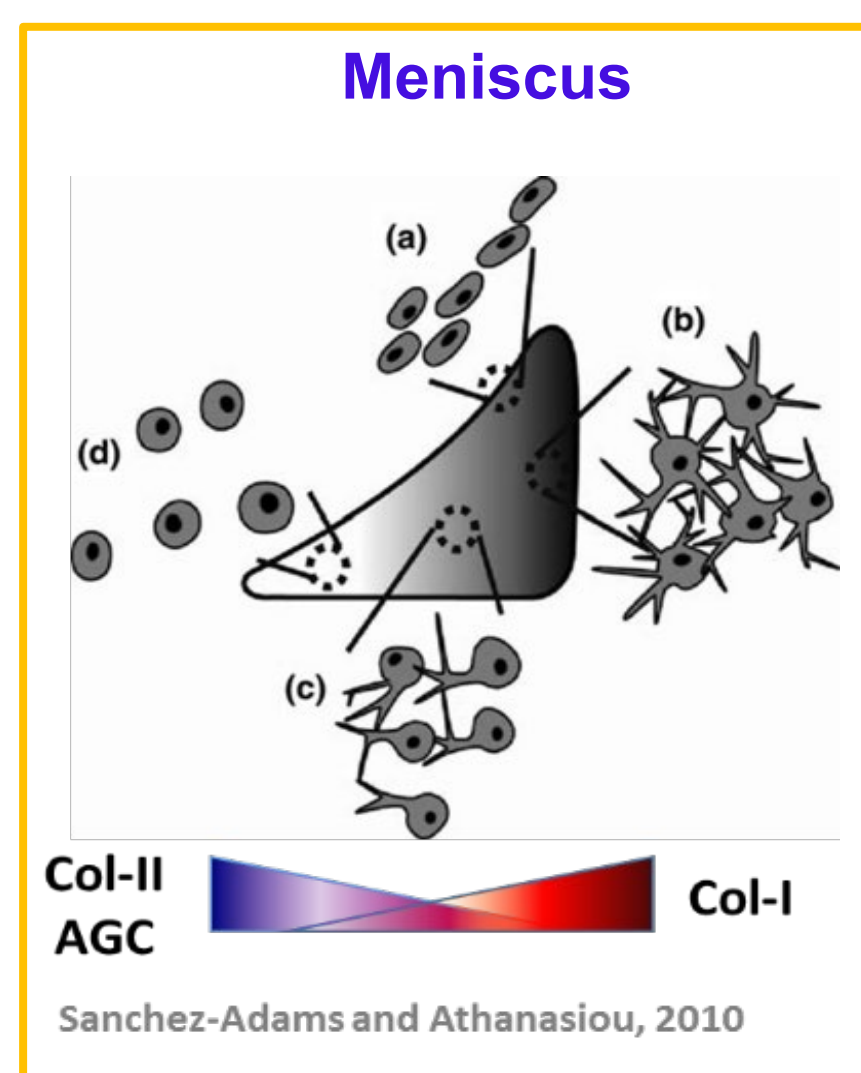
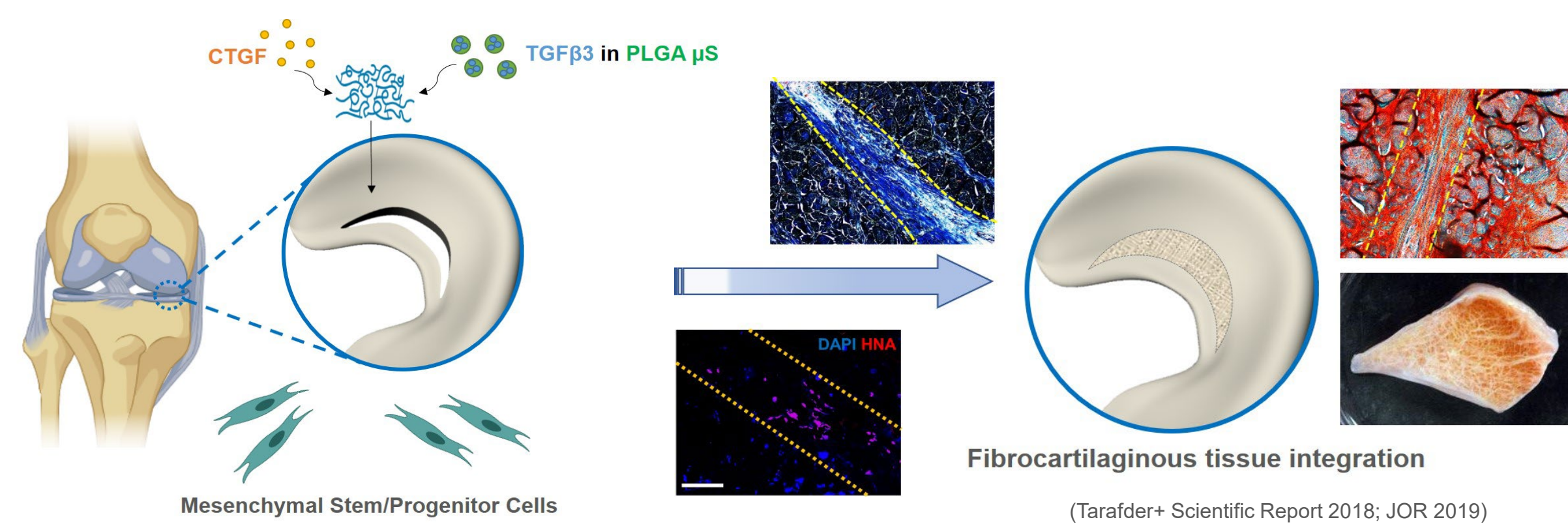


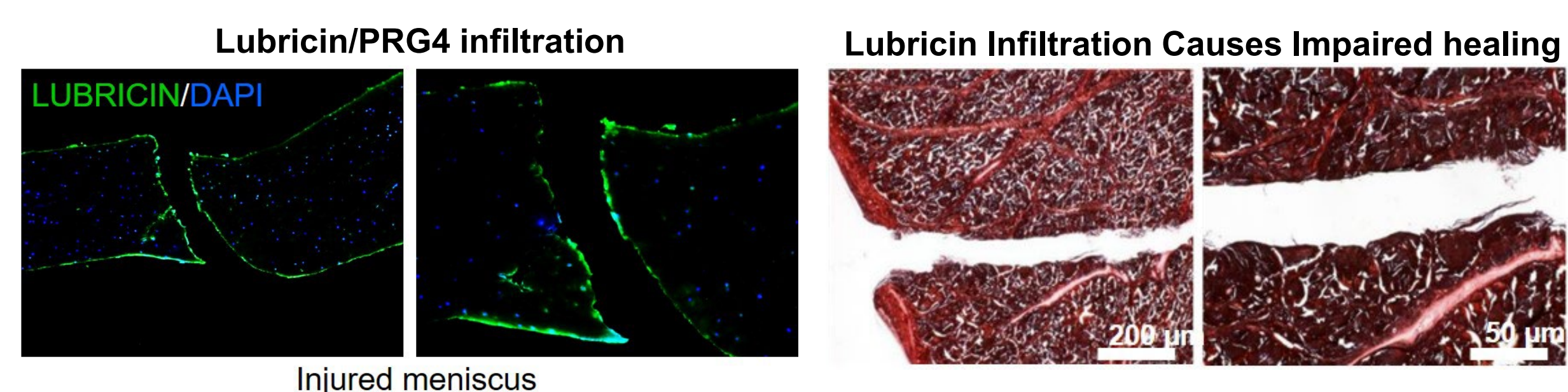
INTRODUCTION



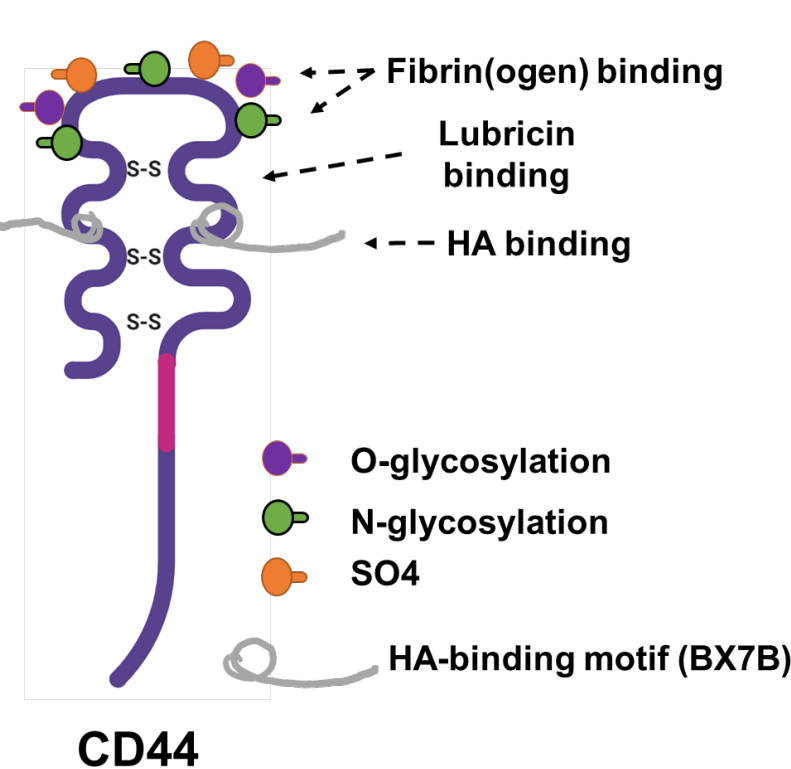
- Meniscus tear is one of the most common knee injury that can lead to a lifelong disease of osteoarthritis
- Patients normally take 3 to 4 weeks to be diagnosed during which time the torn surface of the meniscus is infiltrated and coated with lubricin/PRG4 from the synovial fluid
- Due to lubricin/PRG4's lubricative property, it prevents adhesion and healing of meniscus
- Regenerative healing of meniscus can be promoted through recruiting endogenous stem/progenitor cells through bioactive glues releasing connective tissue growth factor (CTGF) and transforming growth factor-beta 3 (TGF-β3)



- Regenerative healing strategy for intrasynovial fibrocartilaginous tissues (e.g., knee meniscus and TMJ disc) by recruiting stem/progenitor cells through bioactive glues and delivering growth factors

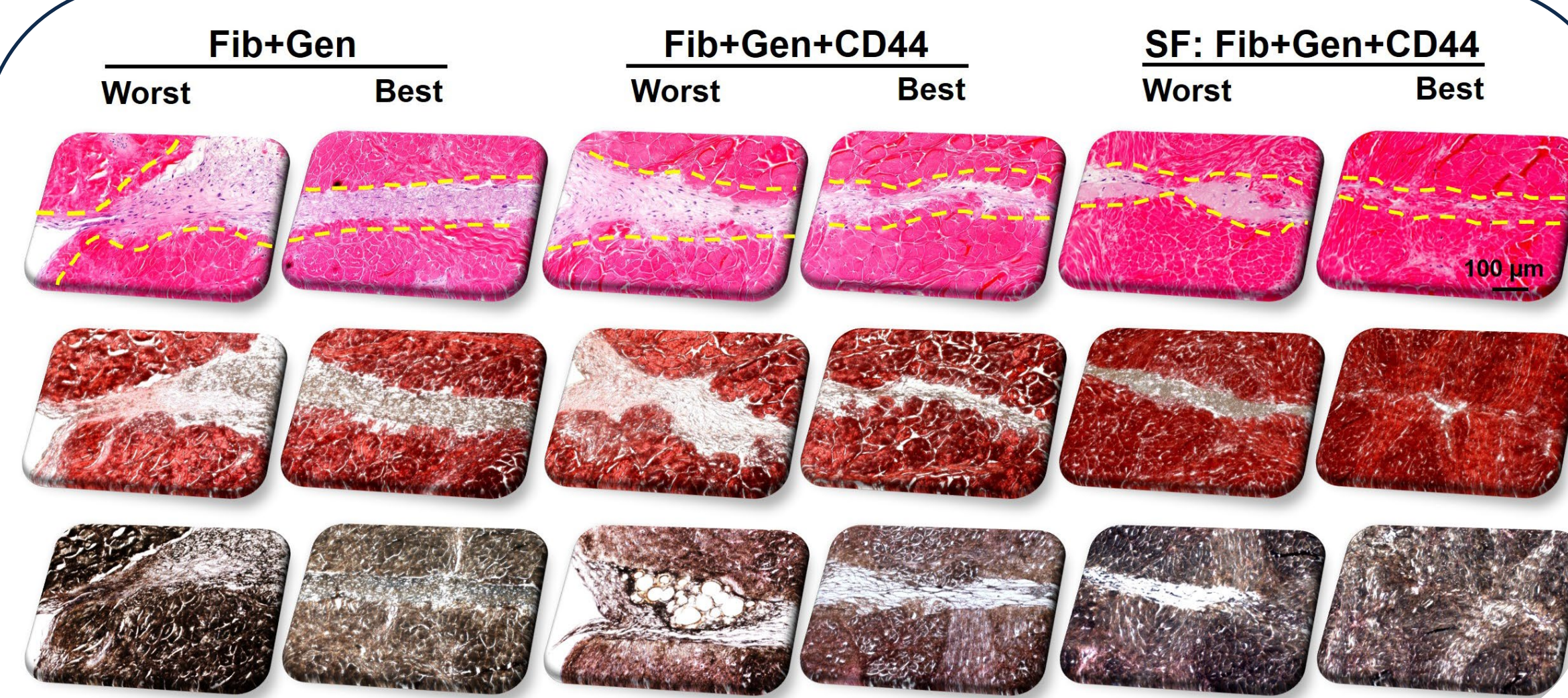


- Lubricin infiltration into the defect site shows harmful effect on meniscus healing

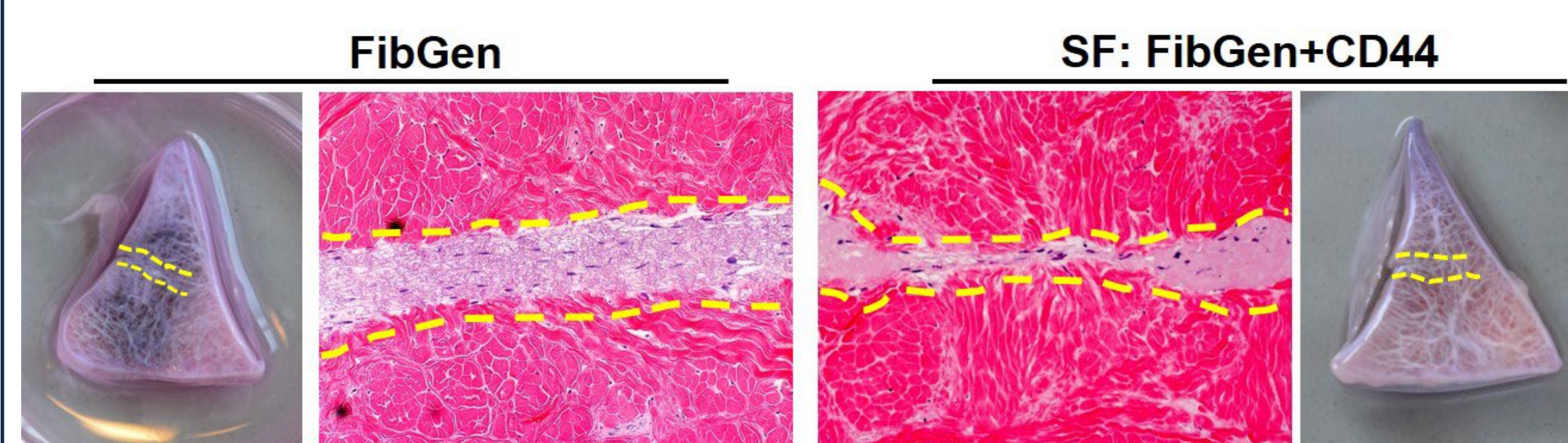


- CD44 is a transmembrane glycoprotein with a strong binding affinity to lubricin/PRG4
- It also interacts with various ligands including hyaluronic acid (HA), osteopontin (OPN), collagens, and matrix metalloproteinases (MMPs)
- Due to these properties, the research investigated the mechanism of lubricin/PRG4 retention on the injured surface of meniscus as well as developing a strategy to improve the healing of lubricin/PRG4-infiltrated fibrocartilaginous tissues by tethering lubricin/PRG4 to CD44.

RESULTS



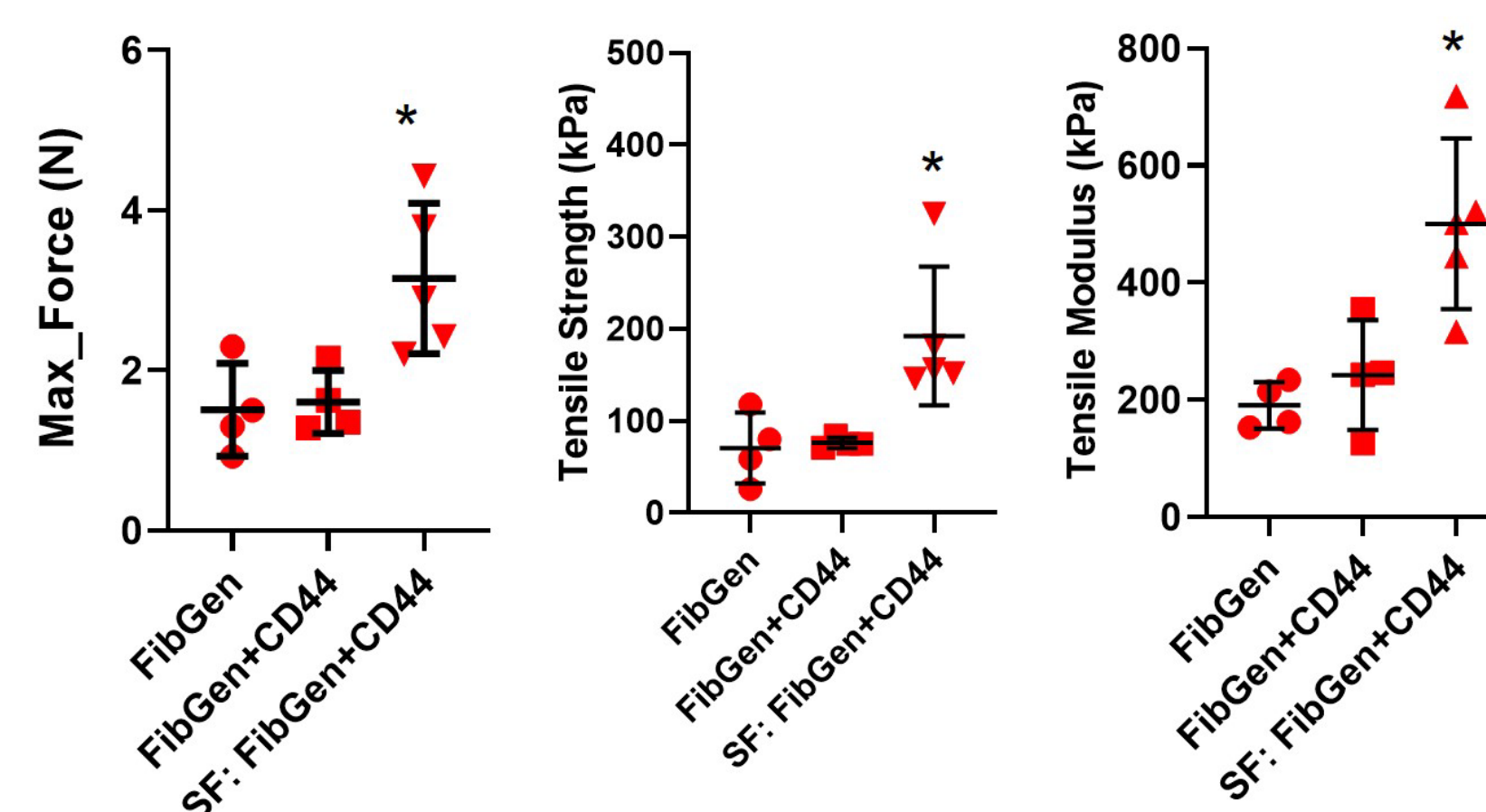
- When CD44 was incorporated into the original bioactive glue mixture of fibrin crosslinked genipin (FibGen), improved healing was demonstrated in lubricin coated meniscus tears as shown by the narrower gap between the torn tissues in SF: Fib+Gen+CD44 column.
- There was minimal improvement when CD44-incorporated biogel was used on non lubricin coated meniscus tears



- The narrower gap between the injured surfaces demonstrates that CD44-incorporated biogel improved healing and enhanced tissue integration

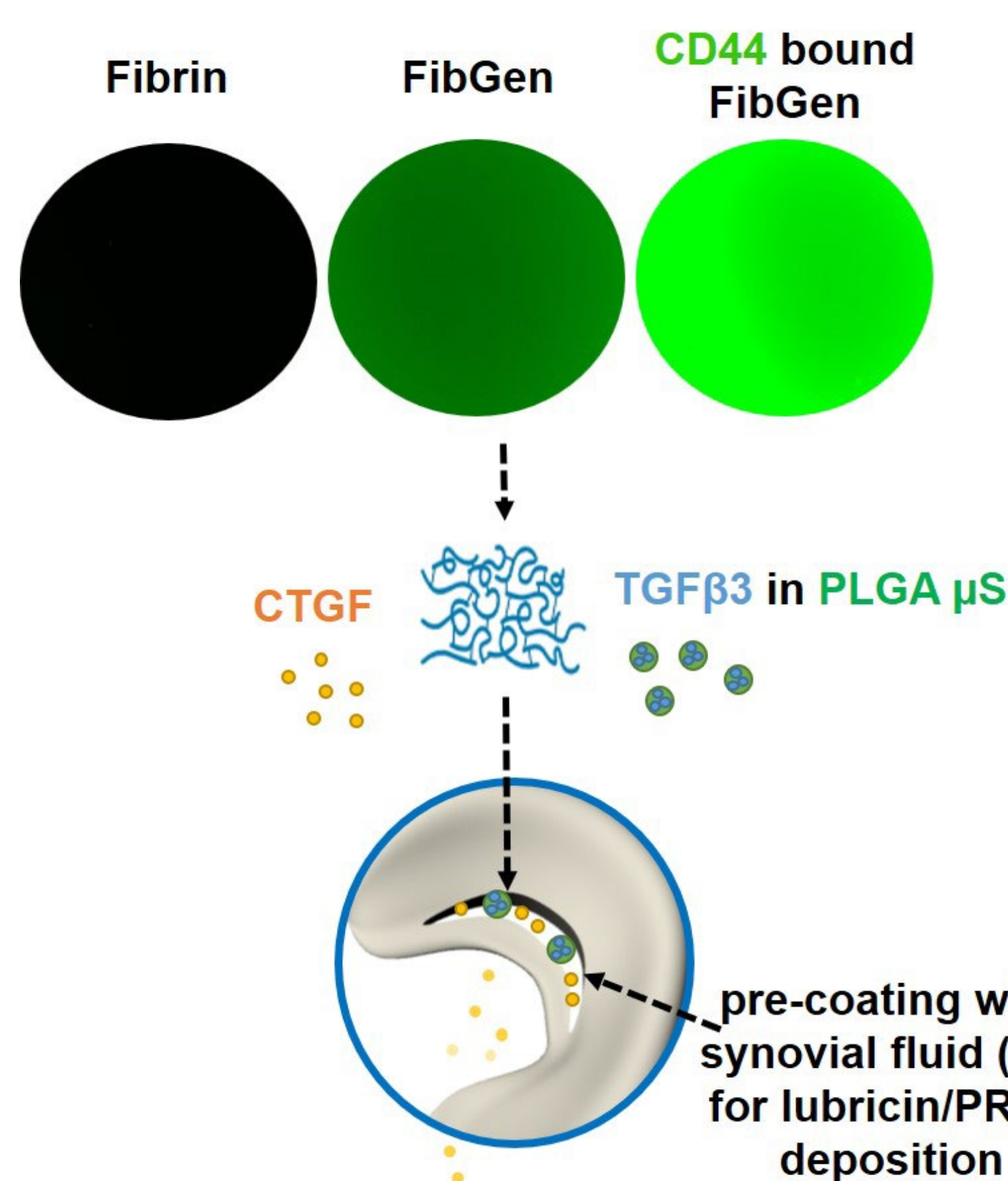


- CD44-incorporated biogel increased cell migrations to the torn surfaces which indicates higher cellular activity in the injured areas
- There is no significant difference in hardness modulus of CD44-incorporated biogel compared to the original glue



- Lap-Shear tests shows that CD44-incorporated biogel demonstrated increased tensile properties

METHODS & MATERIAL



- CD44-bound FibGen was prepared to tether lubricin-infiltrated meniscus injuries.
- Fluorescent-labeled CD44 was used to confirm the CD44's incorporation into the FibGen.
- Lap shear test was performed to evaluate the initial bonding strength.
- The CD44-FibGen with CTGF and TGFβ3 μS was applied for our well-established meniscus explant healing model.

DISCUSSION & CONCLUSION

- Injured menisci are not diagnosed until 3 – 4 weeks post injury.
- Lubricin on the torn surface of meniscus impairs healing and this coating process is facilitated by HA.
- CD44 shows strong binding affinity to lubricin/PRG4 and HA.
- In-vitro explant injury model and Lap-Shear tests show that CD44-incorporated bioactive glue provides a significantly stronger tensile strength.
- CD44-incorporated bioactive glue demonstrates strong potential to improve healing and regeneration of meniscus.
- In conclusion, CD44-bound FibGen may serve as a novel, efficient tissue adhesive for stem cell-guided healing of fibrocartilaginous tissues including meniscus and TMJ discs.

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