Elastin-like recombinamers as advanced biomaterials for biomedical applications

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Elastin-like recombinamers, ELRs, are a class of polymeric material whose composition is bioinspired in natural elastin and obtained by recombinant DNA technologies. Their tailor made design allows to include, with a complete sequence control, both functional groups and bioactive domains specifically for each application. These biomaterials are characterized by their biocompatibility, biodegradability, stimuli responsiveness, self-assembly and excellent mechanical properties. Their thermoresponsiveness has allowed us to obtain nanoparticles like nanovesicles for tuberculosis vaccine from elastin-like block core combinamers. Other nanostructures for intracellular gene delivery applications, design from ELRs and aptamers, are polyplexes that protect therapeutic DNA and act as non-viral cell type specific vectors in breast cancer therapy. Drug controlled release has been also tackled by elastin-based hydrogels formed from thermogelificable ELRs for glaucoma treatment. Their adequate mechanical properties have allowed them to have been electrospun to form fibers and micropatterned to give hydrogels with different and reliable topographies, necessary for the study of cell behavior, with proved moldability. Moreover, ELRs biofunctionalized surfaces are especially useful for implant biocompatibility and, as smart surfaces, for cell and cell-sheet harvesting once exploiting their self organized nanostructure with temperature that makes these thermoresponsive surfaces to switch between cell adherent and non adherent states to be applied as a reliable way to harvest different cell lines. Chemically crosslinked ELRs hydrogels have been obtained by clean, fast and atom economy click methodology, and *in vitro* assays for cellular adhesion and proliferation with different cell lines confirm their viability and bioactivity. ELRs hydrogels have been used for different biomedical applications as implant recoveries or as injectable hydrogels at physiological conditions. Within the field of tissue engineering, they have been applied for cartilage regeneration or for osteochondral bone tissue defects repairing.

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Self-assembling bioactive peptide-ELP fusion protein nanoparticles for wound healing and regenerative medicine

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A number of skin substitutes have been developed over the years to promote wound healing in acute and chronic wounds. While it has been proposed that the addition of growth factors and other agents could improve the efficacy of healing and regeneration, this strategy does not work because purified peptide growth factors are short-lived in the highly proteolytic wound environment. To address this limitation, we have developed long-lived nanoparticle technologies that can release bioactive peptides to help improve wound healing. These nanoparticles consist of fusion proteins of elastin-like peptides (ELPs) fused with relevant bioactive peptides that spontaneously self-assemble at physiological temperatures. The technique used enables rapid and inexpensive purification of the fusion proteins through inverse transition cycling, and the nanoparticles thus formed are small enough to be easily incorporated into existing skin substitutes. Results will be shown using three different bioactive peptides: ARA290, SDF-1 and KGF. ARA290 is a peptide from erythropoietin that increases the tolerance of cells to stress, and helps preserve functionality of the microvascular network around the primary injury. SDF-1 is a growth factor that has been shown to inhibit wound contraction and promote dermal regeneration *in vivo*. KGF is known to stimulate epidermal cell proliferation and migration; Due to the versatility of the ELP-based technology, one can develop ELP fusion proteins that target many different aspects of the healing process. Although here we chose to target cell viability (ARA290), the dermis (SDF-1), and the epidermis (KGF), once could consider ELP-based nanoparticles that incorporate other peptides secreted by M2 macrophages, such as TGF-beta and IL-10, as well as cationic bactericidal peptides. The nanoparticles may also be useful in a variety of applications to treat injuries to tissues other than skin, where in many instances pre-formed or injectable matrices are used to promote tissue repair and regeneration.

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