Alginate-based hydrogels for stem cell chondrogenesis

Maria Laura Vieri
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LifETIME CDT EPSRC-SFI funded PhD project

University of Glasgow

Aims

Development of a hydrogel-based 3D osteochondral model for osteoarthritis research, using induced pluripotent stem cells (iPSCs) as cell source.

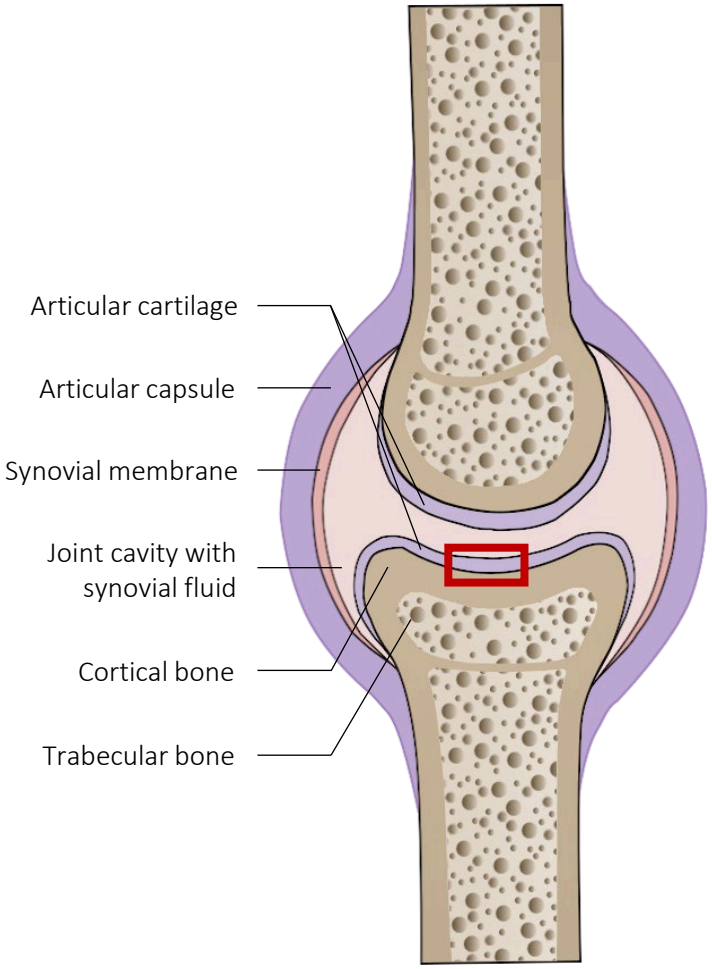
Use the model to study the role of protease activated receptor 2 (PAR-2) in osteoarthritis (OA) pathogenesis.

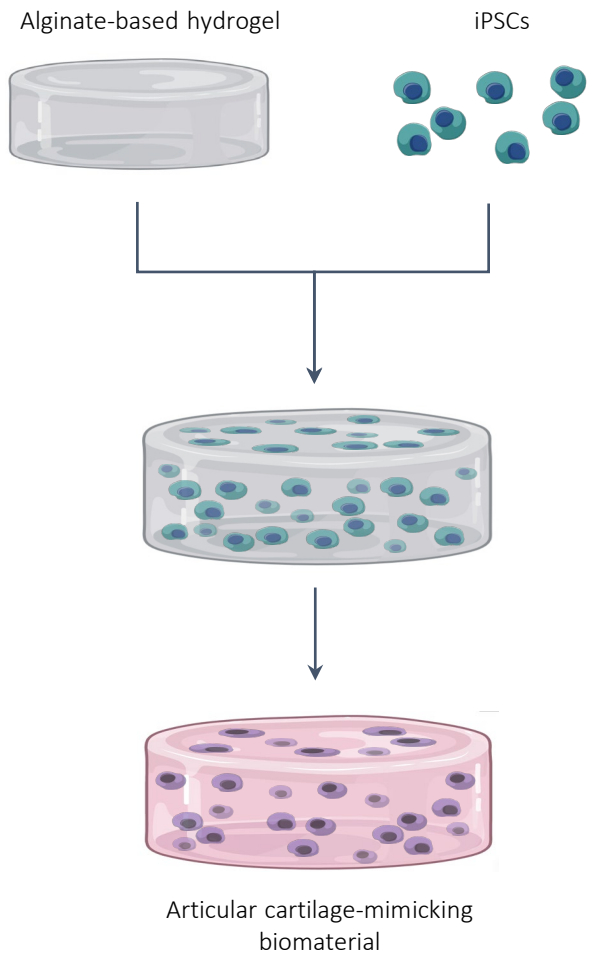
Sub-aims

Development of an alginate-based hydrogel to drive stem cell chondrogenesis.

→ Choose optimal stiffness.
→ Hydrogel functionalisation.

Use of human induced pluripotent stem cells (iPSCs): optimisation of differentiation protocol into mesenchymal stem cells (iMSCs).





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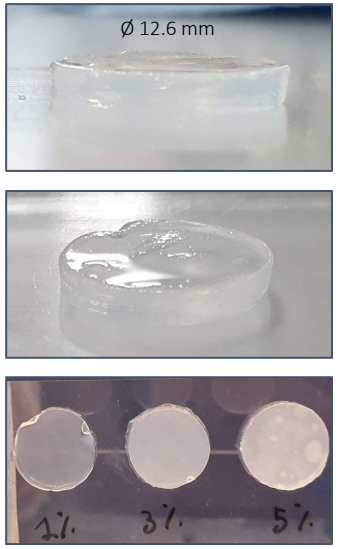
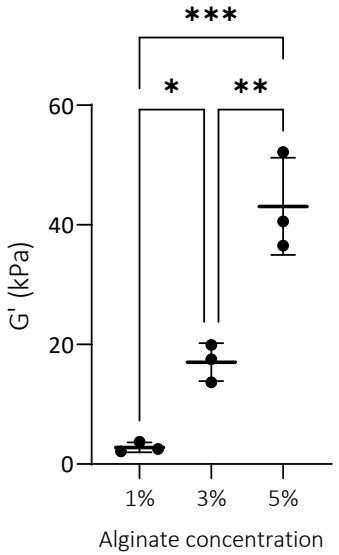
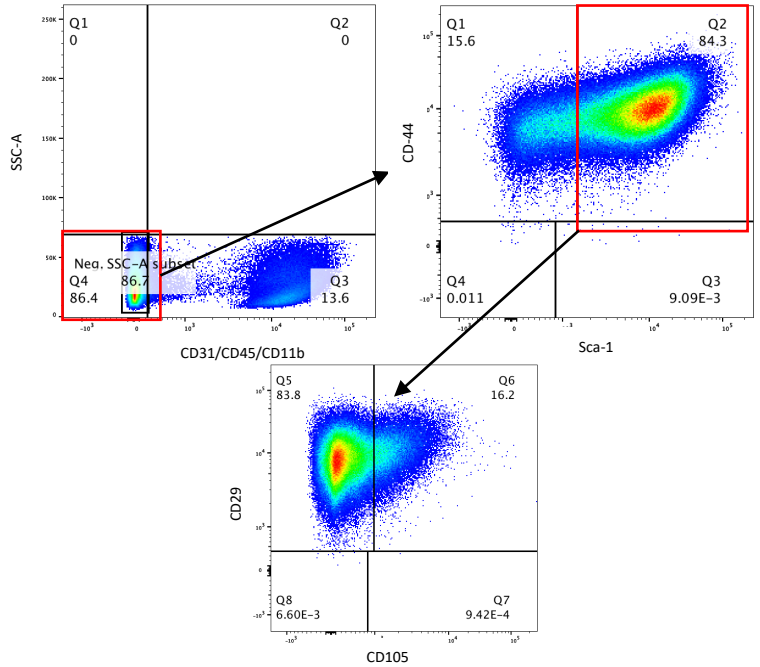
Results

1%, 3% and 5% (w/v) sodium alginate solutions were used to create gels discs with an elastic modulus (G') of 2.8±0.8 kPa, 17±3.1 kPa and 43.1±8.1 kPa respectively. UV sterilization had no effect on gels' mechanical properties.

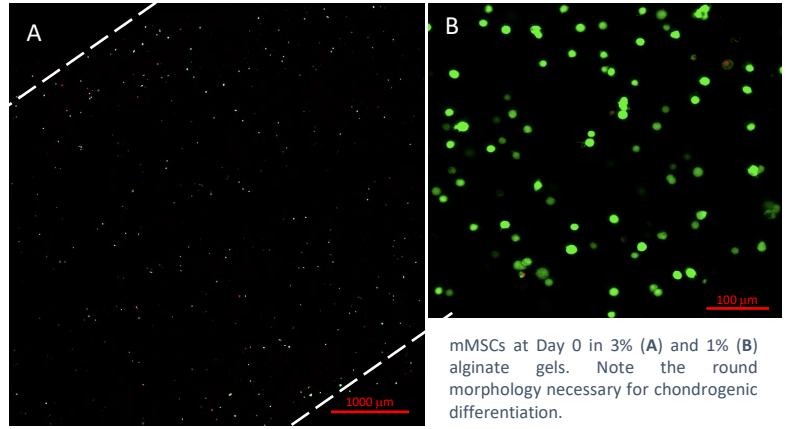




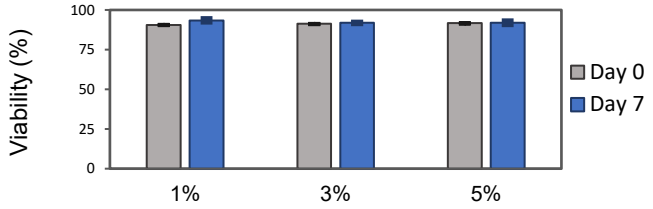
Compact bone derive mouse MSCs were characterised using flow cytometry at different passages: at P4, ≈80% of cells were $CD31^-/CD45^-/CD31^-$, of which ≈84% $Sca\text{-}1^+/CD44^+/ CD29^+$, but with low $CD105^+$ cells.



Viability (Live/Dead assay) was ≈90% at Day 0, with no significant reduction at Day 7 and no significant difference between alginate concentrations (seeding density $1x10^6$ cells ml^{-1} alginate).



mMSCs at Day 0 in 3% (**A**) and 1% (**B**) alginate gels. Note the round morphology necessary for chondrogenic differentiation.



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Conclusion

- Alginate gel discs of three different G' values were successfully synthesised.
- Murine MSCs from compact bone were characterised and used at passage 4 and 5, highlighting low abundance of CD105+ cells, as previously reported.
- A viability assay showed high cell survival in alginate gels, with no significant difference between gels' stiffnesses.

Future work

- Protocol optimisation for chondrogenic markers expression and histological analysis (currently ongoing).
- Functionalisation of gels with biofactors.
- Incorporation of iMSCs and osteogenic hydrogel (subchondral bone).
- Use of CRISPR-Cas9 technology to genetically modify pathways and determine their therapeutic utility.

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