ABSTRACT

GENERATION OF HUMAN BIOARTIFICIAL TISSUES BY TISSUE ENGINEERING AS NOVEL ADVANCED THERAPIES FOR THE TREATMENT OF COMPLEX HUMAN DISEASES

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The clinical management of severe conditions affecting the human cornea, skin and palate remains highly challenging, especially in cases when large amounts of tissue are damaged or lost. Over the last decades, researchers described the successful development of human tissue-like substitutes generated by tissue engineering able to mimic the structure of the native tissues. These advanced-therapies medicinal products (ATMP) demonstrated clinical usefulness for the treatment of severe conditions for which a curative treatment is not currently available. By combining human cells with fibrin-agarose biomaterials subjected to nanostructuration methods, the Tissue Engineering Group of the University of Granada has generated and transferred to the clinical setting three ATMP generated by tissue engineering, including the artificial cornea NANOULCOR, the artificial skin UGRSKIN and the artificial palate mucosa UGRPALATE. After a thorough process of tissue characterization and quality control performed both *ex vivo* and *in vivo* in laboratory animals to demonstrate biosafety and functionality, we were able to generate these three ATMP as medicinal products in a GMP facility. This achievement allowed us to translate these products into the clinical practice, with authorization from the Spanish Medicines Agency (AEMPS). In the case of the NANOULCOR artificial cornea, we previously developed a phase-I clinical trial that demonstrated that the product was safe for the patients, and a phase-II clinical trial is currently undergoing to evaluate its clinical efficacy in patients with severe corneal ulcers. Furthermore, we are currently developing a phase-I clinical trial in children with cleft palate (BIOCLEFT clinical trial), and 5 patients have been grafted with the UGRPALATE substitute, with promising results. Finally, the UGRSKIN substitute has been successfully implanted in more than 20 severely burnt patients, initially as compassionate use. The positive results obtained in these patients allowed us to obtain AEMPS authorization for consolidate use in the Spanish Health System, making it the first tissue-engineered ATMP receiving this authorization. Overall, these results highlight the potential of tissue-like ATMP generated by tissue engineering for the regenerative treatment of severe diseases and confirm the potential role of histology in advancing patient care. This work was supported by grants ICI19/00024 (BIOCLEFT), ICI21/00010 (NANOULCOR) and FIS PI23/00335, Instituto de Salud Carlos III (ISCIII), Ministry of Science, Innovation and Universities. Cofinanced by the European Union – NextGenerationEU.