Marie Skłodowska-Curie Actions (MSCA)
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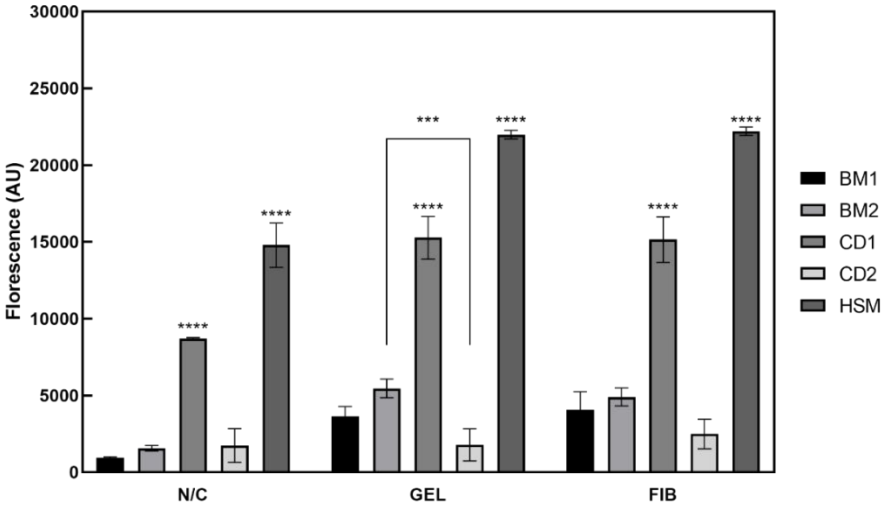
Development of Osteoinductive Spinal Implants (Fusion Cages)

Previous results

1st year public report

Serum-free hMSC expansion

- Primary hMSCs (passage 4)
- Standard cell culture media (BM1, BM2)
- Serum-free media (CD1, CD2)
- Specialized human serum media (HSM)



Metabolic activity of primary MSCs in different culture conditions (*** $p \leq 0.001$, **** $p < 0.0001$; n=3).

- Standard media can be a source a variability
- HSM shows the best results
- CD1 appears as viable option
- Presence of coating improves hMSC expansion

Previous results

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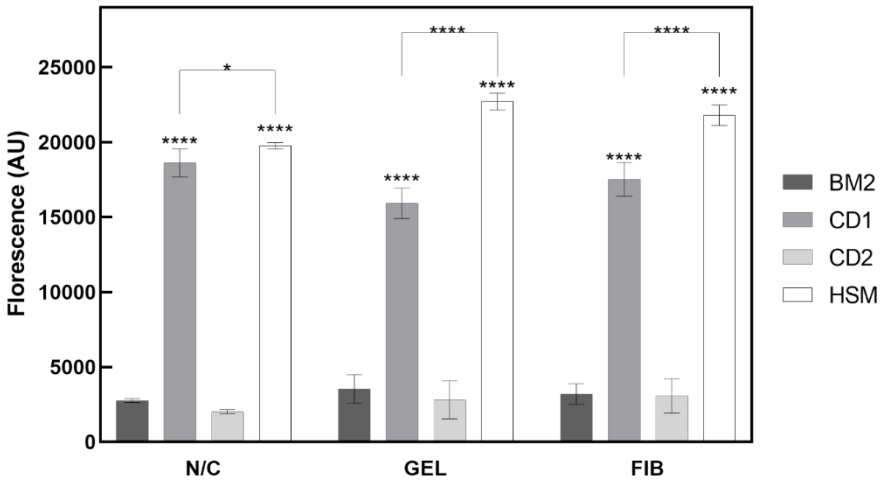
Serum-free hMSC expansion

- hTERT-MSCs (Y201, passage 8)
- Standard cell culture media (BM2)
- Serum-free media (CD1, CD2)
- Specialized human serum media (HSM)

- HSM shows the best results
- CD1 appears as viable option
- Presence of coating improves hMSC expansion, except when using CD1+GEL coating



Metabolic activity of hTERT-MSCs in different culture conditions (* $p \leq 0.001$, **** $p < 0.0001$; n=3).

Previous results

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Synthesis of osteoinductive material

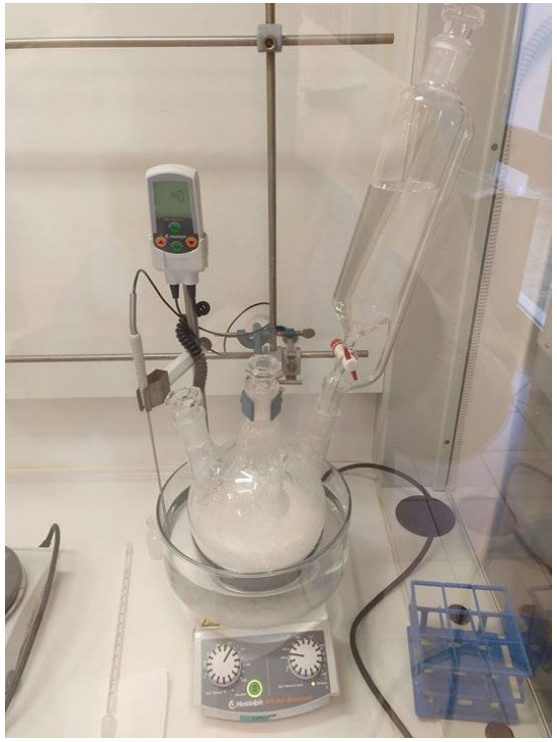
- DoE to study sintering conditions
- Organic residues evaluated by TGA
- Linear model obtained
- High temperature for longer sintering times provide best results
- Fast heating rate necessary for time constraints

Previous results

Deliverable 2.1

Synthesis of sHAP

- Precipitation method
- Mg and Sr substitutions
- Five different formulations tested



Precipitation method: experimental set-up.

Current developments

- Synthesis of osteoinductive material through sol-gel chemistry
  - New drying conditions
  - Improving synthesis yield
  - crystallization DoE - ongoing
- Synthesis of sHAP through precipitation method
  - New washing method
  - sHAP synthesis DoE - ongoing

Synthesis of osteoinductive material through sol-gel chemistry

New drying conditions

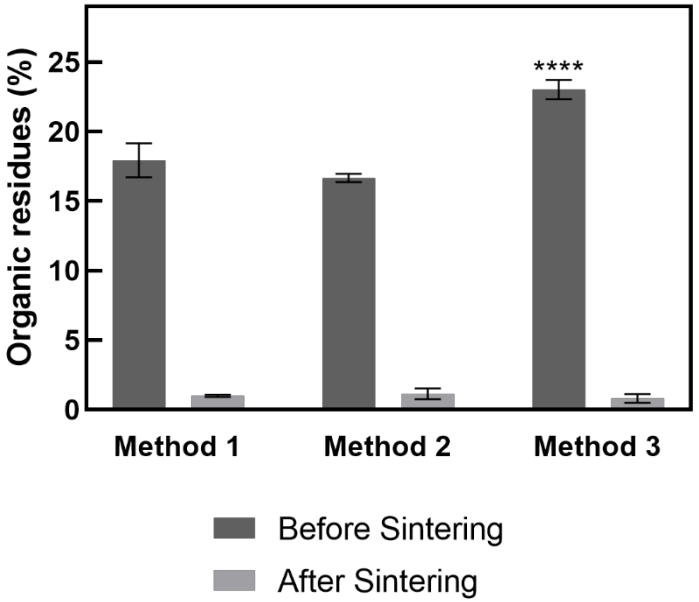
- Three methods tested
- All samples dried for 24 hours
- Samples analysed by TGA before and after sintering

Synthesis of osteoinductive material through sol-gel chemistry

New drying conditions – results

- Method 3 provides worst results before sintering
- All methods performed similarly after sintering
- After sintering organic residues ≈ 1% wt.

- Method 2 selected for all future synthesis



Organic residues for each drying method.

Synthesis of osteoinductive material through sol-gel chemistry

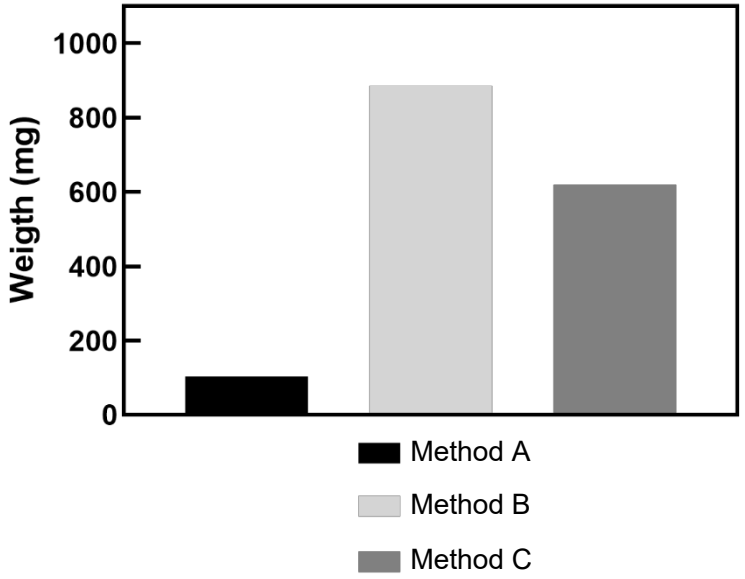
Improving synthesis yield

- Three samples produced with different methods
- All samples dried and sintered at same conditions
- Final weight measured using analytical balance

Synthesis of osteoinductive material through sol-gel chemistry

Improving synthesis yield – results

- Method A resulted in major material losses
- Method B has higher yield, but is slow
- Method C achieves good balance between yield and synthesis time



Yield for each sample.

Synthesis of osteoinductive material through sol-gel chemistry

Crystallization of osteoinductive material

- Crystallinity improves osteointegration
- Temperature of the synthesis based on the thermal resistance of substrate
- Crystallization temperature can be adjusted by synthesis conditions

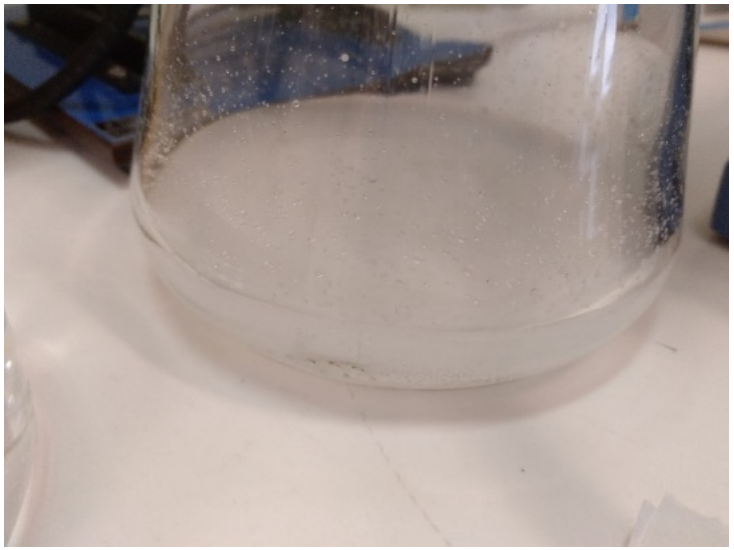
→DoE approach:

- Samples analysed by TGA/DSC and XRD
- Experiment still ongoing

Synthesis of sHAP through precipitation method

New washing method

- Method 1 was too time consuming
- Method 2 resulted in significant material loss
- Methods 3 and 4 were equivalent
- Method 4 chosen



Material loss from method 2.

Synthesis of sHAP through precipitation method

sHAP synthesis DoE

- Different substitutions might have different biological properties
- It is necessary to control the pH but agent responsible for pH control might effect negatively biological properties
- DoE approach allows to simultaneously study the effect of substitutions and ph-control agent on the synthesis of sHAP and its biological properties

Synthesis of sHAP through precipitation method

sHAP synthesis DoE

- FFD with 3 factors
- Samples analysed by FTIR, ICP, XRD and *in vitro* biological testing
- Experiment still ongoing

Future work

- Finish SOP for hMSC expansion and osteogenic differentiation – together with ESR1
- Finish crystallization DoE
- Finish sHAP synthesis DoE – together with ESR1
- Development of final osteoinductive material for spinal application

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THANK YOU