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Investigation of the Mechanism of CTGF-Induced Migration of Synovial/Mesenchymal Stem Cells

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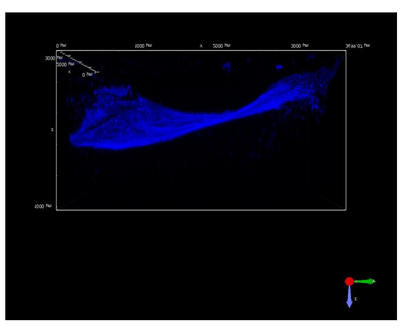
INTRODUCTION

- Temporomandibular Joint (TMJ) degenerative disorders affect millions of Americans each year, inducing myofascial pain and restricting jaw movement for the affected.
- Contemporary treatment includes invasive surgery and artificial TMJ implants that have not established a reliable, pain-free outcome
- A novel approach features harnessing endogenous stem cells and directing them towards the affected area for tissue regeneration
- We aimed to:
  1. Confirm connective tissue growth factor (CTGF) as a chemotactic agent to induce endogenous synovial mesenchymal stem cell (syMSC) migration
  2. Determine surface proteins/potential receptors involved in cellular migration
  3. Quantify a 3D migration assay to determine the underlying mechanism of syMSC migration

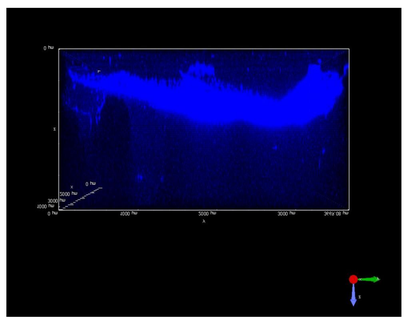
METHODS

- Fabricated 3D-printed scaffolds (5x5x5 mm) embedded with PLGA microspheres encapsulated with CTGF or PBS
- Collagen gel infusion into scaffold microchannels; syMSC's plated on top
- CD44 antibody block was applied to selected scaffolds – groups were either CD44+ or CD44-
- After 1 or 2 wk migration periods, migrated cells were DAPI stained and imaged using two-photon confocal microscopy
- Sliced imaging in 15 μm intervals were reconstructed into 3D images
- NIS-Elements Viewer was utilized to align images and ImageJ was used to randomly select 10 (300x300 μm) columns of interest within each scaffold and allowed us to quantify the migrated cells.

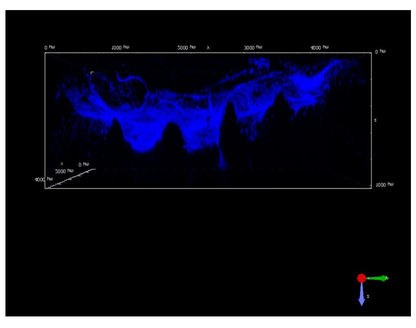
RESULTS



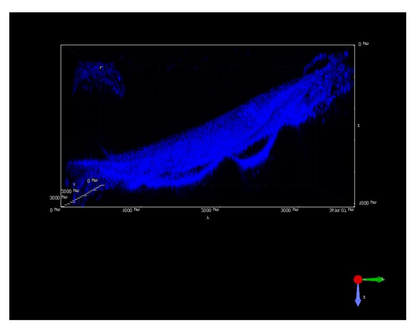
CTGF 1 wk



CTGF 2 wk



Empty 1 wk



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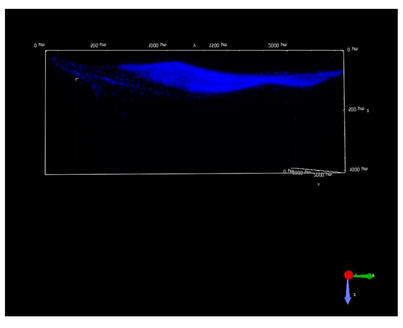
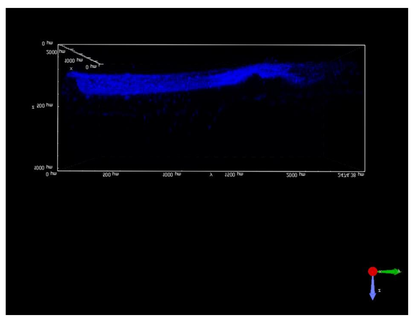
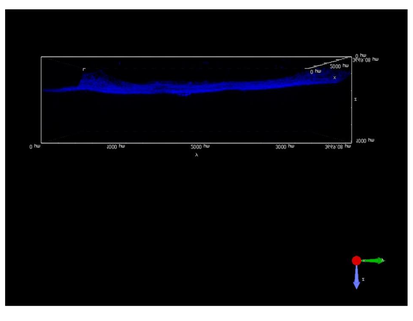


CTGF w/CD44 Ab 1 wk



CTGF w/CD44 Ab 2 wk



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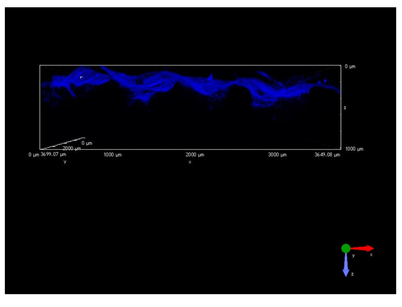

Empty w/CD44 Ab 2 wk

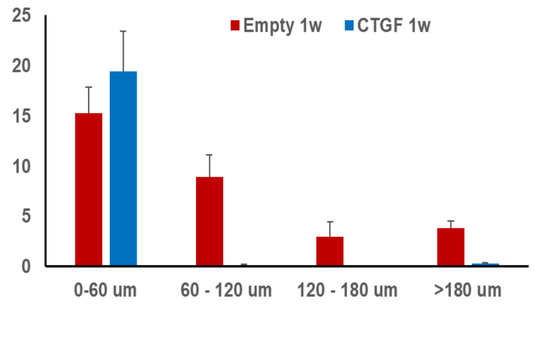

Figure 1: CTGF vs. Empty scaffold migration 1 wk

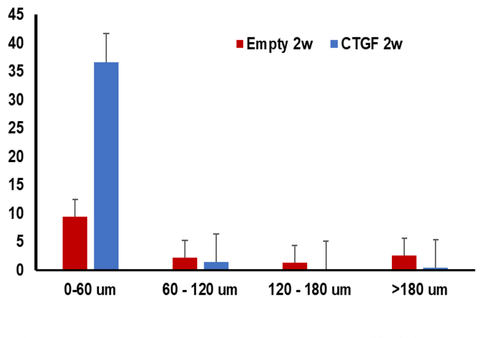

Figure 2: CTGF vs. Empty scaffold migration 2 wks

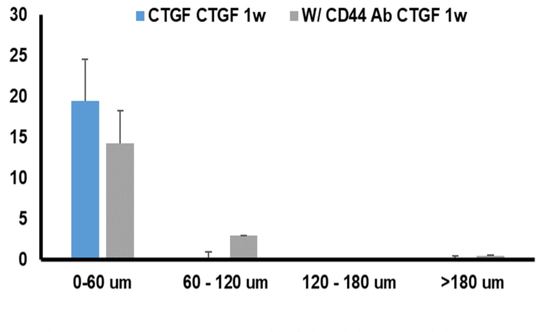

Figure 3: CTGF scaffold with or without CD44 ab block 1 wk

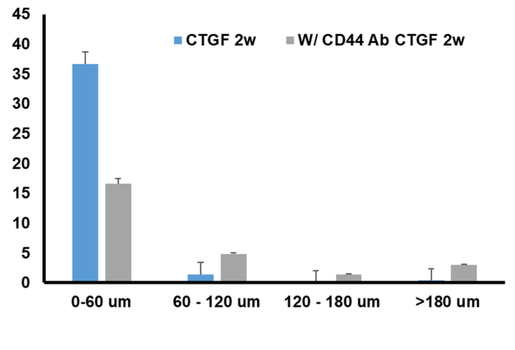

Figure 4: CTGF scaffold with or without CD44 ab block 2 wk

CONCLUSIONS

- Findings suggest that CTGF plays an important role in inducing syMSC proliferation and migration
- Findings also suggest that CD44 is likely involved with CTGF-directed migration of syMSC in 3D-printed scaffolds
- Overall, study has implication in mechanism of CTGF-guided stem cell recruitment towards in situ regeneration of craniofacial tissues
- Limitation includes not being able to fully observe the mechanism and role of CTGF
- For future studies: print scaffolds with better dimensions and equivalent structure and perform better collagen gel infusion to get better scaffold cell cluster baseline.

ACKNOWLEDGEMENTS

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