Cellular and Structural Analyses of Intervertebral Disc Degeneration in NFAT1 Deficient Mice

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Introduction. The intervertebral disc (IVD) has three components: nucleus pulposus (NP), annulus fibrosis (AF), and cartilaginous end plate (CEP). NFAT1 is a member of the nuclear factor of activated T cells (NFAT) transcription factor family. While previous studies linked NFAT1 deficiency with osteoarthritis, the role of NFAT1 in IVD homeostasis remains unknown. Our hypothesis is NFAT1 is essential for maintaining IVD homeostasis and attenuating IVD degeneration.

Methods. Safranin-O stained histologic images of lumbar IVDs of mice (both sexes) were used for quantitative cellular and tissue analysis using ImageJ. The IVD images of NFAT1-deficient ($Nfat1^{-/-}$) mice were analyzed at 2, 6, and 12 months of age; age-matched wild-type (WT) IVD images served as controls. Six $Nfat1^{-/-}$ IVDs and six WT IVDs were analyzed at each age point. Data from three independent researchers were statistically analyzed using unpaired t-tests and ANOVA.

Results. ImageJ-assisted cell counting showed $Nfat1^{-/-}$ IVDs had a significant decrease in cell density at 6 months ($p = 0.001$) and 12 months ($p = 0.011$), compared to the age-matched WT IVDs. An age-dependent decrease in CEP cell density ($p = 0.018$) was detected in $Nfat1^{-/-}$ IVDs, but not in WT IVDs. No significant sex difference in IVD cell counting or structural changes in $Nfat1^{-/-}$ IVDs for the ratio of AF/total IVD area or NP/total IVD area were detected at any timepoint.

Conclusions. These findings suggest that NFAT1 is essential for cellular homeostasis in mouse IVDs. NFAT1 deficiency causes decreased cellular density in the IVD, a cellular feature of IVD degeneration.

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