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Design of calcium phosphate based cement for bone regeneration and drug delivery

The treatment of bone is a challenge due to the difficulty that has the bone to repair itself. Autologous grafting is the gold-standard treatment for bone reconstruction but this procedure presents many limitations including morbidity, long operative time and insufficient quantity. There is therefore a need to develop novel therapeutic strategies able to exploit the natural regenerative potential of bone and that can be delivered in a less invasive manner. Among the materials studied for the development of novel scaffolds, calcium phosphate cements provide many advantages thanks to their biological performances, including biocompatibility, osteoconductivity and biodegradability. Additionally, many innovative methods of drug delivery have been developed. A wide range of technics are used, particularly in cancer treatment, based on drug encapsulation in a carrier. Compared with the direct administration, these approaches enhance drug stability and targeted delivery, and decrease toxic side effects.

The aim of this thesis is the development and characterization of novel calcium phosphate-based cements allowing drug delivery for bone regeneration and tumor growth inhibition of vertebral metastases. The objective is to develop an inorganic matrix, based on phosphate calcium cements, used as vector to transport drugs by carrier encapsulation. The final target of this combined scaffold will be the treatment of vertebral bone metastasis. These metastases provoke vertebral compression fractures, by weakening bone in the tumor area. The combined matrix can offer the support to reinforce the trabecular bone and, at the same time, deliver the required drugs to stimulate bone formation activity and limit tumor cell propagation. Intermediary objective could be envisaged, with the delivery of antalgic or antibiotics. The thesis is divided in three main parts corresponding to the design of calcium phosphatebased cements, the monitoring of the in vitro / in vivo biocompatibility and the measurement of efficacy for bone regeneration and tumour treatment.