Effect of Cross-Linking on Mechanical Function in the Degenerate Nucleus Pulposus

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Motivation

- Low back pain
  - #2 reason Americans see their doctor
  - #2 reason for missing a workday
  - #1 cause of disability
- Intervertebral disc (IVD) degeneration

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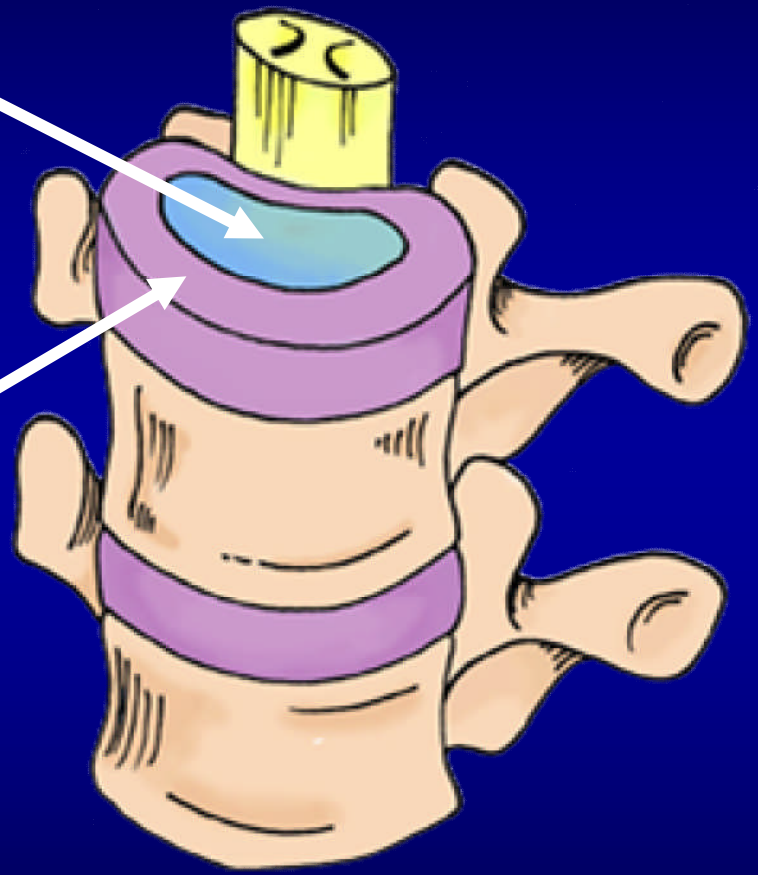
Intervertebral Disc

- **Nucleus Pulposus (NP)**
  - High proteoglycan content
  - Hydrated gel
- **Annulus Fibrosus (AF)**
  - High collagen content
  - Organized fibers



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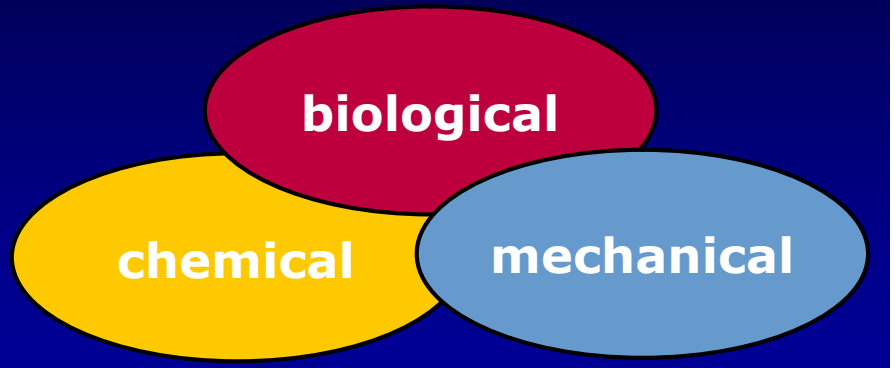
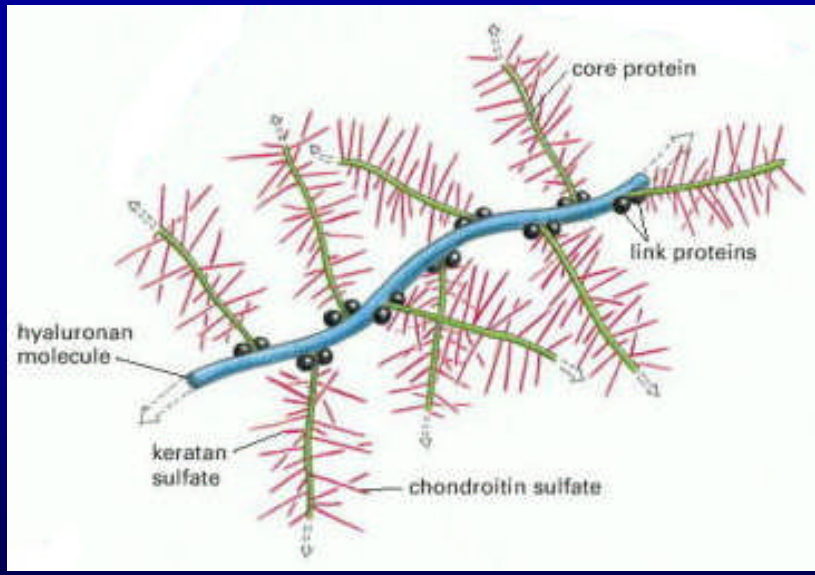
Intervertebral Disc Degeneration

- **Complex process**



- **Proteoglycan content**
  - **Decreases in NP with degeneration**
  - **Changes in mechanical properties**
    - **Significant decrease in swelling pressure**



Proteoglycan
(Alberts, *Molecular Biology of the Cell*)

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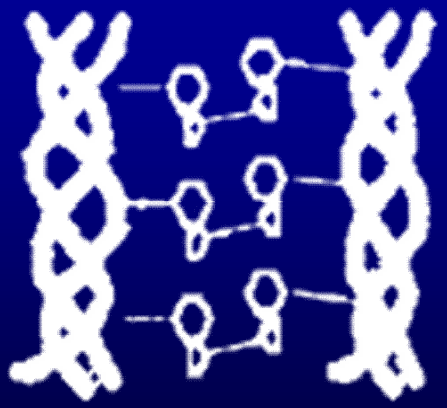
Cross-Linking

- Provide mechanical loading support
- Formed by reactions between amino side groups
- Cross-linking agent: Genipin

Intramolecuar



Intermolecular

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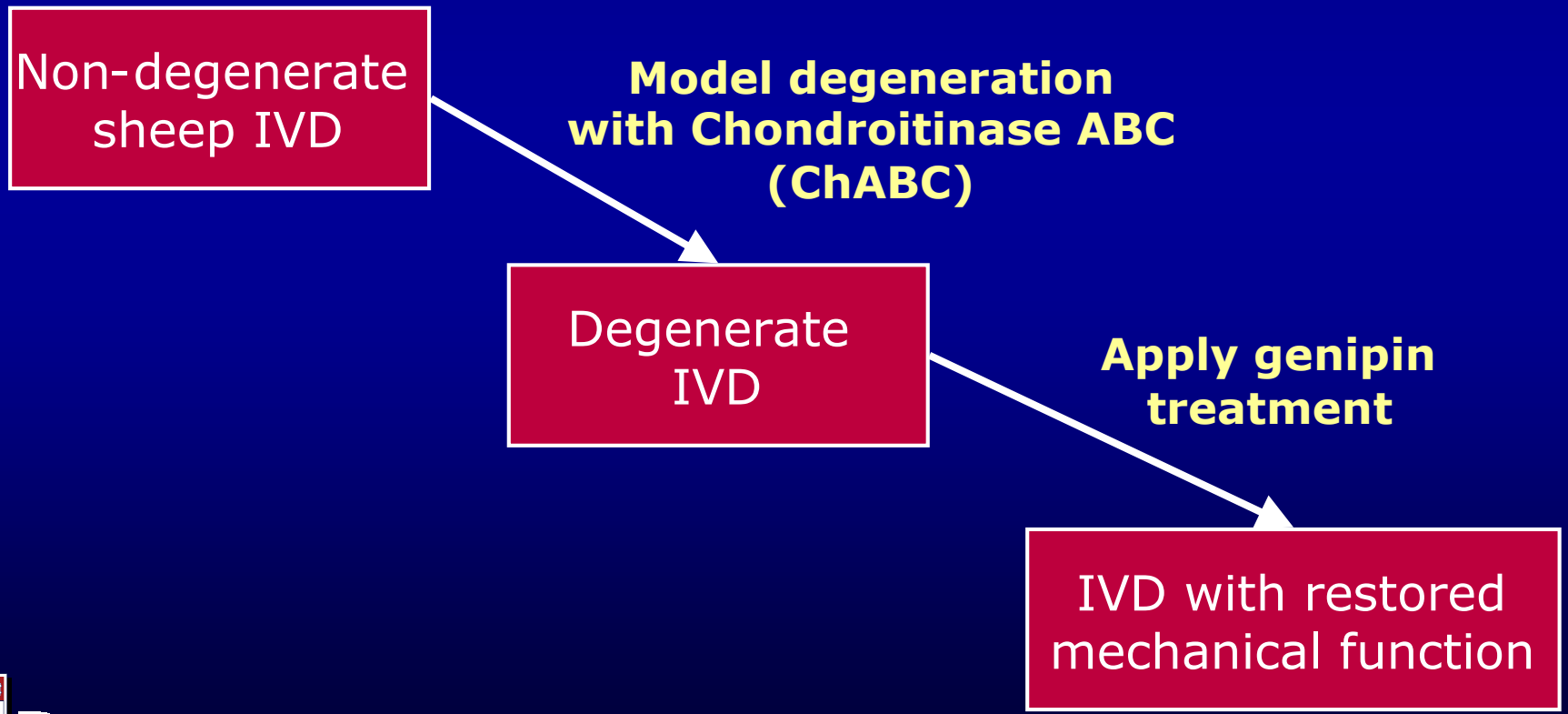
Study Hypothesis

Hypothesis:

Cross-linking will restore mechanical function in the degenerate nucleus pulposus



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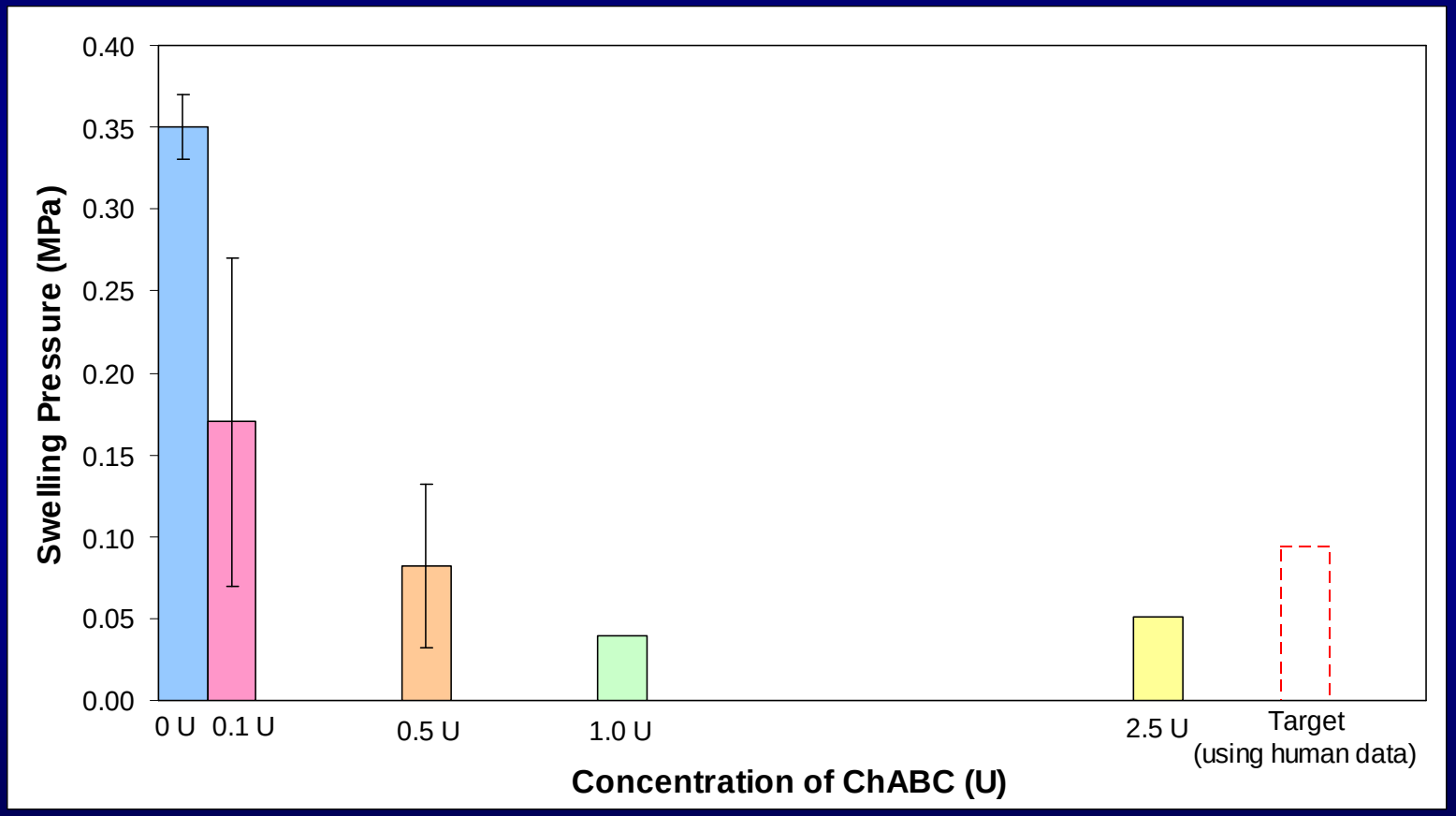
ChABC Dose Finding Results



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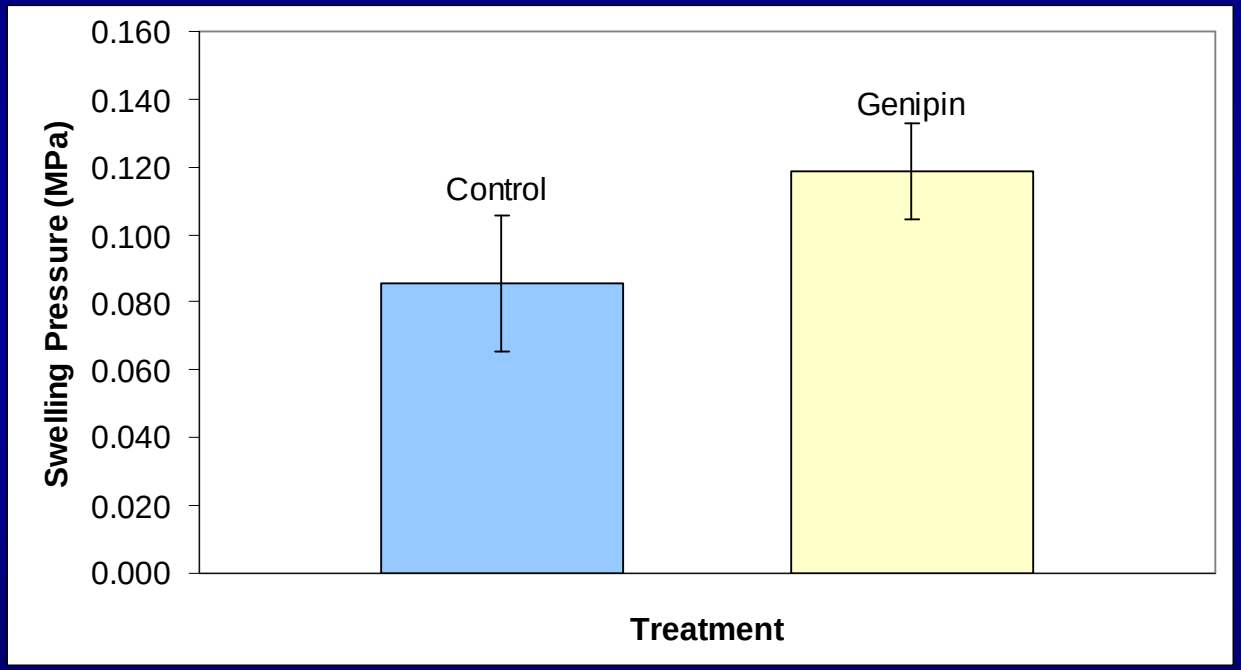
Genipin Cross-Linking Results



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Next Step: Quantifying Cross-Linking

- **Spectrophotometry**
  - **Measures amount of light absorbed by a substance**
  - **Beer's Law: [Absorbance] = k[Concentration]**
  - **Standards of known concentrations are used to make a standard curve**

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Ninhydrin Assay

- Spectrophotometry protocol for free amino acid group determination
- More cross-linking
  - Lower concentration of free amino acid groups
  - Lower absorbance measured

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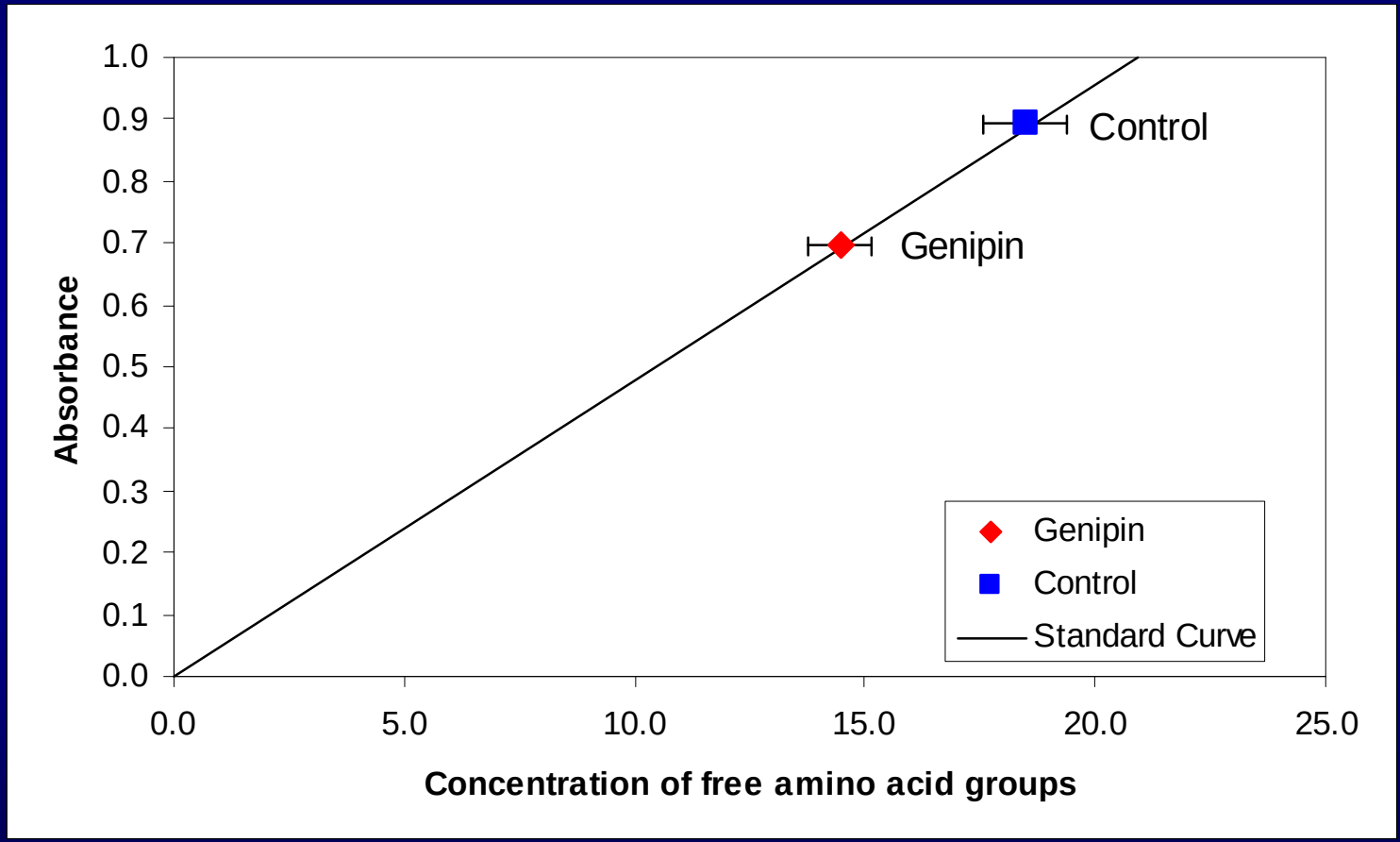
Preliminary Ninhydrin Data

More cross-linking



More cross-linking

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Future Work

- **Finalize ChABC dosage**
- **Test ChABC and genipin together**
- **Quantify genipin cross-linking**

By understanding the effects of cross-linking, an alternative treatment for disc degeneration and low back pain may be developed.

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Thank You

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National Science Foundation
WHERE DISCOVERIES BEGIN