve clinic tendon repair. BMP-12 has been shown to be functionally different from BMP-2. Our previous data demonstrated that BMP-12 gene transfer could enhance chicken tendon cell growth and Type I collagen expression. The present study further demonstrates that BMP-12 gene transfer can augment tendon repair in an in vivo model of complete tendon laceration. These finding indicate a potential for BMP-12 as a gene therapy agent to improve the early strength of healing flexor tendons.

**Acknowledgments**

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**References**