

Safety and Bioactivity of Disc-Derived Progenitor Cells to Treat Degenerative Disc Disease in a Rabbit Disc Model (GLP Study)

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INTRODUCTION

- Our group recently received FDA allowance to begin clinical testing of IDCT, a cell therapy product to treat lumbar degenerative disc disease.
- The treatment contains live cells, known as Discogenic Cells, that are modified from proliferated adult nucleus pulposus tissue, combined with a viscous carrier.
- The safety and bioactivity of IDCT was evaluated in a GLP rabbit study. We hypothesized that no safety concerns would be noted, and that bioactivity would be observed. This study tested IDCT manufactured in a manner analogous to the future human clinical trial (cGMP, clean rooms, etc), contributing to the safety profile of the product as well as supporting the proposed mechanism of action.

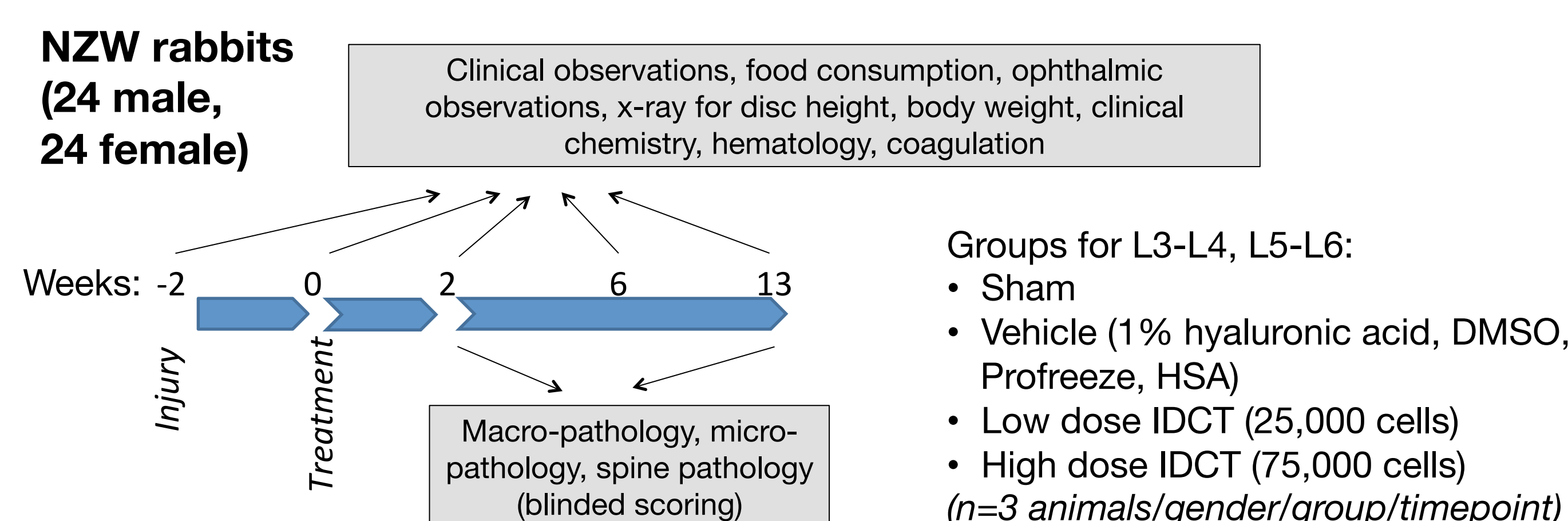


Figure 1: Production of IDCT in clean rooms.

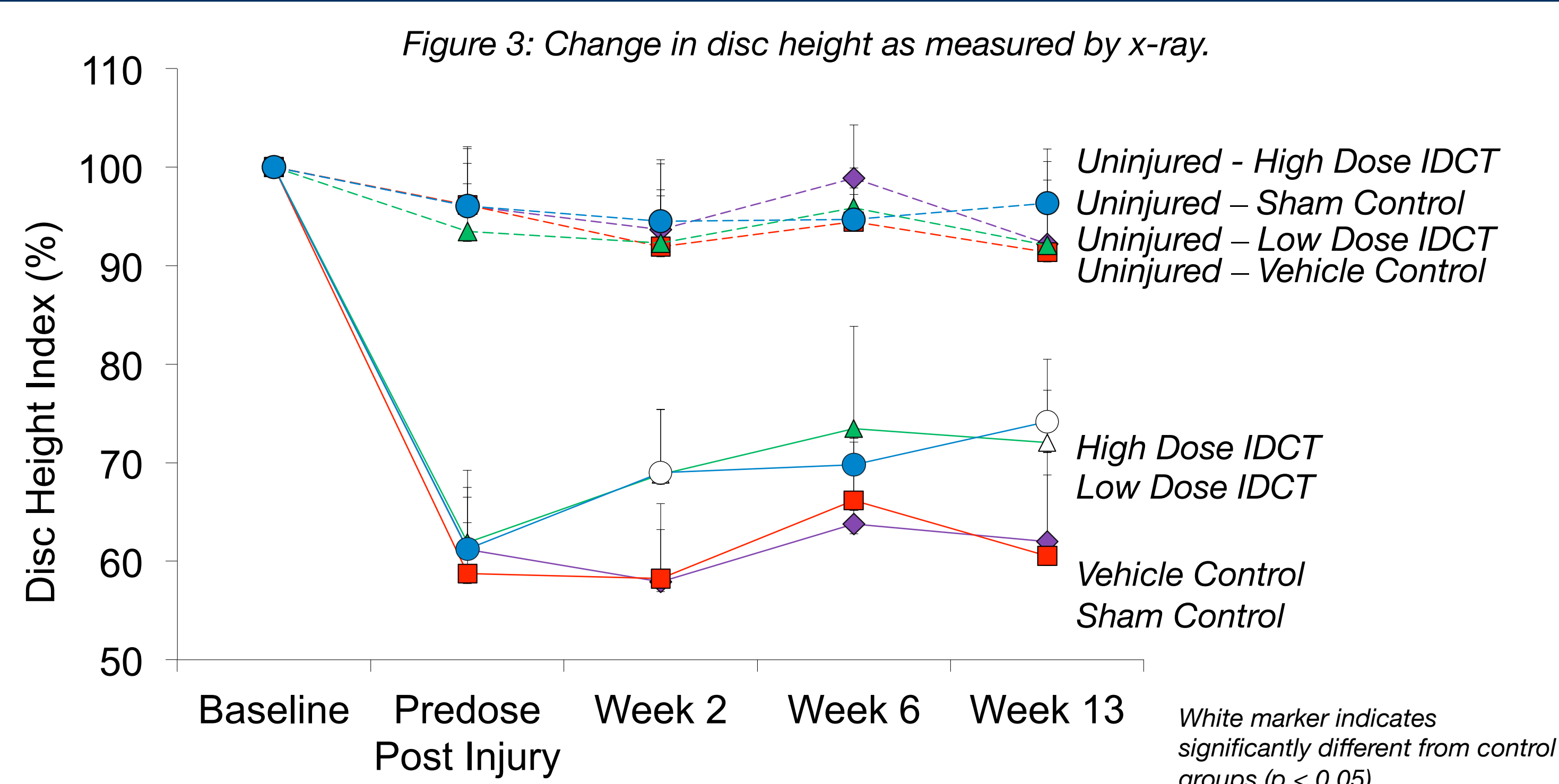
METHODS

- This study was performed with oversight from a private IACUC and adhered to US Good Laboratory Practice (GLP) standards. Evaluations were performed by a certified pathologist in a blinded manner.
- In each animal, discs L3-L4 and L5-L6 were injured via 18-gauge needle puncture and two weeks later, animals were dosed with 25 μ L of treatment in each disc, as shown in **Figure 2**.
- Rabbits were evaluated in-life and post-mortem (2 and 13 weeks after dosing) as shown in **Figure 2**.

Figure 2: Study design schematic.



RESULTS



- No IDCT-related safety concerns were noted across all of the parameters evaluated.
- After 2 and 13 weeks, animals administered Low or High IDCT showed disc height improvement (10% and 13%, respectively) that was statistically higher than sham or vehicle ($p < 0.05$, **Figure 3**).

RESULTS

- After 2 weeks (**Figure 4**) and 13 weeks (**Figure 5**), sham and vehicle discs were abnormal compared to health discs. IDCT-treated discs looked more similar to normal than sham or vehicle discs, especially for the Low Dose.
- Blinded scoring of the discs showed for the total score (combination of safety and structural parameters), the Low Dose IDCT was not significantly different than the uninjured, although higher in score (**Figure 6**). The safety parameters were comparable between groups and relatively low. Structural parameters were not different between Low Dose IDCT and healthy discs at 2 weeks, whereas other groups were different. An increase in ventral prolapse by 13 weeks may mask subsequent positive changes seen at 2 weeks (**Figure 6**).

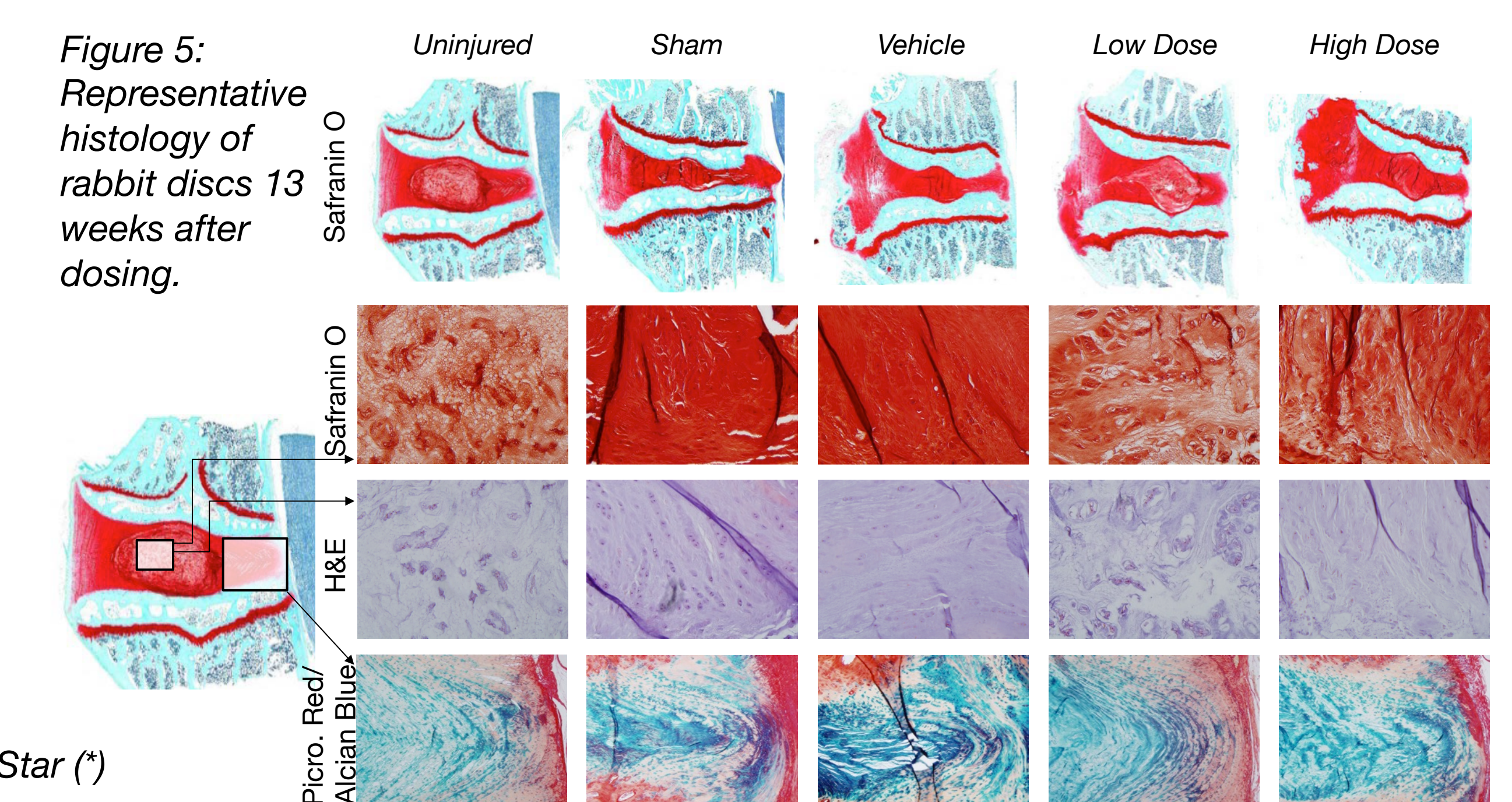
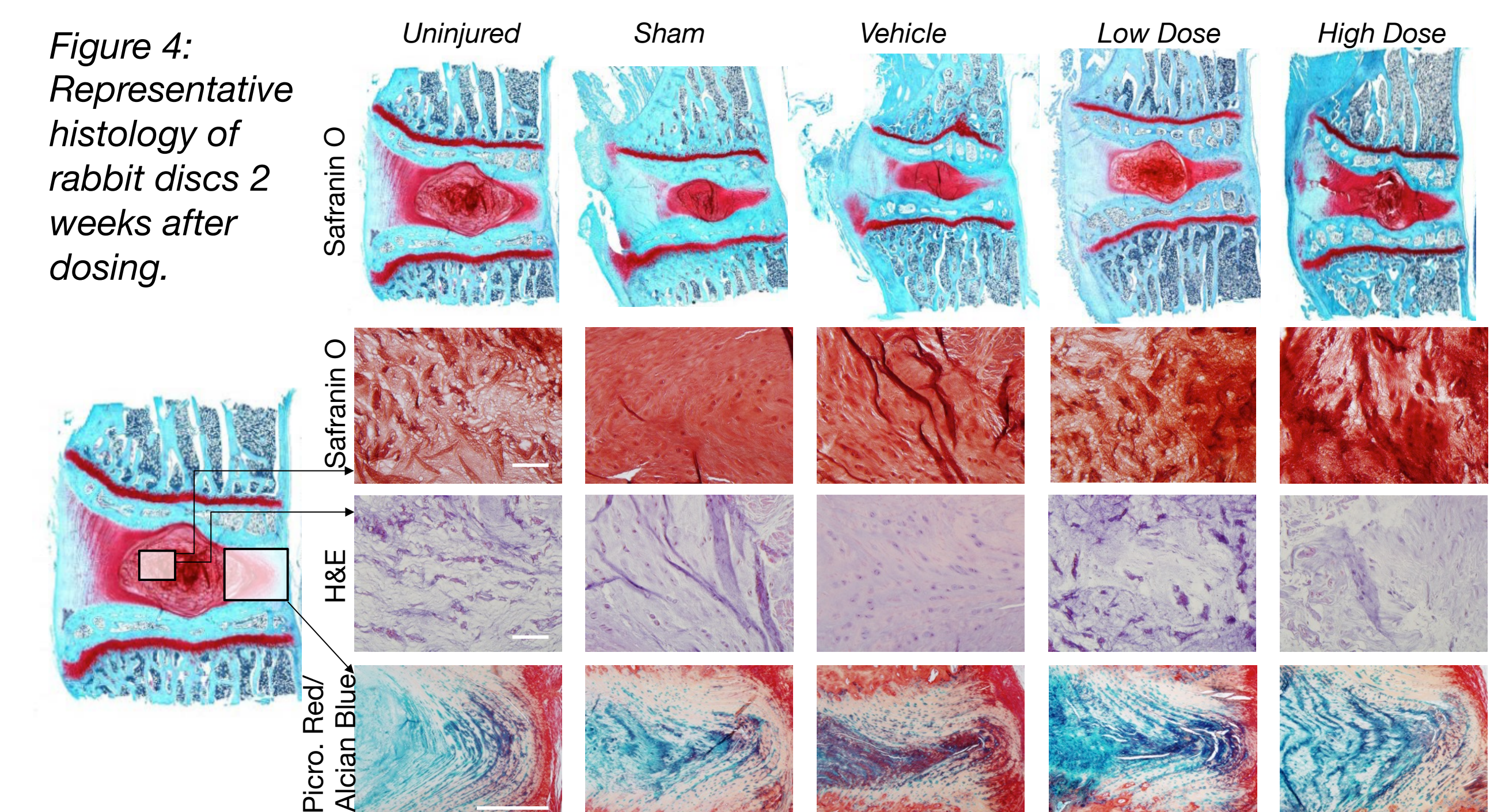
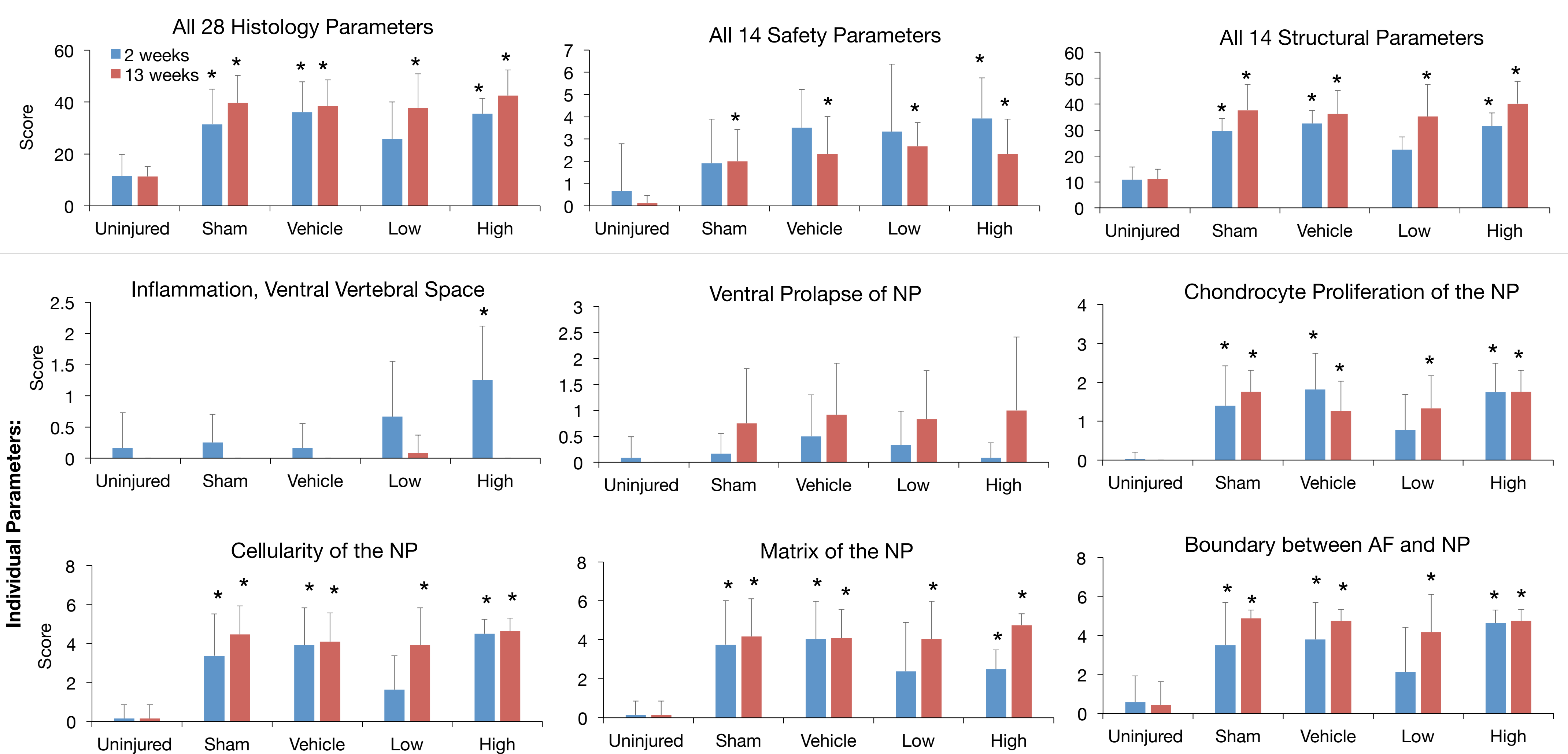


Figure 6: Blinded scoring of disc histology by pathologist. Star (*) indicates difference from uninjured at each timepoint.



CONCLUSIONS

- In this GLP study, two discs per animal were dosed with either IDCT, vehicle control, or a sham procedure. Discs within each animal received the same treatment in order to evaluate systemic safety. No safety concerns associated with either dose of IDCT or the vehicle were observed in the animals, both locally and systemically.
- No significant gender differences were noted. No effect of IDCT was noted on the adjacent disc, although the injury did impact the adjacent disc. The disc height improved within two weeks of treatment with both doses of IDCT but not vehicle or sham, and was also improved after 13 weeks. Histologically, delivery of Low Dose IDCT resulted in normalization of tissue architecture after 2 weeks.
- In conclusion, IDCT manufactured using the same process as the human clinical trial showed safety and bioactivity in a rabbit model of disc degeneration. Human clinical testing is ongoing.