NATURALLY-DERIVED HYDROGELS AND NANOCOMPOSITES AS BUILDING BLOCKS OF SCAFFOLDS FOR TISSUE REGENERATION

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Introduction
Naturally-derived hydrogels are developed as bioinspired polymer-based biomaterials for the fabrication of scaffolds and as key ingredients for the engineering of biomaterial surfaces for controlled biointeractions. Such hydrogels can be produced by cross-linking of pure polymers [1,2] or cross-linking of natural polymers derivatives [3,4], as multicomponent systems with combined properties [3,4], they can be (bio)functionalized for specific applications [5] or used as components in (nano)(bio)composites [6,7]. Recently, hydrogel precursors of natural origin have become appealing for development of viscous formulations for (bio)fabrication such as electrospinning and 3D printing [6,7].

Materials and Methods
We developed naturally-derived hydrogels based on pure or modified proteins and polysaccharides, available for tissue regeneration applications. Pure or modified gelatins, mucin, sericin, alginate, nanocellulose and pectin are used to tune the characteristics of different scaffolds. Obtained through covalent or ionic cross-linking, through network-forming photopolymerization sometimes combined with radical polymerization of synthetic monomers, biofunctionalized with cell-adhesive peptides, our hydrogels are designed to tissue regeneration and generation of bioartificial implants.

Results and Discussion
The design, synthesis and fabrication of the scaffolds based on naturally-derived hydrogels are based on bio-inspired approaches. The surface and bulk microstructure and functional properties including elasticity, permeability, biodegradation of the developed scaffolds are evaluated by advanced investigation methods since they play important roles in the stimulation of suitable biointeractions with cells [1-7]. We established methods for the use of hydrogels in the fabrication of porous scaffolds, membranes, films, fibers or particles with predefined properties. Conventional fabrication techniques and more recently electrospinning, electrostatic bead generation and 3D printing are used to produce cell-interactive scaffolds for tissue regeneration. Rheological properties of precursors, cell-friendly cross-linking protocols, specific biofunctionalization and stability tests are required for each type of hydrogel and application. Special consideration is given to the behaviour of hydrogel-based scaffolds in physiologically simulated conditions including bio-dynamic testing in simulated media, cell-interactions in 3D systems including the use of cell spheroids. As an example, FIG. 1 presents nanobiocomposite particles with controlled microstructure and composition designed to obtain osteoblasts adhesive surfaces, fabricated by electrostatic bead generation. FIG. 2 is representative for the stimulation of cell adherence by coating of a polypropylene mesh for abdominal wall fixation with methacrylamide gelatin hydrogels.

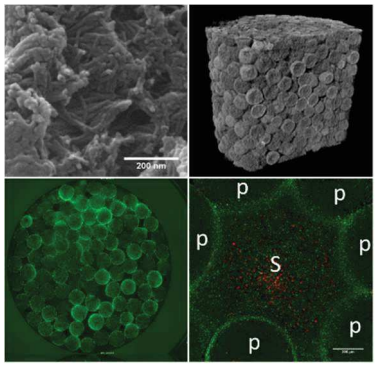

FIG. 1. Bio-inspired nanobiocomposites based on naturally derived hydrogels and nanoapatite. a, b - morpho-structural features (a – SEM; b – microCT); c – osteoblasts adhere on the surface of the beads ; d – the osteoblasts from a spheroid (S) immediately covered the surface of nanobiocomposite particles (P) proving the potential of such scaffolds both as a bone-filling biomaterial but also as a 3D scaffold for the next generation of smart bone regenerative fillers seeded with autologous cells, for personalized medicine.

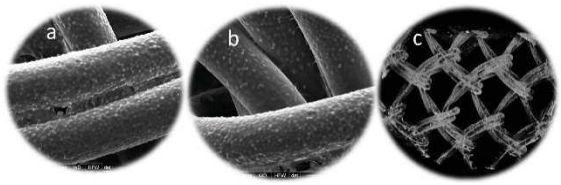

FIG. 2. Polypropylene meshes coated with gelatin-based hydrogels promote fibroblasts adhesion: a,b – SEM micrographs, c – micro-CT

Conclusions
Our research on the development of naturally-derived hydrogels for tissue regeneration emphasizes the importance of microstructural control at the interface biomaterial-cells and acknowledge the need for more appropriate *in vitro* testing conditions to simulate cellular phenomena required for tissue regeneration.

Acknowledgments
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