According to the statistics of the World Health Organization from 2021, over 20 million people around the world are affected by the problem of hard-to-heal skin tissue wounds. This number is indirectly intensified by the occurrence of lifestyle diseases, in particular diabetes. The skin, as the human organ with the largest surface area, performs an important protective function and even in the case of minor but long-term damage, it may be associated with the occurrence of chronic inflammation, infection or necrosis. The global problem of ineffective methods of personalized treatment of damaged or diseased skin tissue makes it necessary to look for new ways and tools to improve the effectiveness of this process thanks to scientific work in the field of tissue engineering: cell research, scaffolds for their cultivation and testing, and signaling factors. Bioprinting is a new rapidly developing tool for tissue engineering. The creation of functional tissues in vitro using bioprinting has become possible with the development of 3D printing technology, materials science and stem cell biology. However, the key problem in bioprinting is still the use of such biomaterials that meet all the scaffold criteria: biodegradability, biocompatibility, non-cytotoxicity and porosity, which provide the conditions necessary for the formation of new tissue and support cell growth throughout the regeneration period. In addition, cellular scaffolds must adhere well to the application site, have appropriate mechanical properties and allow the exchange of gases and cellular metabolites. The fact that hydrogels have a structure similar to the extracellular matrix (ECM) makes them materials with potential applications in tissue engineering. Thanks to their high porosity, they also have the ability to transport low-molecular substances and nutrients that are necessary for cellular activity. Promising materials with chemical similarities to ECM are marine-derived natural polymers: chitosan, agarose, collagen. The project plans to use the first two as a non-cytotoxic composite base with antimicrobial activity and known characteristics of the sol-gel phase transition to create printable primers for skin regeneration. The controlled phase transition of the composite is possible thanks to the use of chitosan hydrogel produced by an innovative method of saturation with gaseous carbon dioxide, which, compared to the use of classic acidic solutions of this polymer, results in the lack of gelling ability of chitosan-agarose composites, the reduction of its gelation rate or the creation of unstable gels, not suitable for creating 3D objects. Approaching the structure of the ECM will also be checked by using the addition of collagen proteins isolated from fish skins as a native equivalent in the designed research model of the skin regeneration starter. In the same function, the QHREDGS peptide, whose biological properties are associated with inducing the migration of primary skin keratinocytes through significantly accelerated wound healing and increased formation of granular tissue, will also be tested.

The main goal of the research project is to develop a multilayer and dynamic model of a skin substitute using two connected robots capable of creating tissue systems with a network of transport vessels containing a nutrient medium for cells placed in alternating layers, with a composition similar to the extracellular matrix (ECM). The model will be created on the basis of a chitosan-agarose composite doped with collagen proteins and/or QHREDGS peptide in free form or covalently bound to chitosan using maleimidoglycine as an efficient and mild cross-linking agent. The pioneering research of the consortium members will be used in the development of a universal multilayer skin regenerative model, in which the multiplication and differentiation of cells and the biodegradation of the scaffold already populated by cells can take place independently during the culture. It is the only non-commercial model adapted to hydrogel materials characterized by a fast phase transition in the cell-safe temperature range, and the only model that, thanks to the use of knowledge and new technologies, will allow to get as close as possible to the skin model as a new analytical tool.

Current scientific works do not indicate the possibility of using the above materials together with the proposed technology of their processing. Both the method of preparation of biocompatible chitosan hydrogel (PG), its composite with agarose, composition and application (PG and MUG) and the use of maleimidoglycine in polymer coupling (UG) are pioneering research of the team, which are the subject of granted patents (PL 223280, PL 222739, EP 2920240) or are in the final stage of filing an invention. Thus, the combination of the competences of the consortium members and their achievements to date has a chance to initiate a new path of research in the field of skin tissue regeneration, especially the one burdened with disease.