

Mechanical Induction of Inflammatory Signalling in Cartilage

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INCREASES IN PROTEINASE mRNA IN OA CARTILAGE ARE SMALL

Appleton et al 2007, Arthritis Rheum. 56, 1854-1868

'Global analysis of gene expression in early experimental osteoarthritis'.

Rat articular cartilage 4 weeks post-surgery (ACL section/partial medial meniscectomy)

mRNA	fold increase
ADAMTS-5	2 - 3
MMP13	1.5 - 2
COX2	2

Chia et al unpublished.

Mouse joints 2 weeks post-surgery (destabilisation of medial meniscus)

mRNA	fold increase
ADAMTS-5	1.5
MMP13	2.0

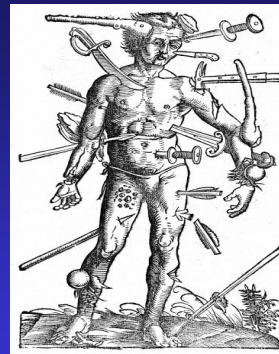
IL-1 receptor family
(e.g. IL-1R, IL-18R,
Toll-like receptors)

TNF receptor family
(e.g. TNFR-p55, CD40,
RANK)



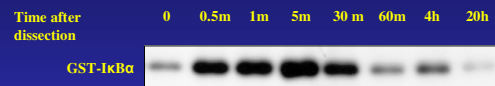
Mitogen-activated
protein kinases

NFκB



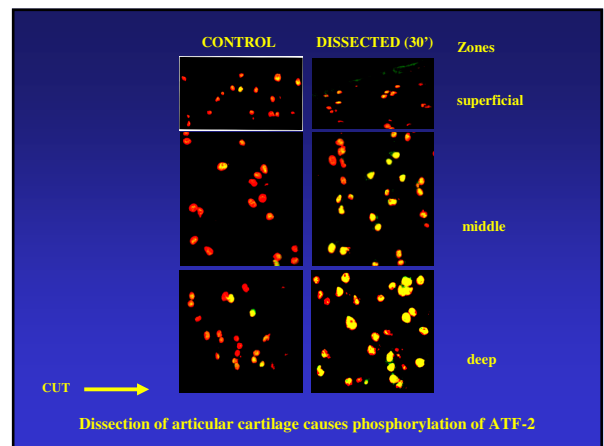
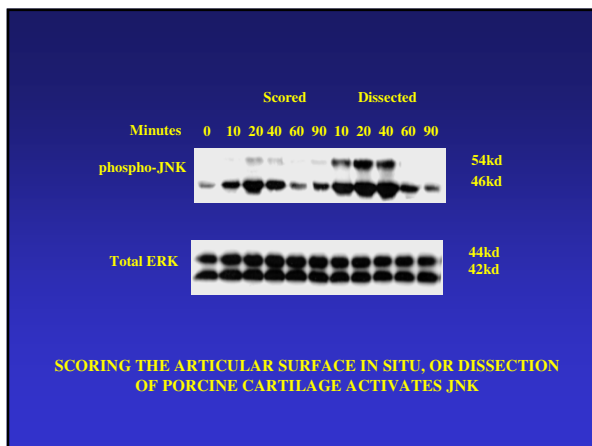
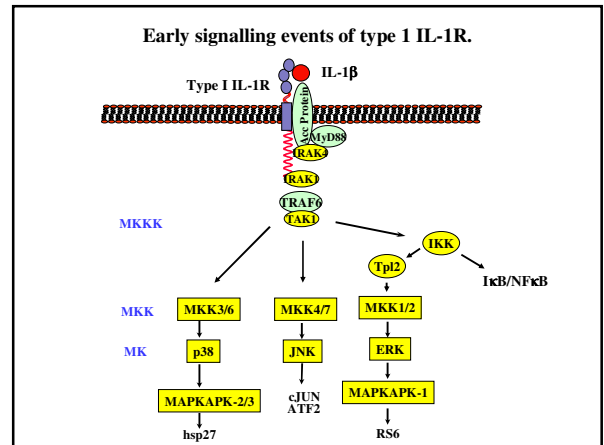
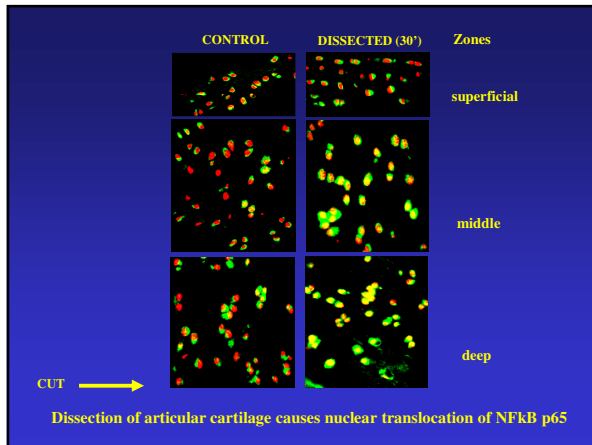
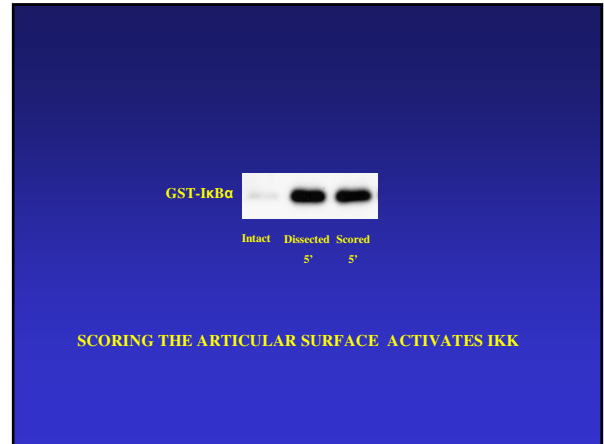
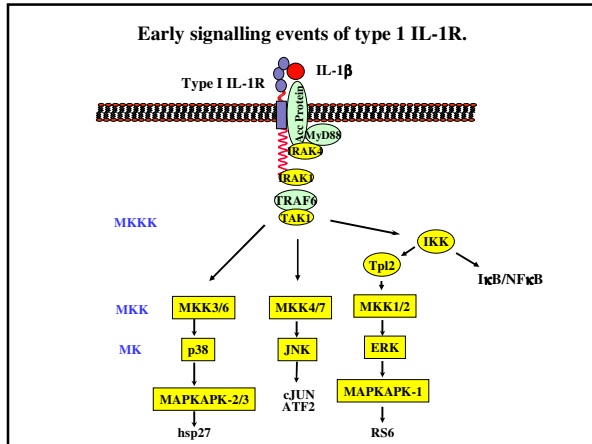
How does injury cause inflammation?

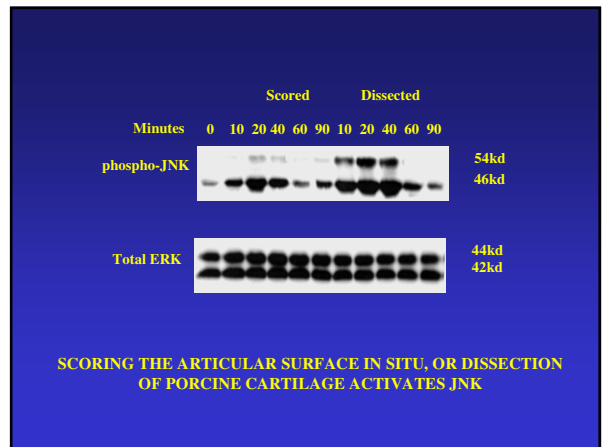
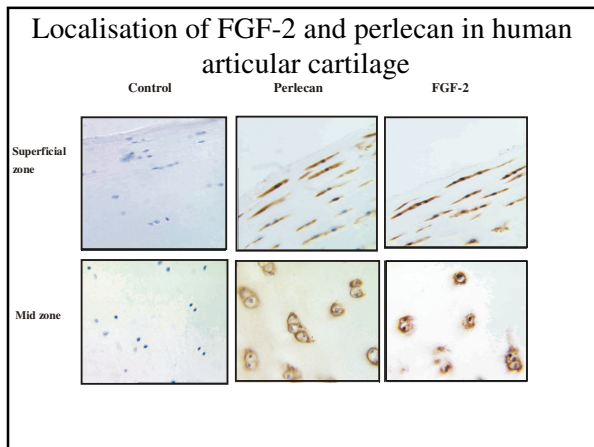
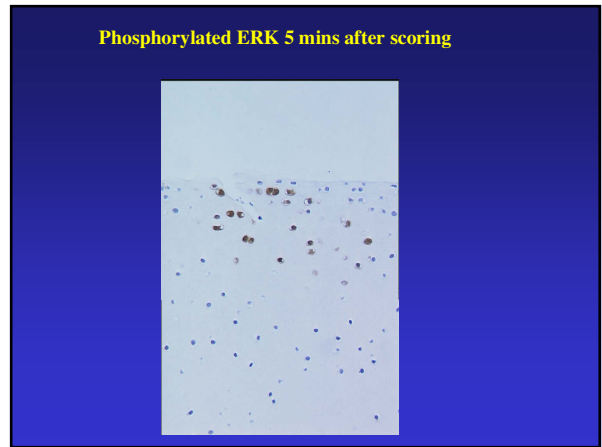
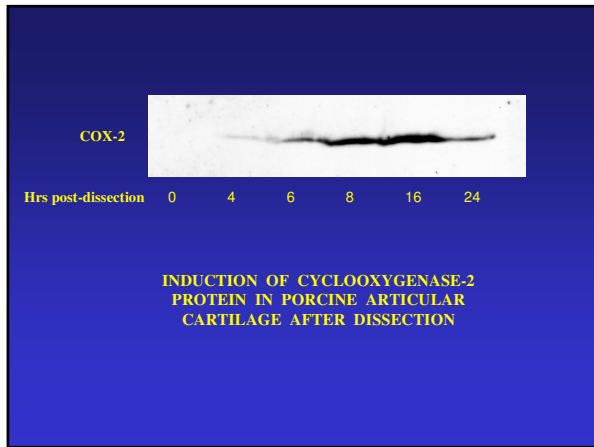
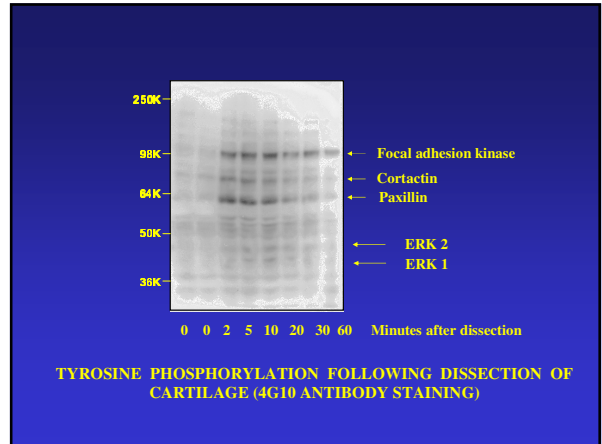
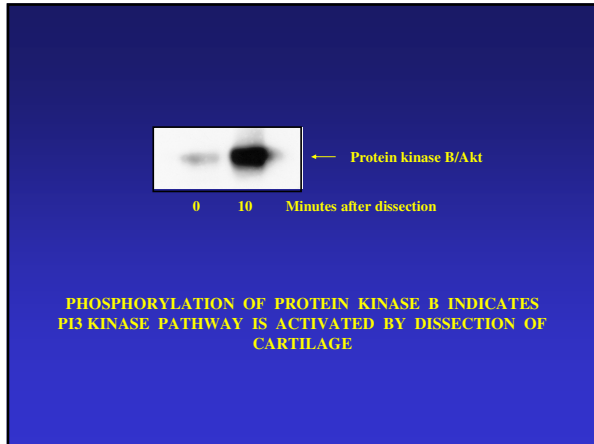
Dissection of porcine MCP cartilage

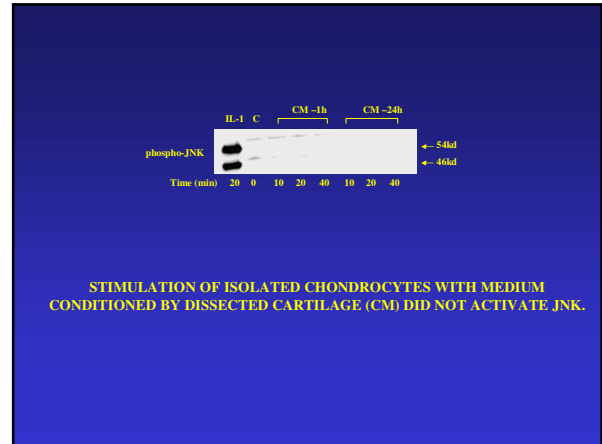
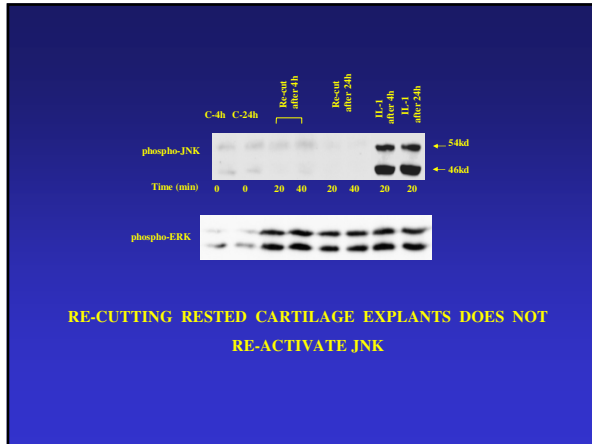


DISSECTION ACTIVATES I kappa B KINASE (IKK).

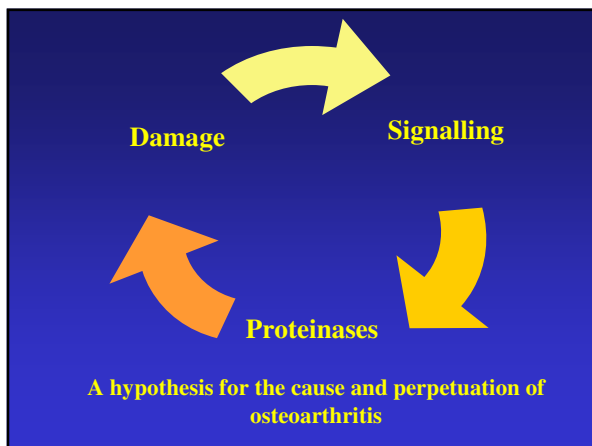
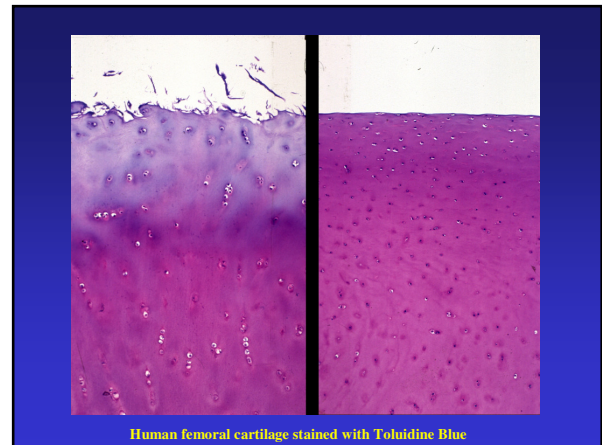
IKK complex immunoprecipitated from cartilage extract and assayed on recombinant IκB with $[\gamma\text{-}^{32}\text{P}]$ ATP.







- SUMMARY**
- 1) Few convincing targets for therapy in OA.
 - 2) Wounding cartilage activates within seconds pathways in chondrocytes:
 - NFkB
 - MAPKs
 - PI3-K
 - Src/FAK
 - 3) Release of pericellular FGF2 explains ERK activation.
 - 4) Inflammatory signalling (JNK/NFkB) is refractory to injury of cultured cartilage.
 - 5) Chondrocytes 'sense' matrix damage: possibly shearing of collagen.



Acknowledgements

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