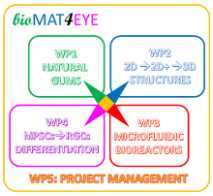

BioMAT4EYE

Neoteric Biomaterials for hiPSCs Monitorized Differentiation to RGCs: Creation, Microfabrication & Microfluidics

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The project bioMAT4EYE proposal addresses the quest for new biomaterials based on polysaccharides of microbial and crustacean origin, ideally obtained from agrowastes to promote circular bio/economy, the construction of bi- and tri-dimensional hierarchical structures based on them and the study of microfluidic conditions and operation, all focused on promoting the differentiation of human induced pluripotent stem cells (hiPSCs) to functional and properly projecting retinal ganglion cells (RGCs), the neurons that selectively die in glaucoma and other optic neuropathies.

We have worked on the microbial production of alginate (*Azotobacter vinelandii*) and pullulan (*Aerobasidium pullulans.* Now, microbial polysaccharide bioproduction has been optimised at shaken flask and bioreactor scale. Polysaccharides has been fully characterised by FTIR, HPLC, SEC. Hydrogels has been formulated with chitosan, alginate, xantham gum and pullulan, while several peptides have been used to activate their surfaces. Hydrogels rheology and morphology have been fully analyzed, having created diverse 3D inks formulated out of several chitosans provided by Chitinor, studying in depth their rheology and printability. Furthermore, the 3D printer supplied by RGD3D to RISE PFI has been modified to control UV crosslinking at cell-adapted temperatures. Microfluidic work with RPCs is advancing with control conditions using Matrigel. Here, the main problem is to follow temporal process variable changes in 2D and 3D systems, in particular small molecules for cell culture (DAPT, BDNF, etc.) are hard to monitor. The on-site measurements of impedance and action potential have yielded good results on retinal progenitors (RPCs) differentiation to retinal ganglion cells (RGCs) using laminin and poly-D-lysine as support material; it is a great success to see signals in the differentiating cells. Initial work with hIPSCs was not succesful on a range of hydrogels, while **work with RPCs is advancing fine results with chitosan and pullulan, where axional growth is clear in several conditions**, including some 2D+ or texturized control runs with poly-d-lysine and laminin.

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