Summary

The bone tissue regeneration induced by biomimetic biomaterials is a very promising and alternative method to treat the fractures caused by a trauma or disease such as osteoporosis compared to the clinical methods normally adopted. The overall goal is the design of nanostructured bioactive scaffolds that are able to reproduce the morphology and physiological features of the native tissue to guide the cells during the regeneration process. In this scenario, collagen-based scaffolds represent a promising tool to mimic the physico-chemical and nano-structural characteristics of bone extracellular matrix (ECM), moreover, the electrospinning (ESP) process can support the design of complex structures with the final shape and porosity similar to the ECM. Moreover, also mesoporous bioactive glasses (MBGs) or nano-hydroxyapatite (nano-HA) can be combined with collagen for the production of multifunctional therapeutic scaffolds; in particular, MBGs have high exposed surface area and pore volume that can be exploited for a surface grafting of different biomolecules, and both MBGs and nano-HA composition can be enriched by the incorporation of therapeutic elements (i.e., Sr). However, ESP require a complex optimization of biomaterial formulations to preserve its high biocompatibility without the loss of the native protein structure.

In this context, the research activities conducted during this PhD, were focused on the design of collagen-based constructs for bone tissue engineering, starting from the development of Sr containing MBGs grafted with a biomolecule to reversibly inhibit osteoclast activity (ICOS-Fc), followed by the optimization and characterization of the material formulations for the ESP process and the most suitable crosslinking strategy.

Concerning MBGs, two synthesis routes were selected for their production with a binary composition based on SiO_2 and CaO enriched with Sr therapeutic ions, a base-catalyzed sol-gel method and an aerosol assisted spray-drying approach. These two syntheses allowed to produce nano-sized particles and micro-sized particles, respectively, with different characteristics. Then MBGs surface were functionalized with amino groups, and the subsequent grafting of ICOS-Fc was performed with a coupling method to link carboxyl groups of ICOS-Fc to the amino groups of MBGs, in order to obtain a multifunctional material that can reversibly and specifically inhibit only the osteoclasts migration and differentiation.

Then, the application of type I collagen was explored for the design of biomimetic scaffolds using the ESP technology, where different collagen concentrations and process parameters were indagated focalizing in particular on the preservation of the protein structure. Subsequently, MBGs or nano-HA were

combined with the optimized solutions, and electrospun to obtain collagen-based constructs with a nano-fibrous morphology and a well dispersed inorganic phase. The effect of the acidic solvent used during the ESP on the grafted ICOS-Fc activity was also studied, resulting in a significant loss of activity only for nanoparticles. Finally, different chemical crosslinking methods were investigated to enhance the mechanical properties of the collagen-based membranes: an N-(3-Dimethylaminopropyl)-N′-ethylcarbodiimide (EDC)/ N-Hydroxysuccinimide (NHS) coupling and a crosslinking with a photoinitiator (Rose Bengal), in order to link the carboxyl and amino groups present in the collagen chains.