



## PROJECT EXAMPLE: FROM ALGAE TO INNOVATIVE BIOPOLYMERS FOR REGENERATIVE MEDICINE

### Starting situation

The use of scaffold structures and coatings for the structuring and imitation of in vivo conditions is becoming increasingly important in biology and regenerative medicine. As far back as 2003 there was a growing awareness that the cultivation of cells as two-dimensional cell layers in plastic cell culture dishes or flasks could hardly reflect the actual conditions in the body. In vivo the cells are in a three-dimensional bond with close cell-cell and cell-matrix contacts in an elastic environment in the range of  $10^2$  to  $10^5$  Pa compared with a value of  $10^8$  Pa on polystyrene surfaces such as are generally used for cell cultivation. This difference can have a decisive effect on the cell properties. It has already been shown, for example, that both chondrocytes and cardiomyocytes lose their characteristics after prolonged cultivation on hard surfaces. For this reason, naturally occurring materials, so-called biopolymers, are increasingly being used to give the cells a surface or scaffold structure that imitates the conditions in the body. The demands on the biopolymers, however, are very high, and can differ greatly depending on the application area. The materials have to be biocompatible, easy to process and available in consistent quality. At the same time the applications range from immune-isolated transplantation, where no adhesion of cells is desired, right up to the automated printing of three-dimensional scaffold structures for the structuring cultivation of cells.

### Problem

The biopolymers currently in use (e. g., gelatine, agarose) do not have the variability, quality and purity required for standardized use in regenerative medicine. In addition to this, commercially available biopolymers are often only available as

a "black box" without any further information about composition and contents, and can only be adapted to a limited extent to the needs of the cells or the application.

### Solution

For this reason, the department Cryo & Stem Cell Technology has made it its business to realize the complete production pipeline of the biopolymer alginate, which is harvested from brown seaweed, from the harvesting of the raw material right up to functionalization of the end product. Quality assurance standards were set to develop a product with high sterility and biocompatibility that is suitable for all in vitro and many in vivo applications. Due to the composition of the alginate, the viscosity and stiffness can be adjusted according to the needs of the cells and the necessity of the application. Preliminary experiments were carried out to show the possible use of the biopolymer to encapsulate pancreatic islets for the immune-isolated transplantation for the treatment of Diabetes mellitus, as well as an expansion of human induced pluripotent stem cells (hiPSCs) on functionalized alginate microcarriers in bioreactors or an improved maturation of cardiomyocytes cultivated on alginate surfaces. For this purpose a functionalization was developed which binds different adhesion proteins (e. g. collagen, vitronectin) covalently to the alginate surface in order to ensure cell growth on the otherwise non-adhesive material. In order to make these biopolymers available to the wider research community, the material will be commercially available from the company Alginatec as of December 2016.

**1** *Maturation of hiPSC-derived cardiomyocytes on alginate layer (green:  $\beta$ -Actinin, blue: cell nucleus).*

**2** *hiPSCs cultivated on alginate microcarrier for large-scale expansion in suspension bioreactors.*