POLYMERIC BIOMATERIALS SUBSTRATES FOR APPLICATION ON REGENERATIVE MEDICINE AND DELIVERY SYSTEMS.

Gennaro Longobardo – Advisor: Prof. Paolo Antonio Netti /Ing. Assunta Borzacchiello

Curriculum: Ingegneria dei Materiali e delle Strutture

The research project intends to study the design and development of scaffolds in the field of regenerative medicine. It is part of the treatment of disease and the regeneration of tissues, such as lung tissue. In particular, the research project aims to develop an innovative therapeutic strategy for the treatment of pathologies, using polymeric biomaterials combined with stem cells that may be able to synergistically improve the development and regeneration of the tissues and possibly the repair of both acute and chronic lesions.

Cell therapy with intravenous administration of mesenchymal stromal cells (MSCs) was proved to be a potential treatment in regenerative medicine for several diseases based on preclinical and clinical studies according to which MSCs modulate the inflammatory and remodelling processes, proliferation, differentiation into different specific cells and restore alveolo-capillary barriers. Moreover, MSCs can secrete soluble factors capable of eliciting a regenerative response from surrounding cells, in order to create a microenvironment to support the regeneration of tissues.

The aim of this research project is therefore the combination of the beneficial effect of stem cells with the use of polymeric scaffolds (such as liquid solutions at room temperature that gel at a body temperature of 37 °C) biocompatible and biodegradable to favour the administration and transport of stem cells into the lung. The biomaterials used, such as natural polymers (for example polysaccharides and proteins) and their derivatives and/or synthetic polymers (for example polyesters) will be optimized for composition, concentrations and molecular weights, evaluating the use of mixtures of them, to obtain a "composite scaffold" that best mimics the host's tissue architecture.

Stem cells will be seeded inside the polymeric biomaterials, thus obtaining a three-dimensional *in vitro* culture system, which better mimics the real physiological conditions of the tissues, and biocompatibility tests will be performed in a first phase (through Alamar Blue assays, MTT). Furthermore, biomaterials will be characterized to establish their physico-chemical, morphological and rheological properties, also through IR and microscopy analysis.

Subsequently, the effect of the biomaterial on the differentiation of stem cells into specific tissue cells will be evaluated, through immunofluorescence techniques, by searching for specific differentiation markers. Through confocal microscopy it will be possible to qualitatively discriminate the differentiated cells as these will show fluorescent spots compared to the undifferentiated controls. Furthermore, it will be possible to quantitatively evaluate the expression of such markers through molecular biology techniques such as Western blot and/or ELISA kit.

The final aspect of the research project will possibly be to test the composite biomaterials seeded with stem cells in *in vivo* animal models. Indeed, numerous animal models of several disease are already known (mice, rats, rabbits, sheep, baboons, etc.) based on various harmful stimuli, such as induction of hyperoxia, inflammation induced by bacterial lipopolysaccharide (LPS), etc.

Gennaro Longobardo, PhD student XXXVII cycle, July 2022