Toward Intelligent Cell-Free Bone Regeneration: iMSC Secretomes and VEGF-Mimetic Functionalized Composite Scaffolds

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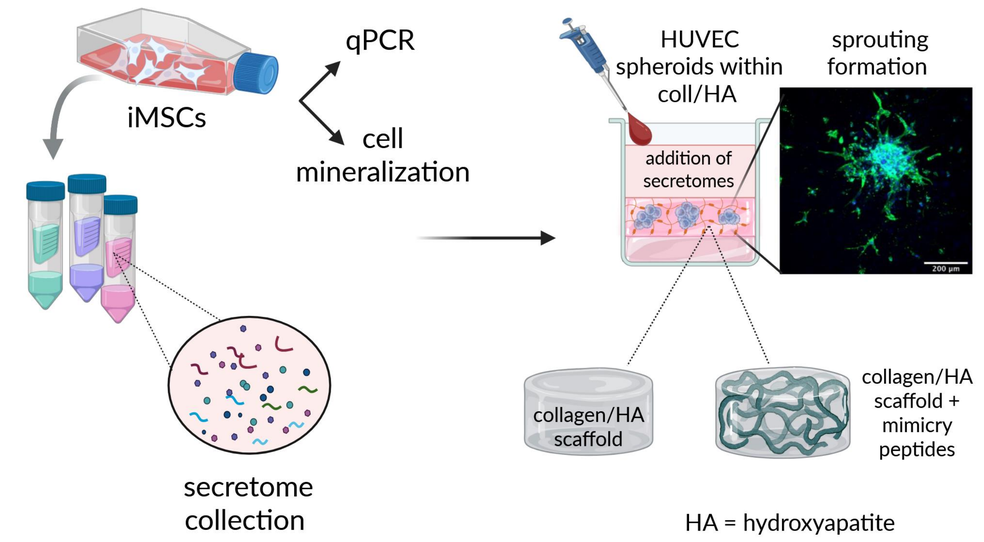
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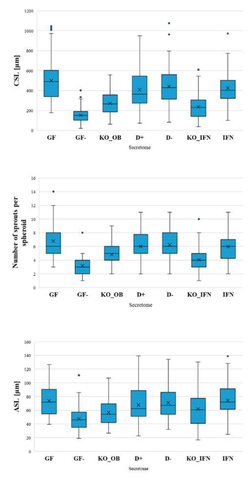
Scientific background and aim of the study

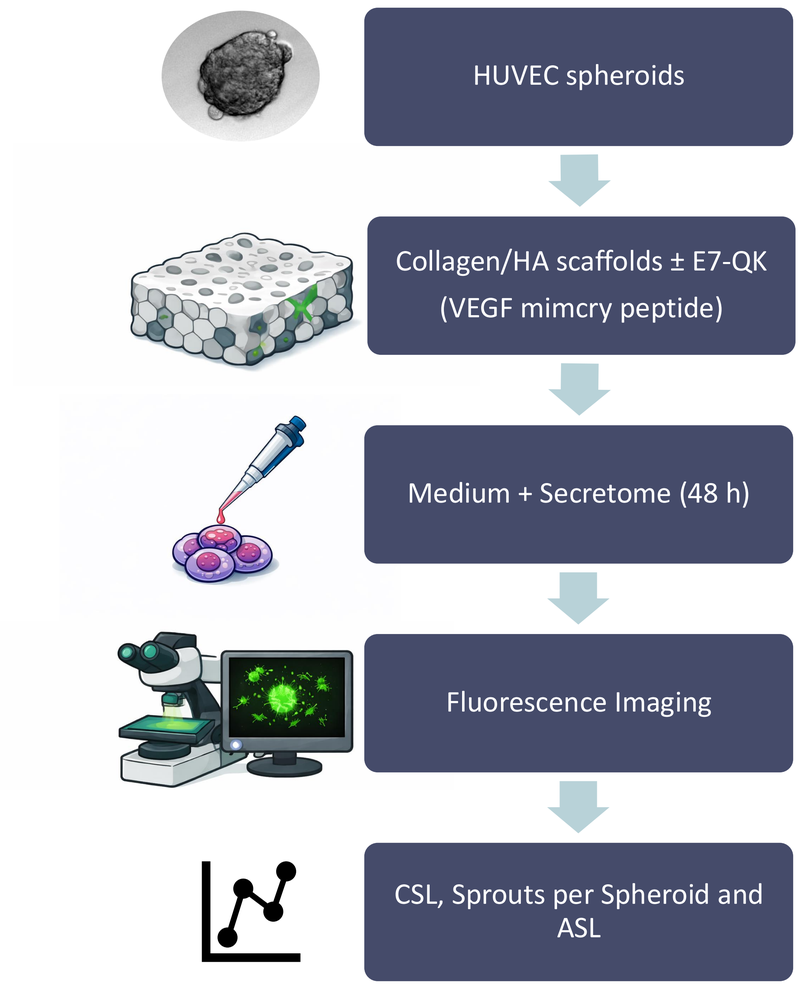
Limitations of Bone tissue engineering:
- Vascularization
- Stem cell survival and immunogenicity
- Mechanical properties of the scaffold

→ Biofunctionalization of scaffolds
Secretome as cell-free alternative

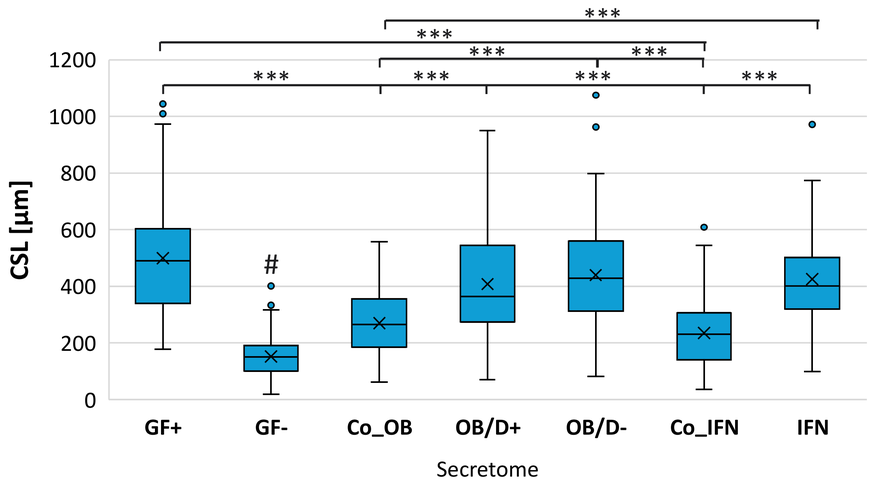


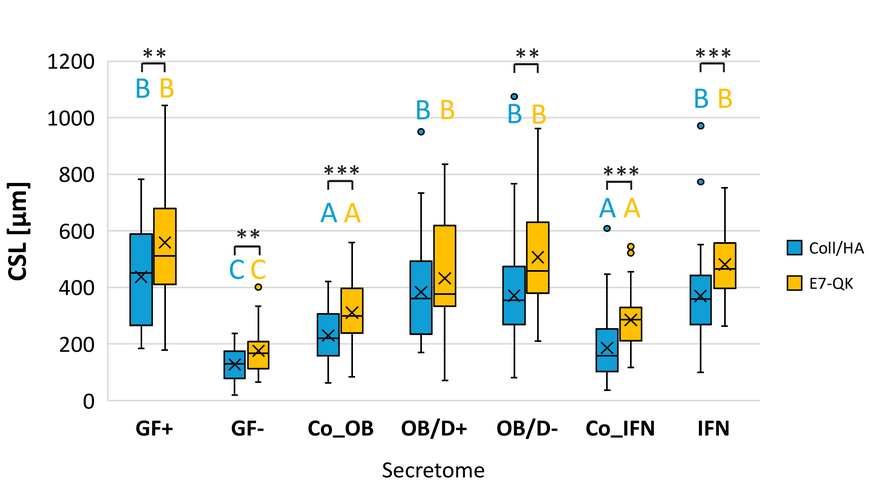
Graphical abstract



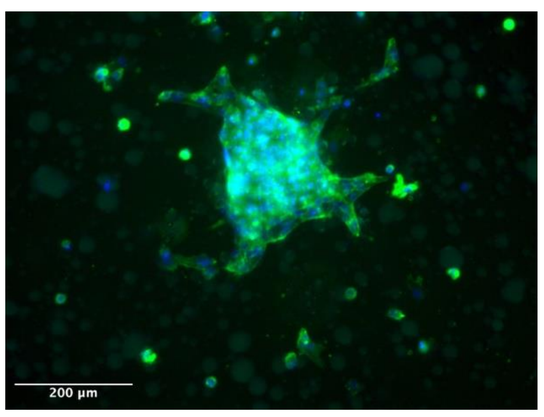


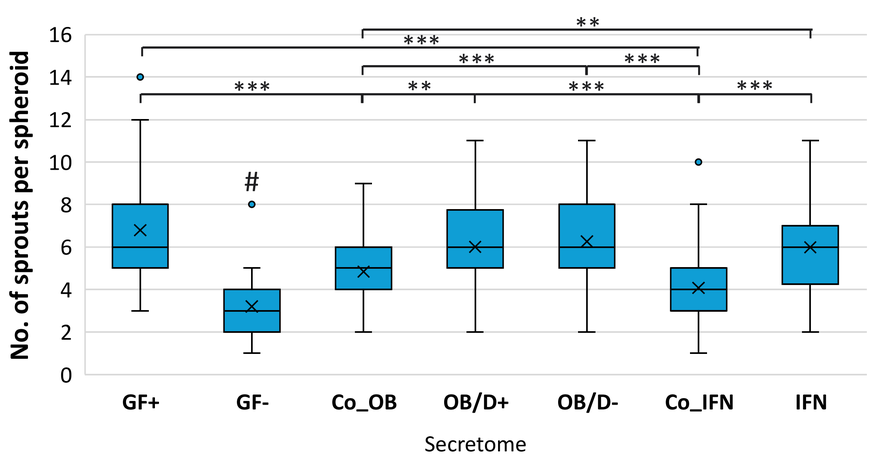
Results

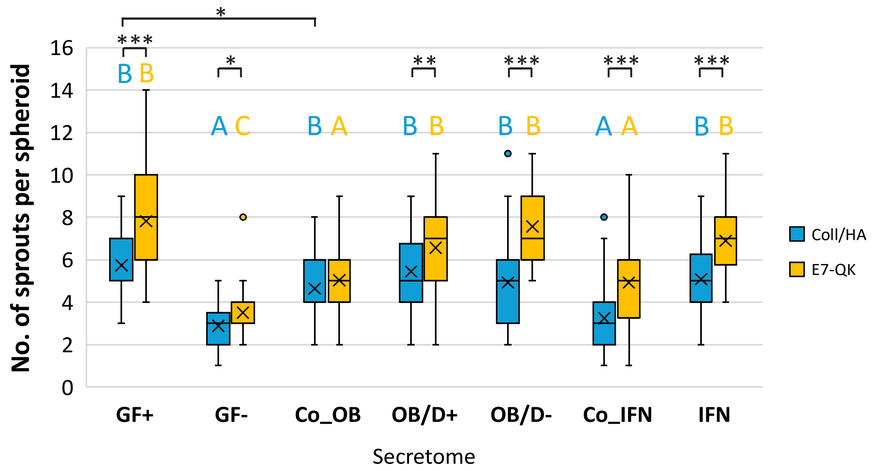




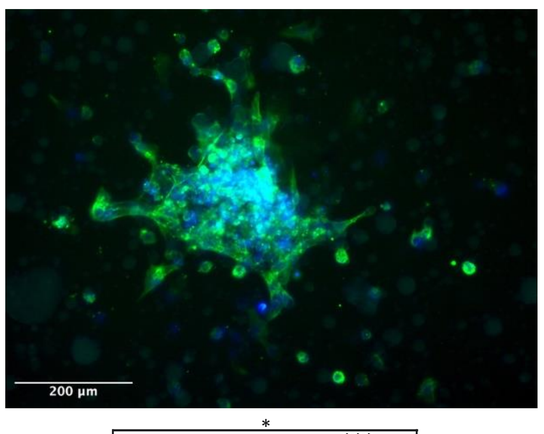
Collagen/HA scaffold, GF+ medium



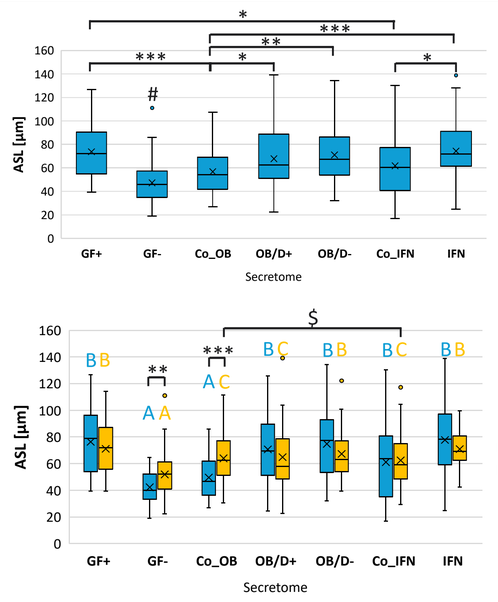


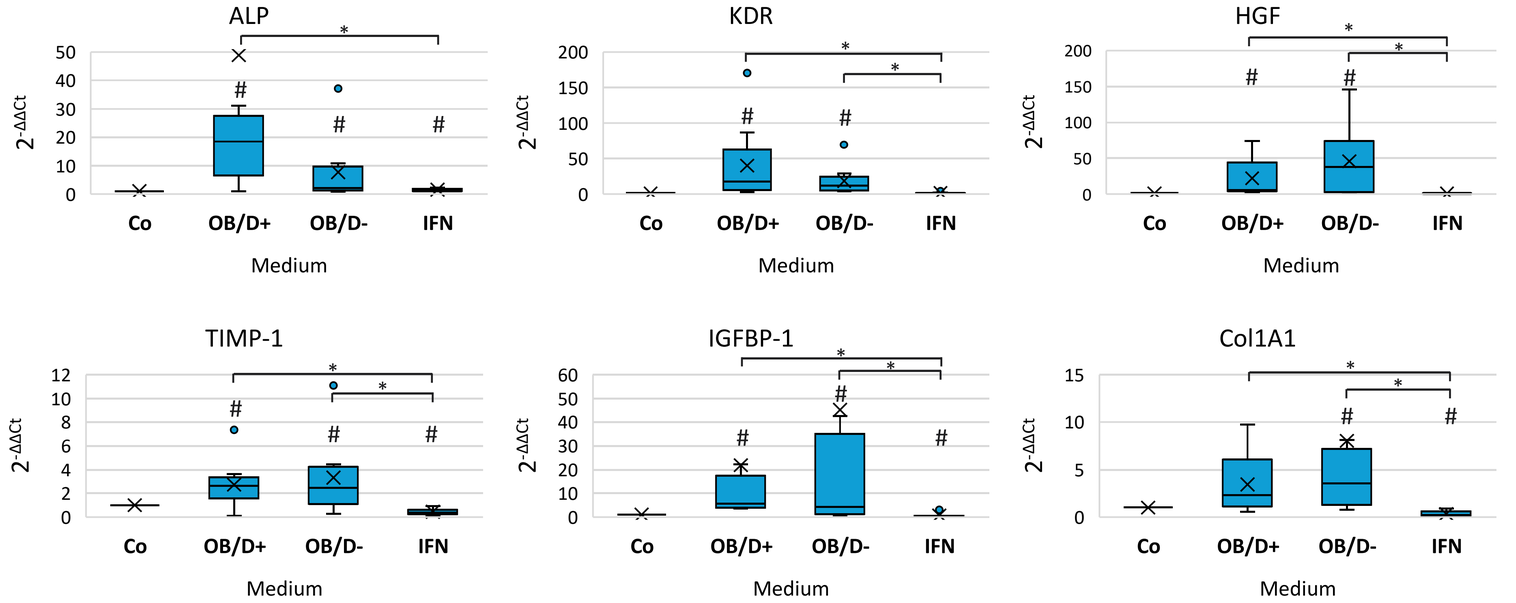


Collagen/HA scaffold+E7-QK, GF+ medium



Effects of secretome and E7-QK on the cumulative sprout length (CSL), number of sprouts/spheroid and average sprout length (ASL) with medium containing or lacking growth factors (GF+ and GF-) or with secretomes from iMSCs treated with control medium (Co_OB), or osteogenic medium with dexamethasone (OB/D+) or without dexamethasone (OB/D-), with control medium under hypoxia (Co_IFN) or with interferon-gamma under hypoxia (IFN). # $p < 0.001$ compared to all other groups. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, Groups with different letters of the same colour show statistically significant differences





Analysis of gene expression in iMSCs, pre-conditioned in 2D cultures with osteogenic medium in the presence or absence of dexamethasone (OB/D+, OB/D-) for 10 days and in the presence of IFN-γ for 5 days by qPCR. Data is represented as $2^{-\Delta\Delta Ct}$ normalized to the control group (Co), which is set to 1. * $p < 0.0083$, # - group shows significant difference to the Co group.

Conclusion

- ❖ iMSC-derived secretomes from osteogenic and pro-inflammatory preconditioning induce angiogenic responses comparable to growth factor-supplemented medium
- ❖ VEGF-mimetic biofunctionalization (E7-QK) significantly enhances angiogenic sprouting, particularly the cumulative sprout length and sprout number
- ❖ The combination of secretomes and functionalized scaffolds demonstrates a synergistic pro-angiogenic effect

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