



Utrecht University



Protective effects of IL-1Ra gene therapy on IVD degeneration: in vitro and in vivo findings in Beagle dogs

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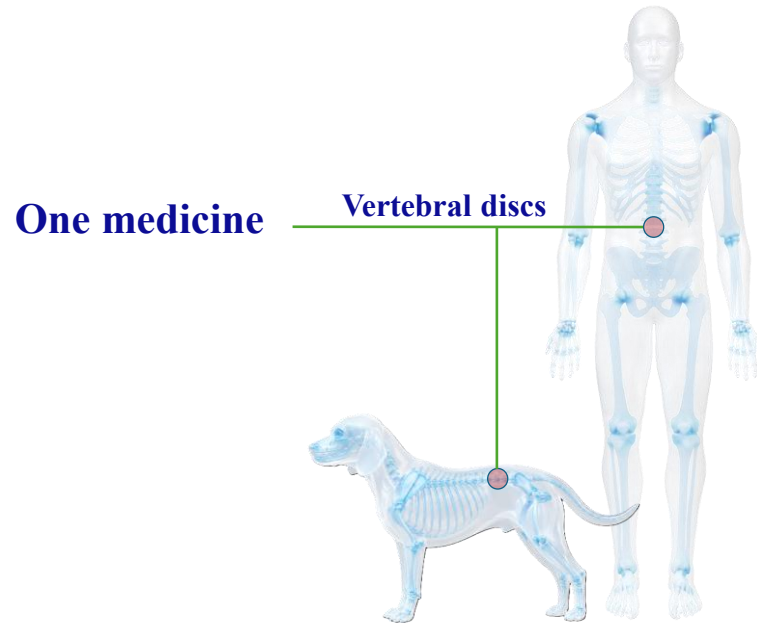
Regenerative Orthopedics group

24/06/2026

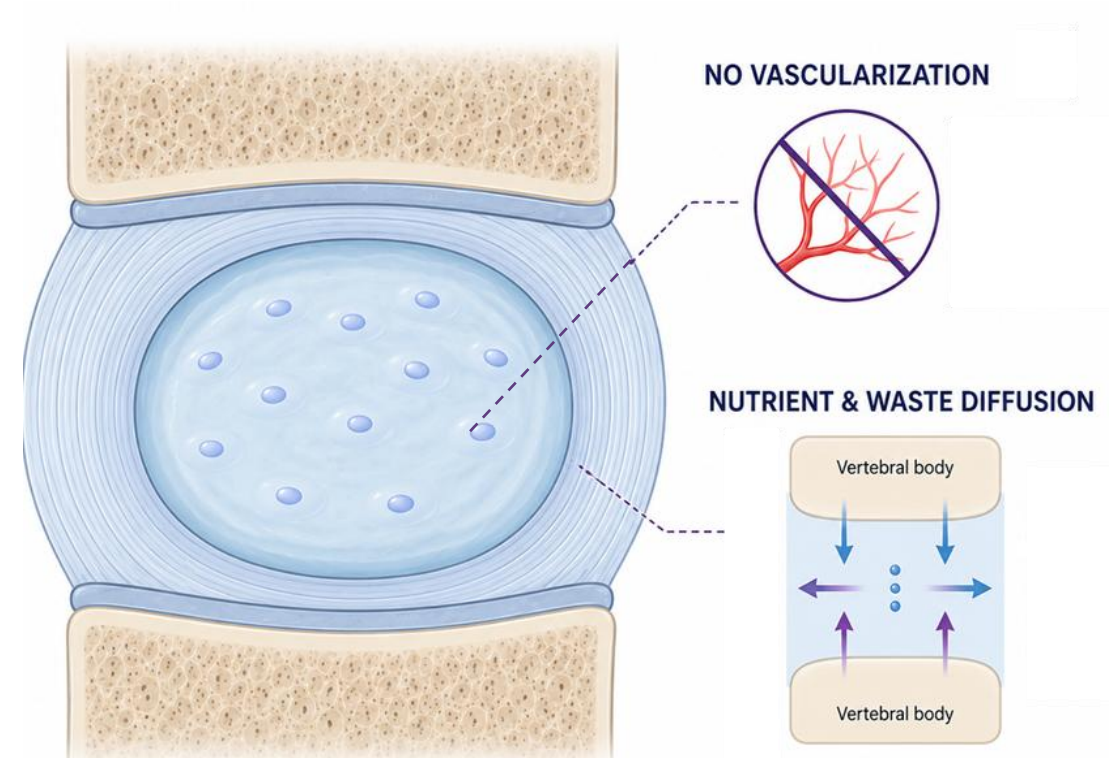


I have no personal conflicts of interest to declare
This research is funded by [Pacira Germany GmbH](#).

Gene therapy for early to moderate IVD degeneration



- Long-term expression
- Closed Compartment for local treatment



Why high-capacity adenoviral vector (HCAAd)?



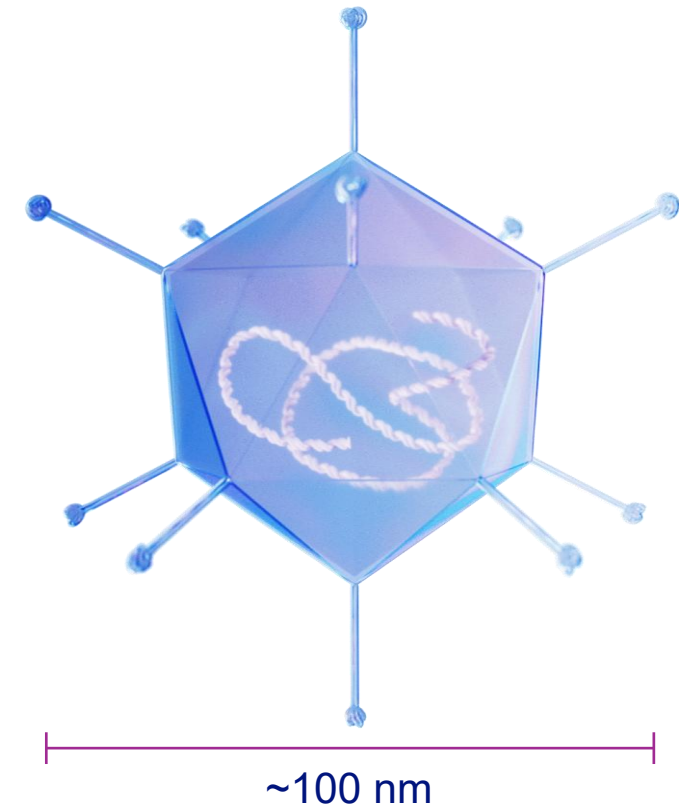
Delivery of larger genes and regulatory elements



Higher transduction efficacy



Safety: Non replicating, episomal



Target Gene



Local IL-1 β inhibition using IL-1 receptor antagonist (IL-1Ra) gene delivery

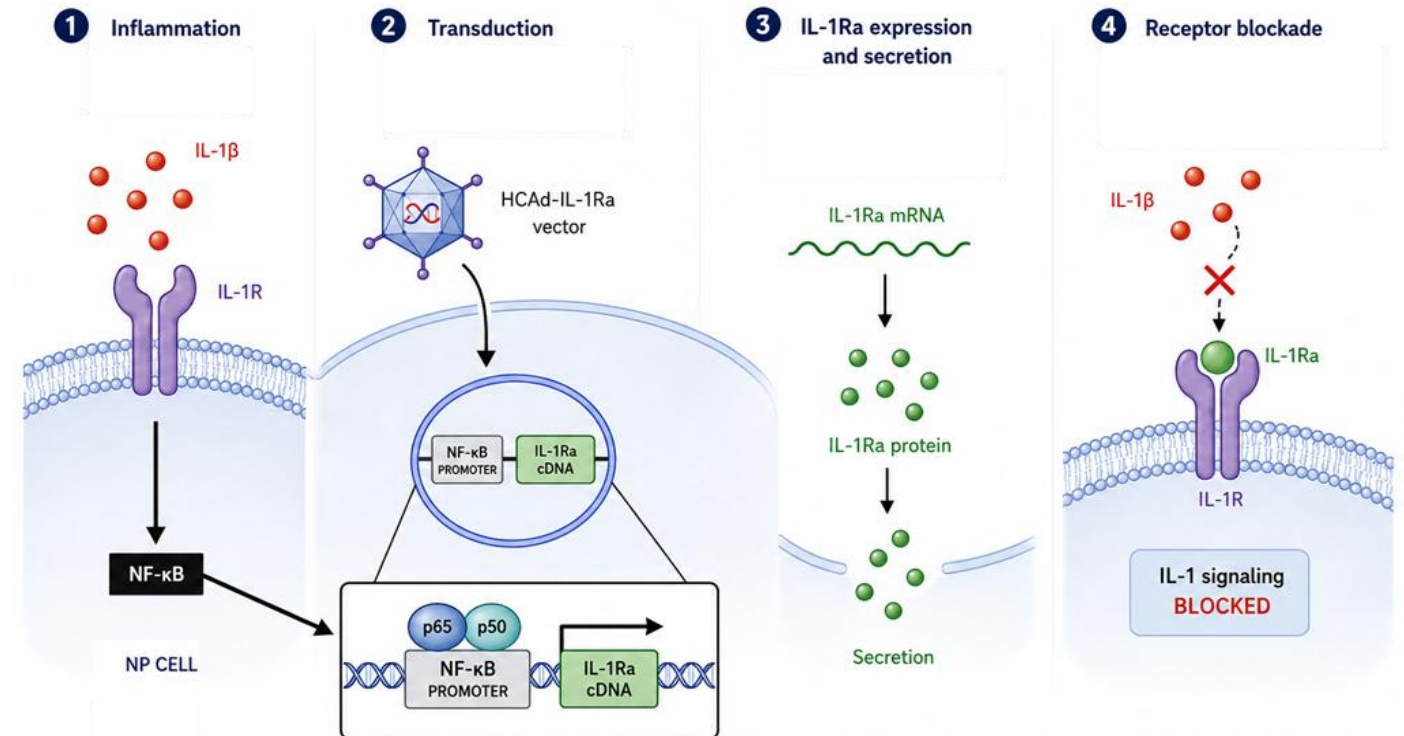
□ NF- κ B promoter => inflammatory-responsive gene therapy



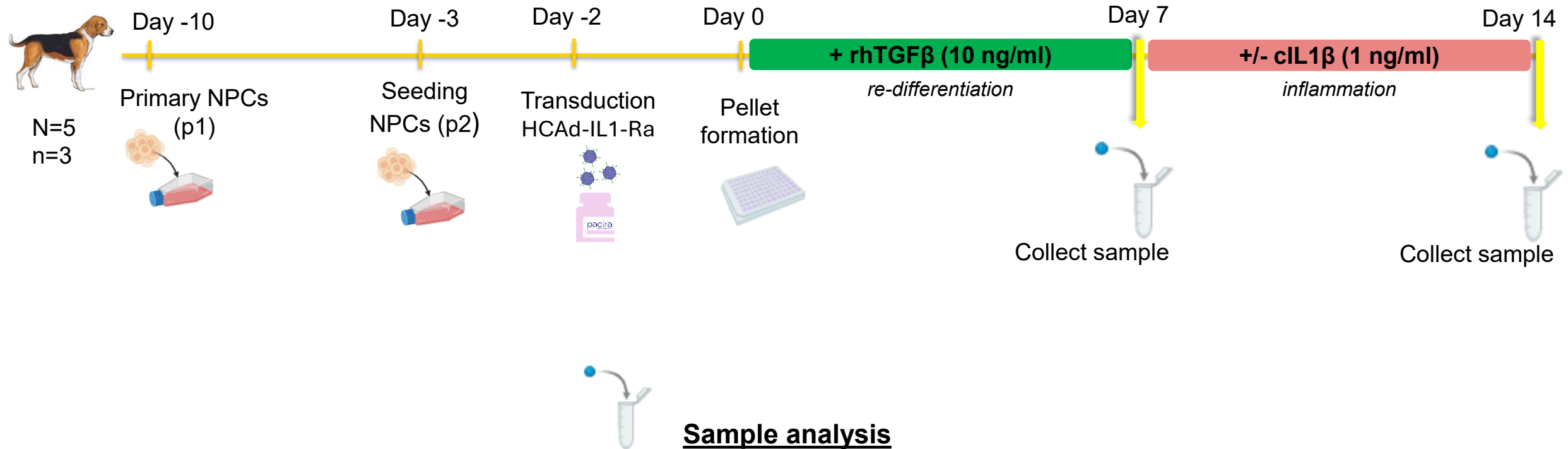
AIM: **translational potential** of IL-1Ra gene therapy.

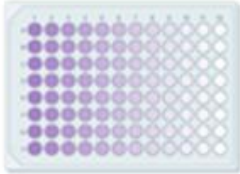
A) *in vitro* model

B) *in vivo* dog degenerated IVD model

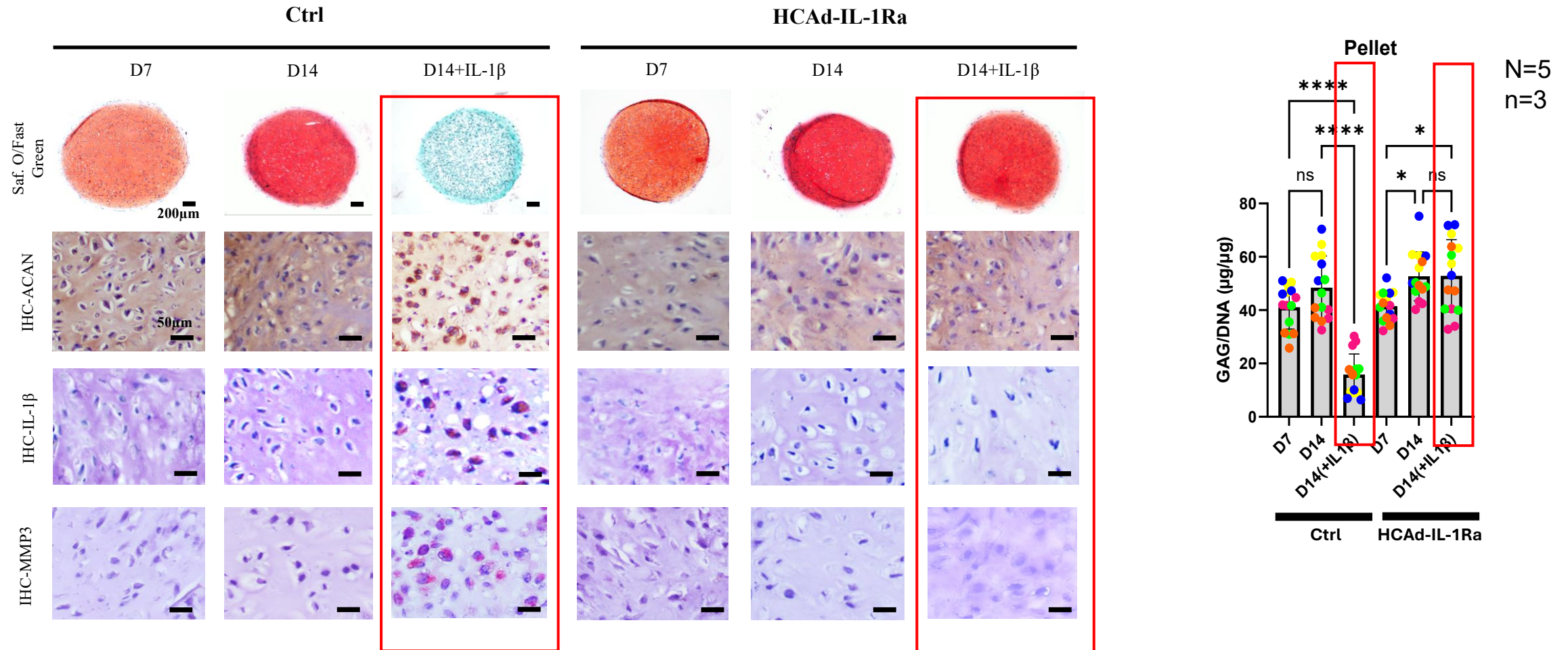


Biological HCAd-IL-1Ra efficacy using a dog inflammation *in vitro* model

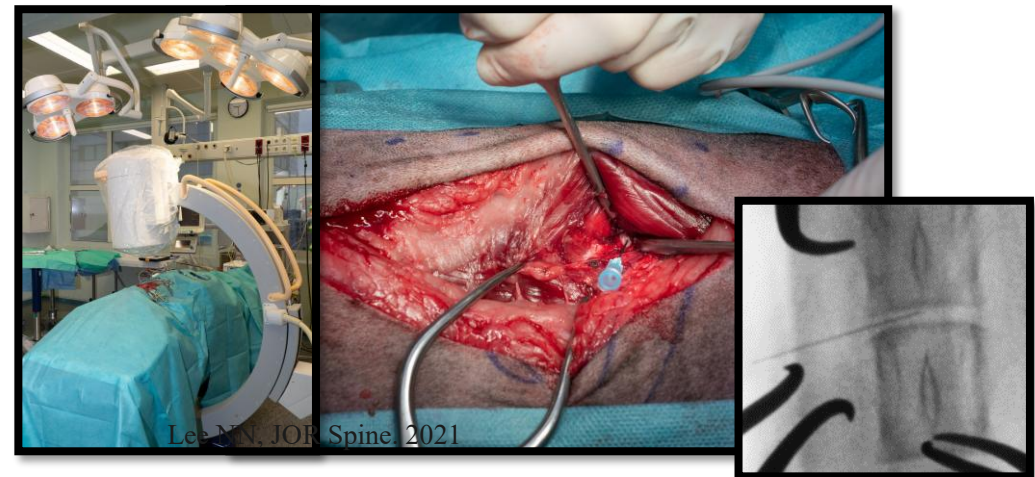
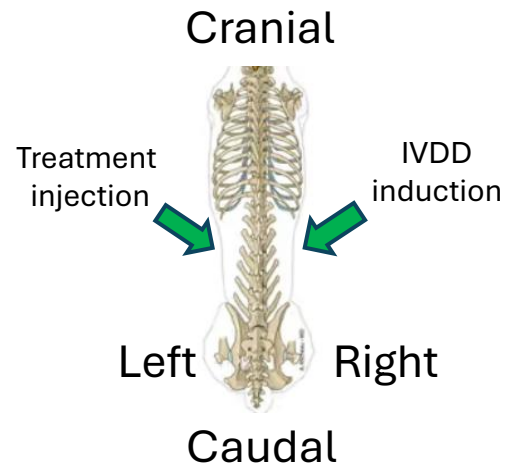
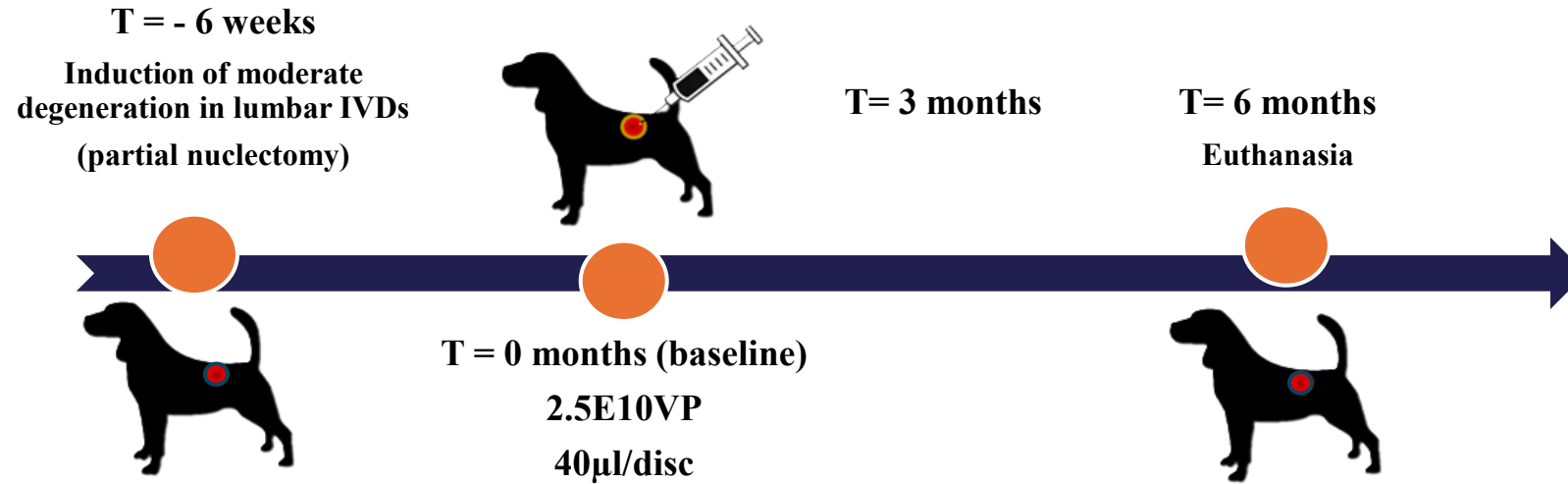


Histology - pellet	Biochemical assays – pellet & media
 • Morphology • Anabolic (ACAN) • Inflammation (IL-1β) • Catabolic (MMP3)	 • GAG (DMMB) • DNA (Qubit)

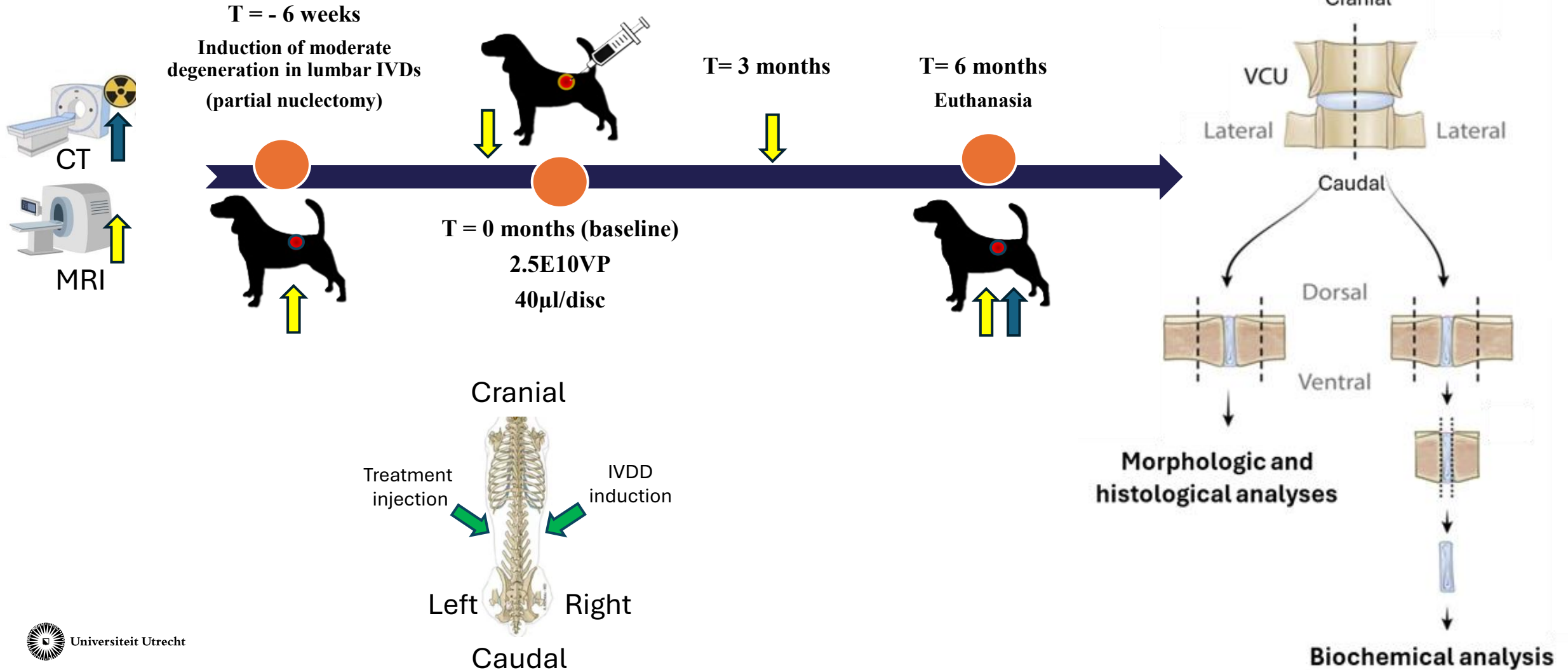
IL-1Ra halts IL-1 β -induced GAG/ACAN loss and arrests IL-1 β -induced MMP3 and IL-1 β expression



In vivo study design & readouts, n= 6 female Beagle dogs



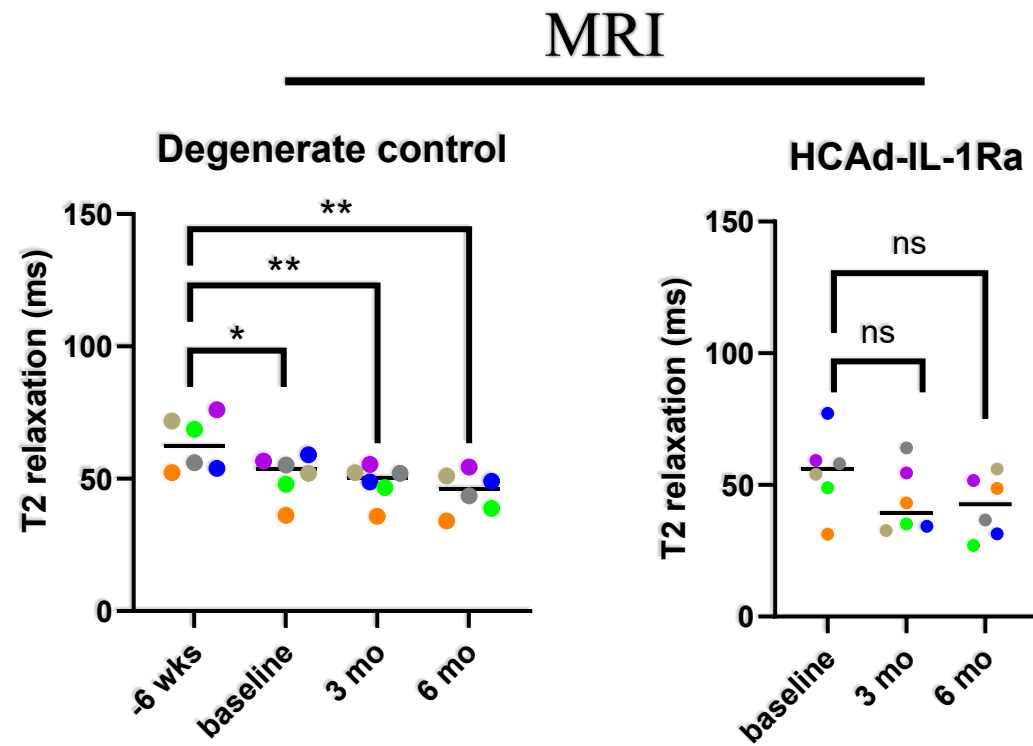
In vivo study design & readouts, n= 6 female Beagle dogs



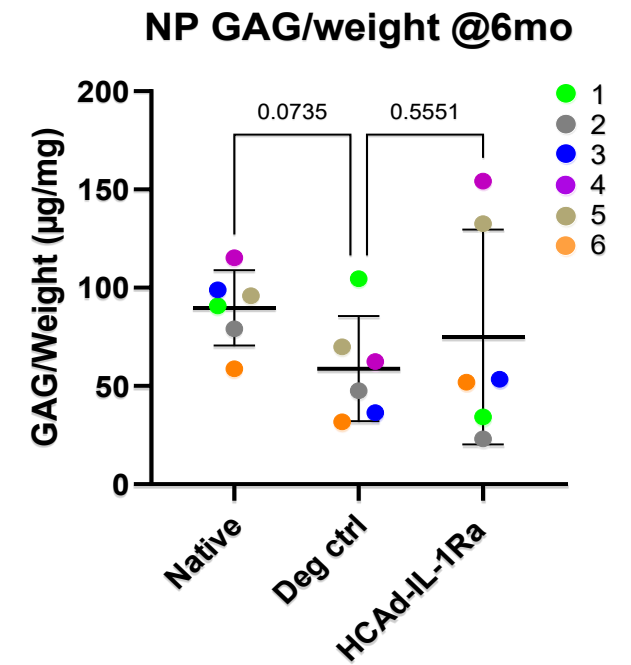
✓ Safety Assessment: No histopathological adverse effects or tissue abnormalities were observed.

- HCAd-IL-1Ra seems to reduce the attenuation of T2 values on MRI

- However, it does not rescue GAG loss at tissue level

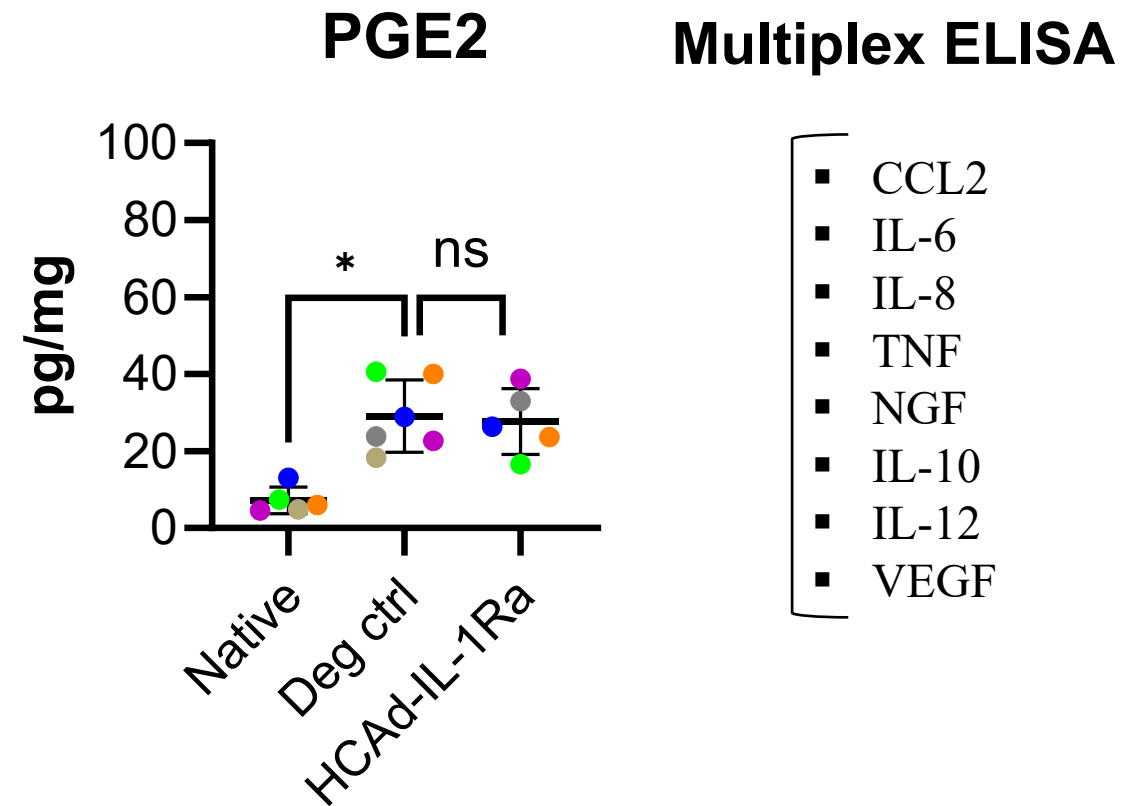
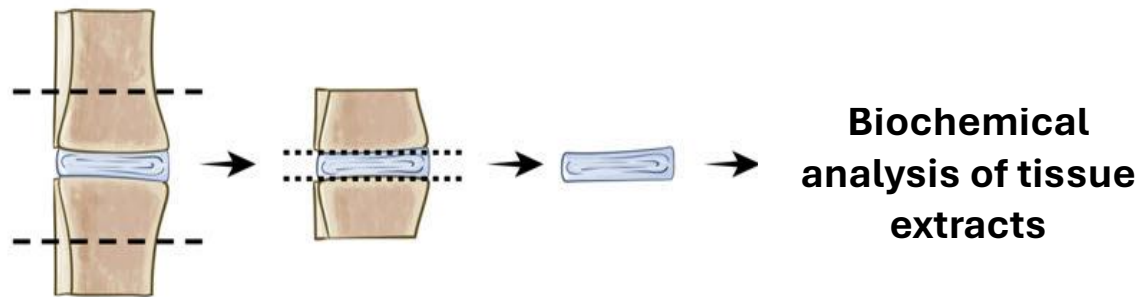


DMMB- GAG content

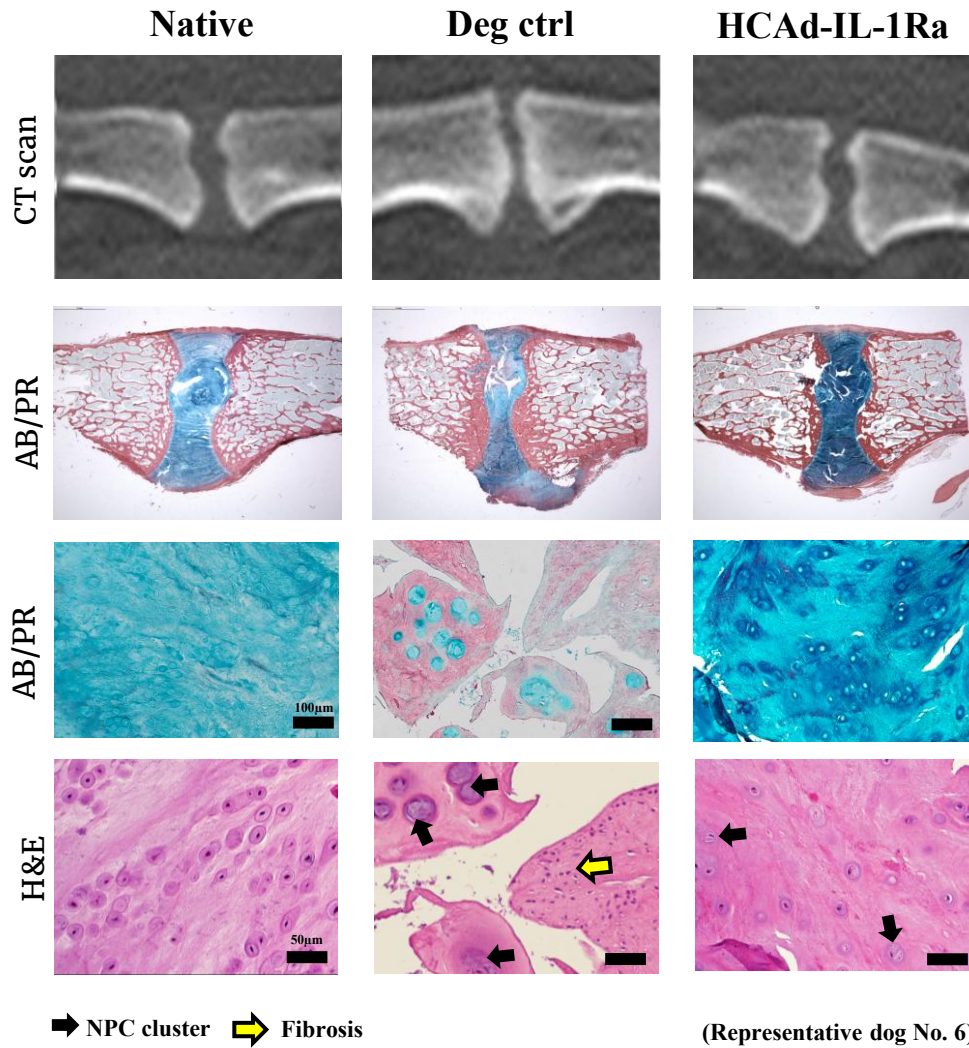
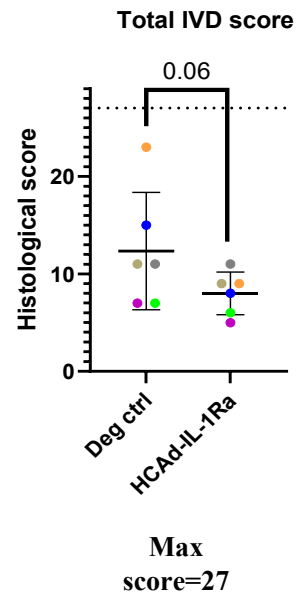


NP tissue: profiling inflammation at 6 months

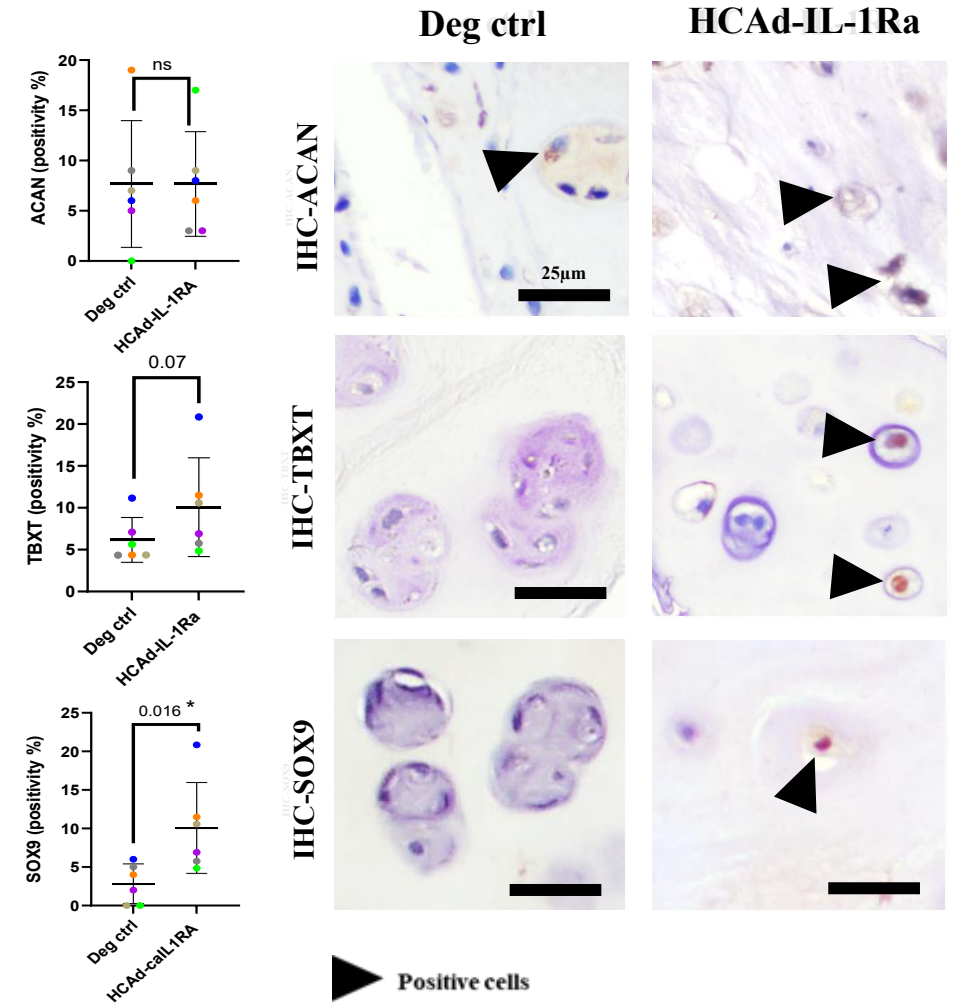
- NP tissue: inflammatory mediators did not differ between conditions



✓ HCAd-IL-1Ra reduced the total histological IVD score



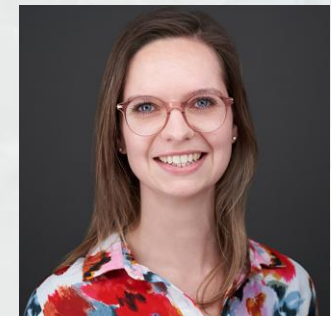
✓ IL-1Ra = 4.5-fold % SOX9⁺ and 1.6-fold % TBXT⁺ NPCs > deg ctrl



HCAd-IL-1Ra may represent a promising therapeutic strategy to halt the progression of IVD degeneration at an early to moderate stage

- **Anti-inflammatory / anti-catabolic effects**
 - The *in vitro* model mimics IL-1 β –driven inflammatory and catabolic degeneration
 - The protective effect of IL-1Ra was confirmed through the *in vitro* study
 - No modulatory effects observed *in vivo*: may be related to the model and the long-term follow-up period
- **Mild protective effects at the matrix level**
 - On histology
 - T2 relaxation time
- **Discussion / follow up steps:**
 - Proteomic analysis of tissue extracts
 - Dose finding

Poster No. 23



Lisanne Laagland



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Acknowledgments

Prof. Marianna Tryfonidou
Chantal Voskamp
Anouk Eversdijk
Saskia Plomp
Irin Kwananocha

Prof. Bjorn Meij
Lisanne Laagland
Michelle Teunissen
Anna Tellegen



paciraTM
GERMANY GMBH



Dr. Kilian Guse



Dr. Stanislav Plutizki



Dr. Oliver Ast



Dr. Gerhard Sponder