Molecular and physiological mechanism of activity of biodegradable cell scaffolds based on an electrospun polymer matrix enriched with carbon-metal nanocomposites as a biomimetic system supporting the regeneration of skin tissue

Autologous cell therapy is based on the use of the patient's own cells as a therapeutic agent due to their repair and regenerative abilities. **Just a few square centimeters of healthy tissue can be an abundant source of a multi-million population of *in vitro* cell cultures**, thus constituting a therapeutic basis for tissue reconstruction. This solves the problem of limiting access to donor sites, which often occurs in the case of extensive burn wounds. However, cell-only therapy may be ineffective due to the unfavorable tissue environment and the lack of physical support for the cells due to the loss of the extracellular matrix.

Cell scaffolds are the perfect complement to cell therapy, providing support for cells to reveal their full healing potential. In the case of skin, the cellular scaffold should be biocompatible, architecturally and geometrically biomimetic in relation to the extracellular matrix and biodegradable, so that with the development of the newly formed tissue it is degraded to degradation products that do not cause a cytotoxic effect. The added value is the enhancement of the biological effect by facilitating cell adhesion and promoting regenerative processes.

The **electrospinning process** consists in forming polymer fibers under the influence of high voltage, which results in obtaining porous nonwovens. **Poly-(L-lactide)** (PLLA) is a polymer, due to its biocompatibility, processability and biodegradation in the tissue environment, is often used to create electrospun nonwovens. PLLA can be coated with **graphene oxide** (GO), a one-atom-thick carbon nanostructure, and thus influence the reaction of cells. This allows the modification of physiological processes at the cell level and accelerates the process of cell adherence to the substrate. In addition, the deposition of **gold nanoparticles** (Au-NPs) on the surface of GO nanoflakes solves the problem of combining nanoparticles into large particles and enables the promotion of regenerative processes leading to tissue reconstruction.

The aim of the project is to explain the molecular and physiological mechanisms of biointeractions between the PLLA/GO-Au NPs scaffold and cells (keratinocytes, dermal fibroblasts, mesenchymal cells) **and human skin tissues** (EpiDerm model) as the basis for regeneration, growth and development of new tissue. Au NPs will be deposited on GO nanoflakes during the sonication process, and then the GO-Au NPs nanocomposite will be attached to the PLLA matrix by electrospinning. In conclusion, electrospun PLLA will provide physical support to cells, GO will serve as an enhancer of substrate adhesion processes, while Au NPs will act as a component accelerating regeneration processes. The biodegradable nature of PLLA will allow the scaffold to temporarily take over the role of the extracellular matrix, which is a natural cellular support, and will gradually degrade and be replaced by newly formed tissue.

As part of the project, the electrospun PLLA/GO-Au NPs scaffold will be **characterized physicochemically**, and then **biological analyzes** will be carried out using cells of human origin (keratinocytes, dermal fibroblasts, mesenchymal cells) and tissues (reconstructed EpiDerm skin tissue derived from human keratinocytes). The physicochemical assessment will include: assessment of scaffold morphology, topography, wettability, chemical composition, degradation. Then, the biocompatibility, proadhesive and proregenerative properties of the scaffolds will be assessed on the cell models. Finally, the biocompatibility of the scaffold at the tissue level and the assessment of tissue-scaffold interactions will be assessed.

The research results will provide a scientific and theoretical basis for the development and creation of advanced and multifunctional cellular scaffolds dedicated to extensive wounds with difficult regeneration processes, thus supplementing the tools of regenerative medicine with a **bio-dressing that restores health and comfort to patients**.