Quantitative CD44 Binding Force to Matrix Proteins on Articular Surface

COLUMBIA
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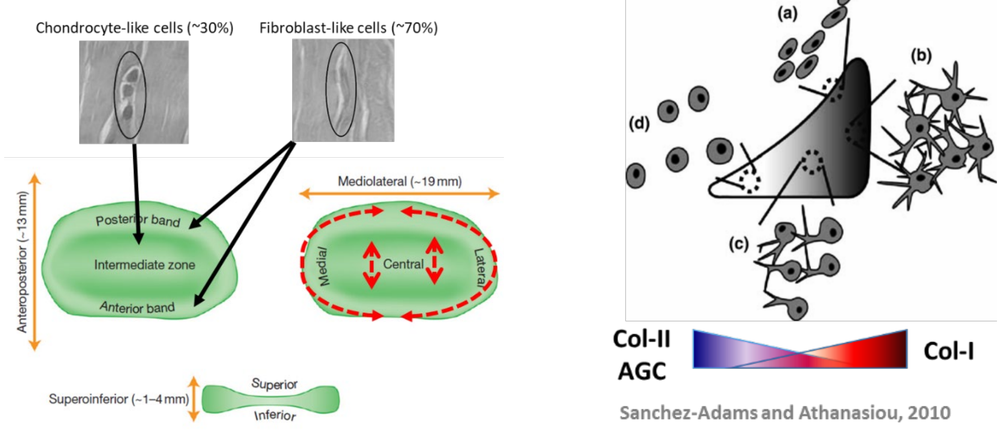
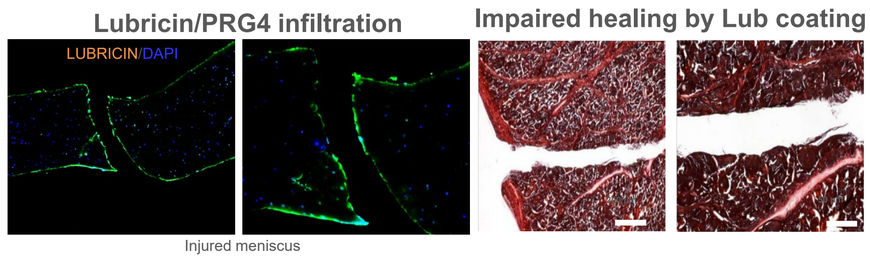
INTRODUCTION

The fibrocartilaginous tissues found in joints such as the menisci or TMJ disc are featured by regionally variant cell and matrix phenotypes. Tears or perforation in these tissues frequently lead to joint deterioration, but no regenerative therapy currently exist.



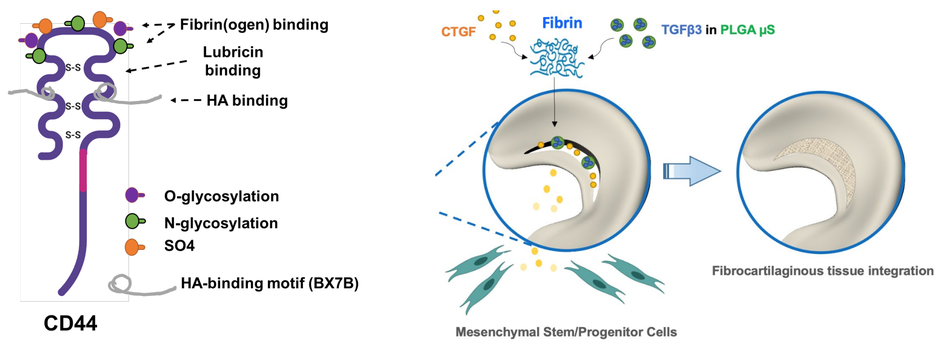
Regionally variant cell/matrix phenotypes and vascularity lead to tears or perforations that rarely heal, frequently progressing to joint deterioration

Lubricin/PRG4, found in synovial fluids and on articular surfaces, enables frictionless joint movement. However, exposure of injured joint tissues to lubricin may disrupt healing by preventing cell/tissue adhesion.



Lubricin infiltration in injury prevents the cell/tissue adhesion necessary for healing

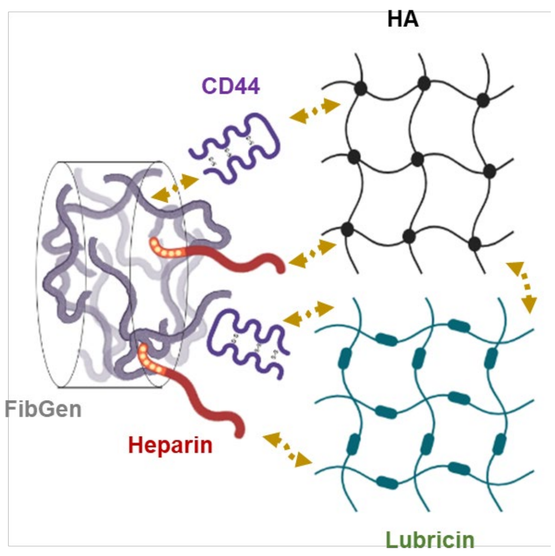
CD44, a surface receptor expressed in various cells, including synovial MSCs, has a strong binding affinity to lubricin present on the articular surface of fibrocartilage tissues. Therefore, CD44 incorporated glue may promote the initial tissue adhesion and stem cell recruitment necessary for healing.



Regenerative strategy by stem cell recruitment into CD44 incorporated bioactive glue

OBJECTIVE

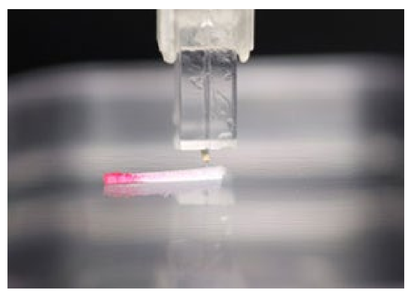
Since lubricin deposits on the torn surface of menisci/TMJ discs as supported by other matrix proteins, this study aimed to quantitatively measure binding forces between CD44 and lubricin coated on other matrix proteins to develop an efficient strategy for improving the healing of lubricin-infiltrated fibrocartilaginous TMJ discs and knee meniscus tissues.



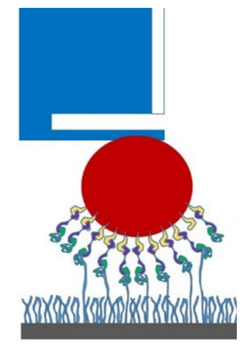
MATERIALS AND METHODS

Quantitative binding forces between CD44 and lubricin/PRG4 coated through matrix proteins on the torn meniscus surface were measured using a PiumaTM nano-indenter. The nano-indenter probe tip was functionalized by CD44, and a series of indentations were performed under a maximum force of 10 mN and 20 μm step size on the hydrogels to measure the adhesion force between CD44 and fibrin, hyaluronic acid (HA), type I and type II collagen gels with and without additional coating of lubricin.

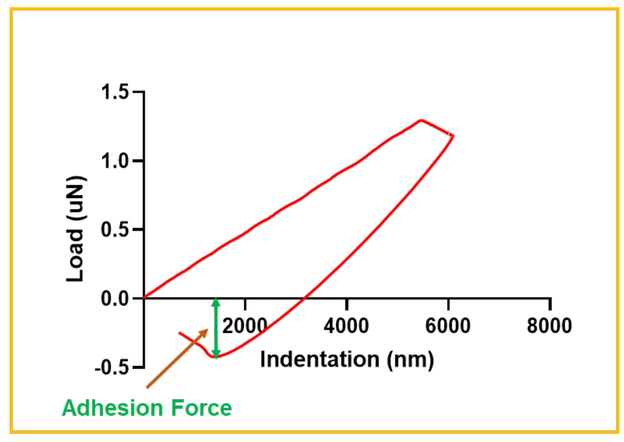
MATERIALS AND METHODS



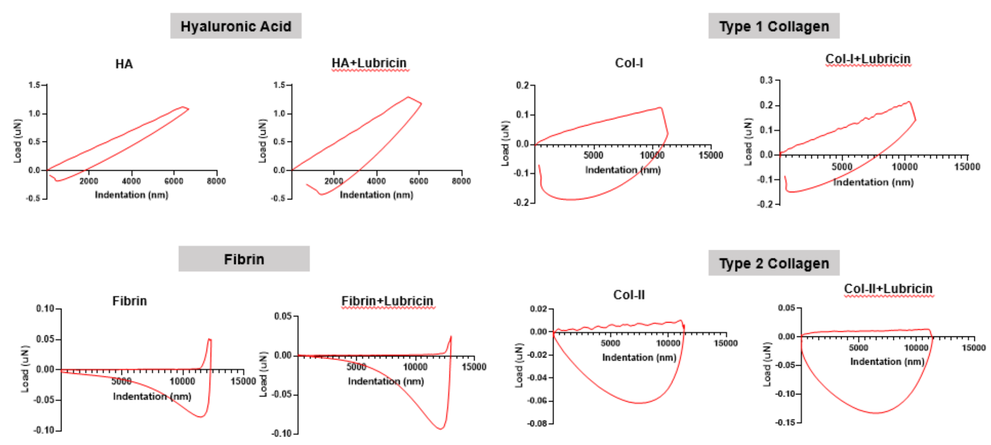
PIUMA™ nano-indenter probe tip functionalized by CD44



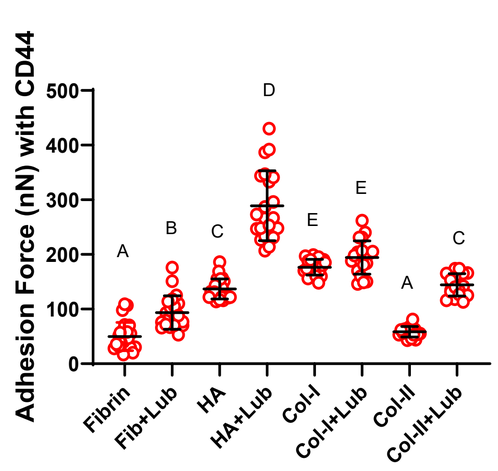
Adhesion force was determined from the maximum deflection from the baseline in the force vs. displacement graph.

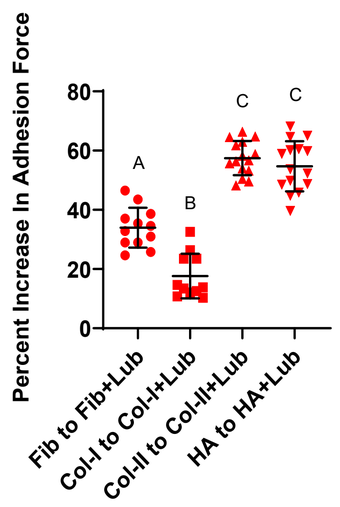


RESULTS & CONCLUSION



Significantly higher CD44 adhesion force for all lubricin/PRG4 coated hydrogels except type I collagen. HA demonstrated the highest binding affinity to lubricin/PRG4, while type I collagen showed the least affinity to lubricin. These results suggest a higher binding affinity of lubricin/PRG4 towards fibrin, type II collagen, and HA.





- CD44 showed the highest adhesion force on HA/lub-coated substrate.

CD44 and its binding to lubricin and HA have been extensively investigated in osteoarthritis initiation and progress in the biological context. Our findings suggest that CD44 can be incorporated in our bioengineering approach to regenerate intrasynovial tissues. Furthermore, reliable, quantitative measurement of CD44 binding forces will lead to optimization of the compositions of bioactive glue to achieve regenerative healing of intrasynovial fibrocartilaginous tissues.

ACKNOWLEDGEMENT

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