Therapeutic siRNA conjugates for osteoarthritis

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VANDERBILT UNIVERSITY

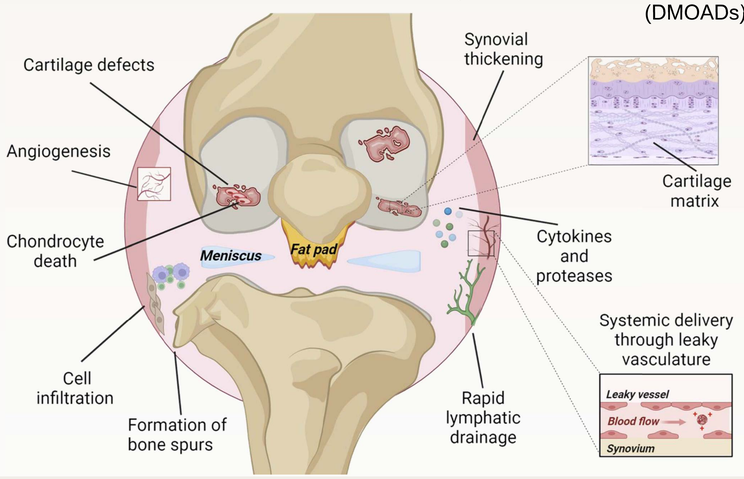
Advanced Therapeutics Laboratory

Disease Modifying Drugs for Osteoarthritis are nonexistent

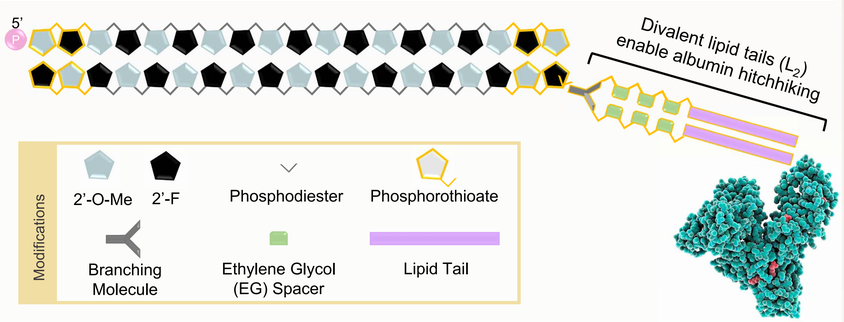
$44 Billion
Annual Financial Burden

67 million
US Adults Diagnosed by 2030

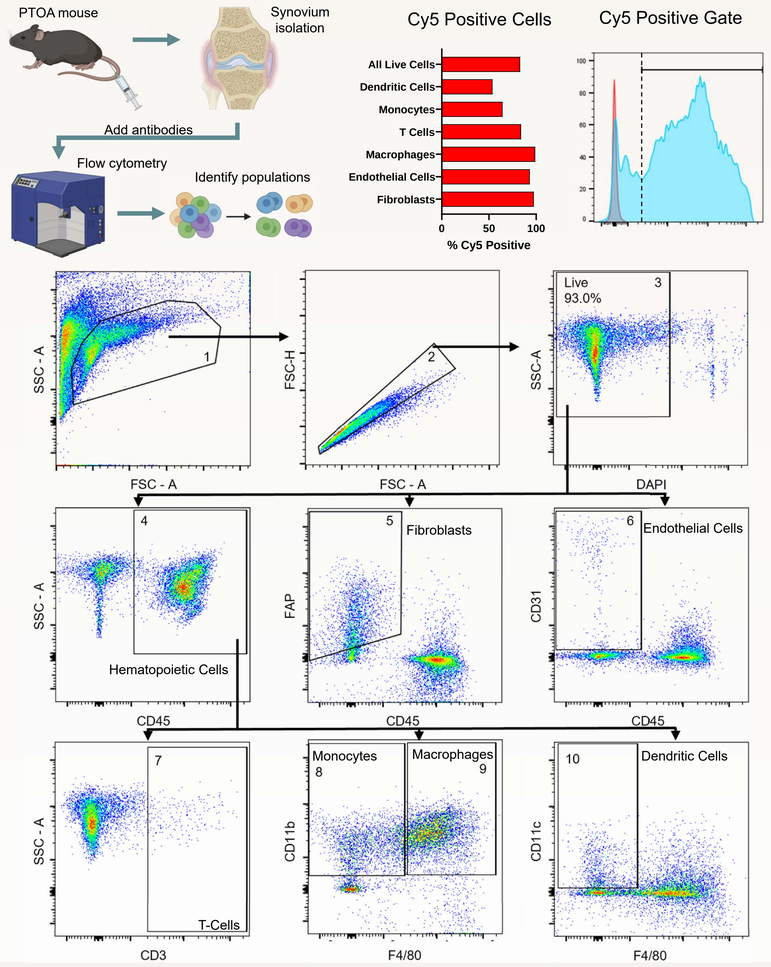
0
Disease Modifying Osteoarthritis Drugs (DMOADs)



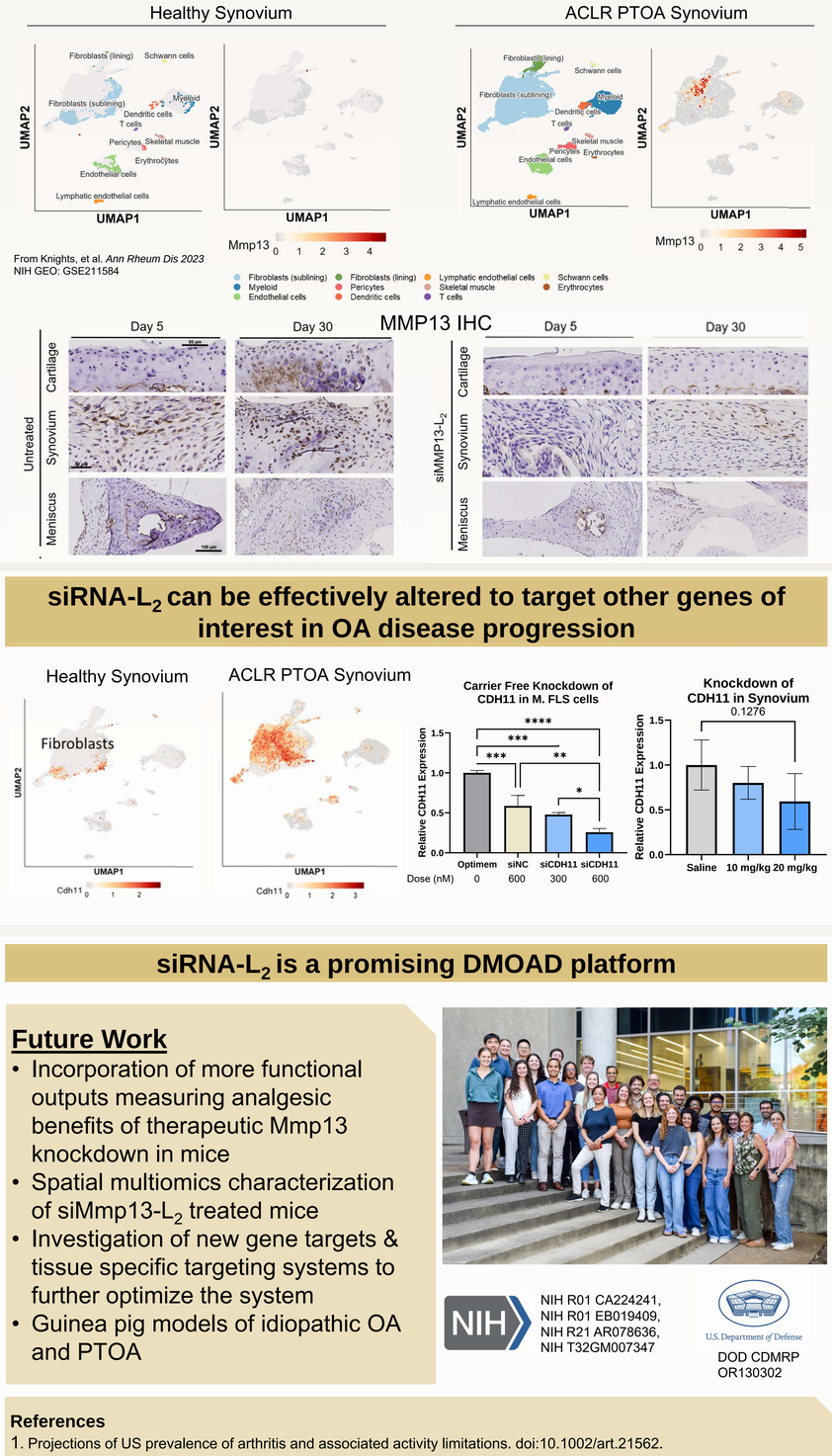
Albumin serves as a natural carrier for siRNA-L_2



All major synovial cell populations uptake siRNA-L_2

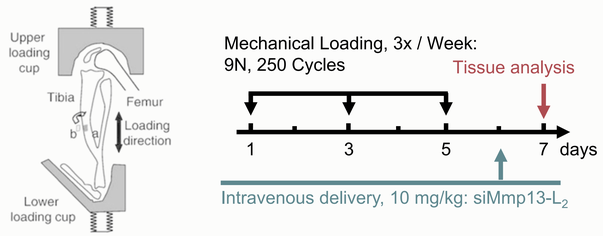


Mmp13 upregulation in PTOA can be effectively silenced via siMmp13-L_2 across joint structures and cell types

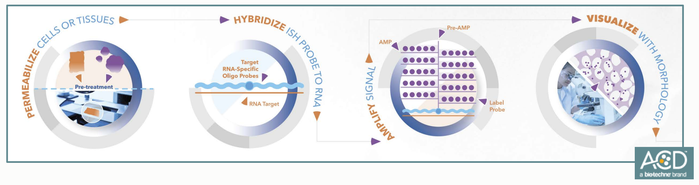


siRNA-L_2 can be effectively altered to target other genes of interest in OA disease progression

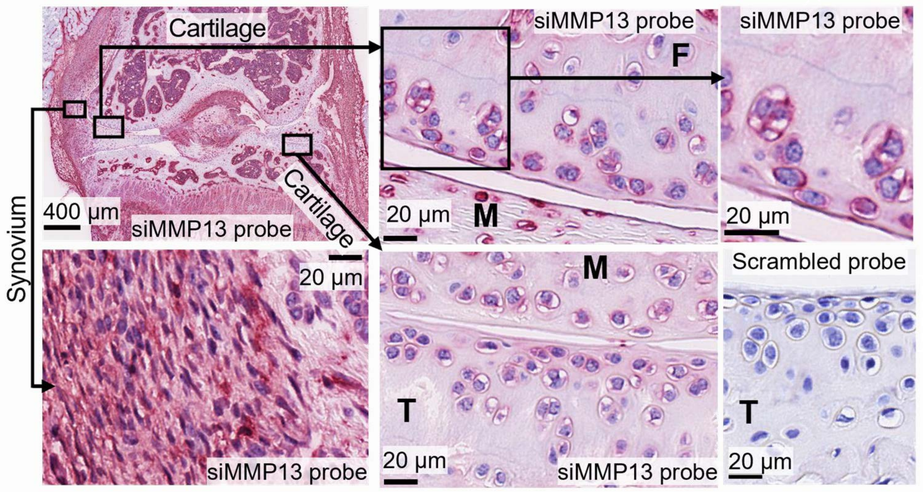
Systemic siRNA-L_2 administration achieves rapid delivery to all major joint structures



Hybridization of probe to siRNA antisense strand



In situ hybridization of siMMP13<(EG_{18}L) in injured mouse joint



siRNA-L_2 is a promising DMOAD platform

Future Work

- Incorporation of more functional outputs measuring analgesic benefits of therapeutic Mmp13 knockdown in mice
- Spatial multiomics characterization of siMmp13-L_2 treated mice
- Investigation of new gene targets & tissue specific targeting systems to further optimize the system
- Guinea pig models of idiopathic OA and PTOA

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NIH R01 EB019409,
NIH R21 AR078636,
NIH T32GM007347

U.S. Department of Defense
DOD CDMRP
OR130302

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3. **Colazo, J., Hoogenboezem, E., et al. Albumin-binding RNAi Conjugate for Carrier Free Treatment of Arthritis. *BioRxiv***