INTRODUCTION: It has previously been reported that the use of OP-1 (rhBMP-7) alone results in a higher rate of posterolateral than autograft alone in a rabbit model. However, the molecular mechanisms involved in this process remain to be elucidated. In this study, we examined the molecular biology of spinal fusion and specifically the effects of OP-1 (rhBMP-7) the expression of the genes encoding for type I collagen, BMP-2, 4, 5 and 7, in the New Zealand white rabbit (Oryctolagus cuniculus) model. Furthermore, gene expression following fusion with OP-1 alone was compared to that seen with autograft alone. In addition, RT-PCR products were used to determine the sequence for Oryctolagus cuniculus genes BMP-5 and OP-1, which had previously been undetermined.

METHODS: Posterolateral intertransverse process lumbar arthrodesis was performed with either iliac crest bone autograft or OP-1 (rhBMP-7) using the New Zealand white rabbit model previously described by Boden (Feiertag et al, Spine 21(1): 27-31, 1996). Two animals in each of the 2 study groups were sacrificed on postoperative days 2, 4, 7, 14, and 35. Inner (central) and outer (juxtatransverse) zone samples of the fusion mass were processed for isolation of mRNA. Primers synthesized from published rabbit sequences or adapted from highly conserved regions in other species were used for quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) analysis. Image analysis software was used to quantify the RT-PCR product for each gene studied with respect to the constitutively expressed GAPDH product and the quantified expression was normalized to the constitutive expression of the various genes in iliac crest autograft at day zero.

RESULTS: Type I collagen was expressed in greatest amounts during days 7 and 14. BMP-2, 4, 5, and 7 mRNA were expressed in both the inner and outer region of the fusion mass. The temporal sequence of gene expression in the autograft animals did not differ significantly from that of the OP-1 treated animals. Expression of
BMP-5 and OP-1 in the developing spinal fusion mass was demonstrated for the first time. The PCR products of BMP-5 and OP-1 were sequenced producing fragments of 1.1 kb of BMP-5 and 1.0 kb of BMP-7. This elucidated a portion of the previously undetermined amino acid sequences of these genes in the rabbit.

CONCLUSIONS: This is the first spinal fusion gene expression study to normalize RT-PCR results to a constitutively expressed (housekeeping) gene and then to compare the results to the baseline expression of the same genes in iliac crest autograft. The similarity in expression of various bone morphogenetic proteins in both the autograft group and the OP-1 group highlights the finding that the application of a single bone morphogenetic protein without supplemental autograft in the fusion bed results in similar BMP gene expression as does autograft alone. The expression of type I collagen in our spinal fusion model is highly consistent with that seen in the fracture repair model. The newly elucidated Oryctolagus cuniculus BMP-5 and OP-1 gene sequences demonstrated near complete homology with the corresponding human and murine sequences. These findings suggest that the use of OP-1 as a single osteoinductive protein may preclude the need for iliac crest bone harvest and its resultant morbidity. The importance of OP-1 in the biology of spinal fusion is underscored by the similarity in molecular events between OP-1 alone and iliac crest autograft fusions.

- If noted, the author indicates something of value received. The codes are identified as: a – research or institutional support, b – miscellaneous funding, c – royalties, d – stock option, e – consultant or employee. For full information, refer to inside back cover.

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