Adipokines and the Intervertebral Disc
A Biochemical Link Between Obesity and Degeneration

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The Fatty Cytokines

ADIPOKINES

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Adipokines

- Leptin
  - Product of the obese gene
  - Pleiotropic effects
  - Inflammatory

- Adiponectin
  - Decreased in obesity

- Hypothesis
  - Obesity → altered adipokines → inflammation → back pain and disc degeneration
METHODS
Methods

- Bovine intervertebral disc
  - Good model for human

- Cells isolated and resuspended in alginate beads

- Cultured under standard conditions and exposed to variable concentrations of:
  - rh Leptin

- Effects on gene expression and production of:
  - matrix macromolecules,
  - degradative enzymes and inhibitors
  - pro-inflammatory cytokines
RESULTS
Effect of Leptin: Gene Expression

Nucleus Pulposus

Matrix | Degradative Enzymes | Inhibitors | Cytokines

Fold Change

ACAN | COL1A1 | COL2A1 | COL6A6 | MMP-1 | MMP-2 | MMP-3 | MMP-7 | MMP-11 | ADAMTS-1 | ADAMTS-4 | ADAMTS-5 | TIMP-1 | TIMP-2 | TIMP-3 | TIMP-4 | IL-1B | IL-6 | TNF-α

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Effect of Leptin: Gene Expression

Annulus Fibrosus

Matrix
Degradative Enzymes
Inhibitors
Cytokines

Fold Change

ACAN  COL1A1  COL2A1  MMP-1  MMP-7  MMP-11  ADAMTS-1  ADAMTS-4  ADAMTS-5  TIMP-1  TIMP-2  TIMP-3  TIMP-4  IL-1  IL-6  TNF-α

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Effect of Leptin: Protease Production

Nucleus Pulposus

[Graph showing fold change to control for proMMP-2, proMMP-3, and MMP-3 at different leptin concentrations (5 µg/mL, 10 µg/mL, 25 µg/mL).]

* *p < 0.05
*** p < 0.001
Effect of Leptin: Protease Production

Annulus Fibrosus

Fold Change to Control

MMP-1 proMMP-2 MMP-2 proMMP-3 MMP-3 MMP-9

5 µg/mL 10 µg/mL 25 µg/mL

*p<0.05   **p<0.01   ***p<0.001
Conclusions

- Leptin leads to both:
  - Changes in gene expression
  - Changes in protease production

- This could initiate and potentiate degeneration and pain

- Further work needed
Where next?

- Pro-inflammatory potentiation
- Spinal fat samples
Acknowledgements