Biomineralized collagen for bone regeneration

Chapter 8

Statement of impact

To appreciate the scientific impact of the work presented in this thesis it is first important to recognize the field in which it is positioned.. Like the majority of biomedical research, it sits at the intersection of disciplines. Starting from fundamental to more applied topics, the studies presented here have aspects of biomineralization, materials science, and regenerative medicine. Inspiration for the use of biomineralized collagen was born out of discoveries made in the field of biomineralization, with its studies concerning processes of natural mineralization of biological tissues (bone in particular), but its contribution fits more completely under the umbrella of regenerative medicine. More specifically, this work contributes to the existing knowledge of biomimetic materials and their applications as *in vitro* models to study (patho)physiological processes and as clinical products. The main contribution to the field of biomimetic materials comes from the results describing interactions between osteoclasts and biomineralized collagen, presented in Chapter 3 and Chapter 4. By showing that osteoclast resorption of biomineralized collagen is possible, we add to the evidence that this material can indeed be considered one of the closest lab-made analogs for bone microenvironment. Osteogenic and osteoclast-related gene expression of hMSCs, explored in Chapter 5, further adds to this evidence.

Above everything else, the results and discussions presented in this thesis are relevant to the scientific community concerned with mimicking the bone microenvironment. On the one hand, they are useful for the continued development of bone graft substitutes, and on the other hand, as mentioned in Chapter 7, for pre-clinical studies of bone (patho)physiology and drug testing, the value of which depends on biomaterials that adequately resemble the native tissue.

Estimating the societal impact of pre-clinical in-vitro studies, like the ones presented in this thesis, is far more difficult, and in my opinion, only a step short of clairvoyance. In fact, currently, there is no direct, appreciable societal impact from the research presented in this thesis. Nonetheless, a few considerations can be made regarding its potential future application.

The contributions of this thesis to the understanding of biomineralized collagen as a biomaterial of choice for mimicking the microenvironment of bone may be valuable to biomedical companies active in the field of medical devices and regenerative medicine products, such as companies that develop bone graft substitute materials. A prospective market study from February 2021 estimates the global bone graft and substitutes market at USD 2.78 billion (2020), with a compound annual growth rate estimated around 5.8% until 2028.[1] Companies such as DePuy Synthes, Stryker, Medtronic, Zimmer Biomet, Integra Orthobiologics, among others, all develop some form of synthetic bone graft substitute, usually comprising a biomimetic composition of calcium phosphate, collagen, or both.[2,3] The market share of synthetic graft substitutes (as opposed to human or animal derived products) has been increasing in the past, and is projected to grow in the coming years. In addition, synthetic bone graft subtitutes have become increasingly more biomimetic, with composite formulations (collagen-CaP) replacing single-component materials, sometimes even with biological growth factors added. However, so far, no commercial product is composed of collagen with intrafibrillar mineral, such as the one investigated in this thesis.

As mentioned in Chapter 1, in many clinical cases, bone defects are large and complex, and require grafting to aid its regeneration. As the population in developed countries skews older, the incidence of situations requiring a bone graft or a bone graft substitute increases, and so does the need for alternatives to the current standard of care (using the patient's own bone tissue).

The road that starts with fundamental discoveries of bone biomineralization processes is long and winding, passing by material design, optimization for regenerative strategies, and many other stops, before (potentially) reaching society at large, in the form of new and improved solutions to clinical challenges. The contributions made to science along that road stand on their own feet, even if the ultimate goal of a society-benefitting product remains elusive.

References

[1] Grand View Research, "Bone Graft And Substitutes Market Size, Share & Trends Analysis Report By Material Type (Allograft, Synthetic), By Application (Craniomaxillofacial, Dental, Foot & Ankle), By Region, And Segment Forecasts, 2021 - 2028," can be found under https://www.grandviewresearch.com/industry-analysis/bone-grafts-substitutes-market, **2021**.

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[3] A. Bow, D. E. Anderson, M. Dhar, *Drug Metab. Rev.* **2019**, *51*, 533.