ISSN NO: 2770-2936
Date of Publication:30-03-2023

History of Retinal Implants

Khayrullayeva Lobar,
Department of Physiology, Faculty of Chemistry and Biology, Karshi State University phone: +998991328554

Abstract
Vision is the ability to perceive light stimuli through the eyes, transport information to the brain, which subsequently interprets it in order to relate to the world around us. In this way we can correctly distinguish between colors, shapes, movements and distances. Vision is an essential tool for day-to-day life and its loss leads to a reduction in the person's independence as well as in their quality of life.

Keywords: *eyes, colors, shapes, movements, retina*

Introduction

Defects in the described pathway can lead to multiple visual disorders. The most frequent pathologies are myopia, astigmatism and amblyopia, more commonly described as lazy eye. Even so, there are many more alterations that, due to their lower prevalence, are less studied, despite their great relevance and affectation of multiple ocular tissues, such as the macula, the optic nerve or the retina. This would be the case of hereditary genetic alterations that present with deficiencies in the optical signal transmission pathway, which are by no means negligible due to their generational transmission.

Some examples of these pathologies are retinal dystrophies, congenital glaucoma, hereditary strabismus and most diseases related to the correct perception of the color spectrum.

Synthetic biology is an expanding field. In the last decade, multiple advances have been made both in gene editing and in 3D bioprinting of functional tissues and organs, as well as in the reprogramming of microorganisms. Mixing knowledge of bioengineering with new cutting-edge biomedical techniques, this project offers the hope of developing new approaches for the treatment of hereditary pathologies related to dysfunctions in the retina, the layer where we find the photoreceptor cells.

Retina and Cornea 3D Printing Background

Some retinal cells such as ganglion and glial cells have begun to be printed without affecting their viability during the printing process. However, this process would need to be expanded to more retinal cells in order to create a functional, artificial retina.1

Unlike the retina, what has been able to be completely bioprinted is a cornea. This process has been carried out using a porous polycarbonate mold where the cells will later be printed, mostly keratinocytes. It should be noted that the subsequent feasibility test had satisfactory results, making the technique successful.

An important aspect was that the bioinks used for corneal 3D printing must have a low viscosity, otherwise it would interfere with the resolution of vision (Hamzayeva Nargiza, 2022).

History of retinal implants

Multiple protocols have been developed for the formation of retinal pigment epithelium (RPE) from pluripotent stem cells. It was shown that an RPE resting on a synthetic parylene substrate reproducing Bruch's membrane characteristics has greater survival than suspension pigment epithelium cells. However, the polymer used as the base of the epithelium thickens over the years and makes it difficult to transport metabolites through it. Synthetic pigment epithelium was implanted in patients with age-related macular degeneration (AMD) and good integration was achieved with the retinal tissue of the subjects. Despite the study demonstrating early signs of safety for a bioengineered retinal implant, there were no significant improvements in study subjects.

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Materials and methods.

Hybrid PEG hybrid and peptide synthesis The synthesis of the hybrid blocks was achieved using 3-isocyanatopropyltriethoxysilane following a previously described procedure.

Bioink preparation: PEG hybrid 1 (10 wt%, 300 mg) and GRGDSP peptide 2 hybrid (1 wt%, 30 mg) were dissolved in DPBS (3 mL) containing sodium fluoride (0.3% weight, 9 mg) Viscometry: Viscosity measurements were made using an SV-10 sine-wave (a&D) vibrometer. The sample beaker was filled with 10 mL of bioink and the viscosity was recorded as a function of time at 37 °C.

3D printing: 3D printing was performed on an nScript strategy prototyping machine (3Dn-300-TE) at RT, using a 3 mL syringe filled with bioinks and provided with a 200 µm tip. The hydrogel was dispensed onto a glass slide at a constant velocity of 3 mm s-1 under a pressure ranging from 0.15 to 0.28 MPa. Biological samples: Samples were isolated from the bone marrow (BM) of C57BL/6 mice. In brief, BM was removed from long bones and the cell suspension was plated in minimal essential medium (MEM)-a supplemented with 10% fetal bovine serum (FBS) (Hyclone, Thermo Fisher Scientific, Brebieres, France). 2 mM glutamine, 100 u mL-1 penicillin, 100 mg mL-1 streptomycin (Lonza, Levallois-Perret, France), and 2 ng mL-1 Basic fibroblast growth factor (bFGF) (R & D Systems, Lille, France). The MSCs were characterized by the capacity for immunophenotyping and differentiation towards 3 lineages (chondrocytes, osteoblasts and adipocytes) (Kamil Elkhoury 1 2, 2022). They were then grown to sub-confluence, and used in the process.

Optogenetics

Optogenetics is a biological technique that involves the use of light to control cells in living tissue, typically neurons, that have been genetically engineered to express light-sensitive ion channels. It is a neuromodulation method that combines optical and genetic techniques to control and monitor the activities of individual neurons in living tissue and precisely measure this manipulation in real time.

Most patients suffering from degenerative diseases of the retina, such as retinitis pigmentosa and macular degeneration, often lose their light-sensitive photoreceptors, rods, and cones, leaving the remaining retinal tissue insensitive to light. Even so, surviving cells may retain functionality and connections to the brain after photosensitivity subsides. For decades, researchers have tried to activate this remaining tissue with electrical stimulation. Nowadays with the advent of optogenetics, photosensitivity and vision can restore cellular resolution. Taking into account previous scientific contributions in the field of vision restoration, 3D printing of different organs, especially the cornea and retina, and the recent and innovative advances in optogenetics, we believe that we are going to contribute with our platform to overcome some of the limits that we find today on the table (Hamzayeva Nargiza, 2022).

On the one hand, we are going to bioprint all the cellular components that belong to the retina in 3D and also without affecting its viability during the process. These cells will be present within special low-viscosity bioinks so that the resolution of the patient's vision is not interfered with. And we are also going to contribute to the study and discrimination of what may be the most appropriate substrate for printing in our context.

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