SOX9-Mediated Gene Therapy in a Degenerative Disc Model
F.M. Phillips, MD; R.C. Haydon, MD, PhD

The objective of this proposal was to determine the efficacy of exogenous SOX9 for the treatment and/or prevention of degenerative disc disease in an animal model. Three specific aims were proposed. The first aim was to determine whether the AdSOX9 vector could efficiently transduce rabbit lumbar intervertebral discs in vivo. The second aim was to determine whether exogenous SOX9 expression could promote the healing of degenerative lumbar discs in an animal model of disc degeneration. The third aim was to determine whether exogenous SOX9 expression could prevent and/or delay the intervertebral disc degenerative process in vivo.

We have recently completed the proposed studies. Specifically, we first demonstrated that recombinant adenoviral vectors expressing SOX9 (ie, AdSOX9) or GFP (ie, AdGFP) effectively transduced disc cells when they were injected into the lumbar intervertebral discs of New Zealand white rabbits. When the intervertebral disc materials of the injected animals were analyzed, expression of exogenous SOX9 and induced production of type II collagen were readily detected in AdSOX9-injected disc tissues using immunohistochemistry.

We next used a stab incision procedure to establish the lumbar intervertebral disc degeneration model of New Zealand white rabbits. To determine the potential therapeutic effect of SOX9, we first introduced stab incision for four weeks, followed by injection of the AdSOX9 or the AdGFP control into the degenerative discs. To determine the possible preventive effect of SOX9 on disc degeneration, we injected the AdSOX9 or AdGFP virus at the same time when the lumbar discs were stabbed. Animals were sacrificed at six and eight weeks after injection and were evaluated using X-ray radiography and MRI. The injected discs were evaluated histologically for preservation of normal disc architecture and the levels of Type II collagen in the nucleus pulposus were immunohistochemically determined.

Findings or Conclusions to Date. We found that AdSOX9 injection effectively transduces intervertebral discs and increases the production of Type II collagen. Using the stab incision-induced disc degeneration model, we have demonstrated that AdSOX9 injection restored the chondroid appearance of normal nucleus pulposus whereas the AdGFP-injected discs showed degenerative changes consistent with annulotomy-induced degeneration. Both plain X-rays and MRIs showed lesser grades of disc degeneration in the SOX9-treated discs. Thus, our findings support the hypothesis of our application, suggesting that SOX9 can be used as a potential therapeutic agent to treat disc degeneration.