Jellyfish meets algae – two marine materials enabling adult stem cells to heal cartilage defects

The regeneration of cartilage in humans is a big challenge, since cartilage tissue cannot regenerate from itself after an injury. Therefore, the application of tissue engineering strategies is very promising for the healing of cartilage defects. Tissue engineering involves the cultivation of cells (often stem cells) on a carrier material in a culture dish. During cultivation in the lab, the cell-loaded carrier material will mature into tissue and can be implanted into the defect. In this context it is very important to develop materials which ideally support the maturation into the respective tissue. Cartilage mainly consists of collagen, water rich carbohydrates and cells which are called chondrocytes.

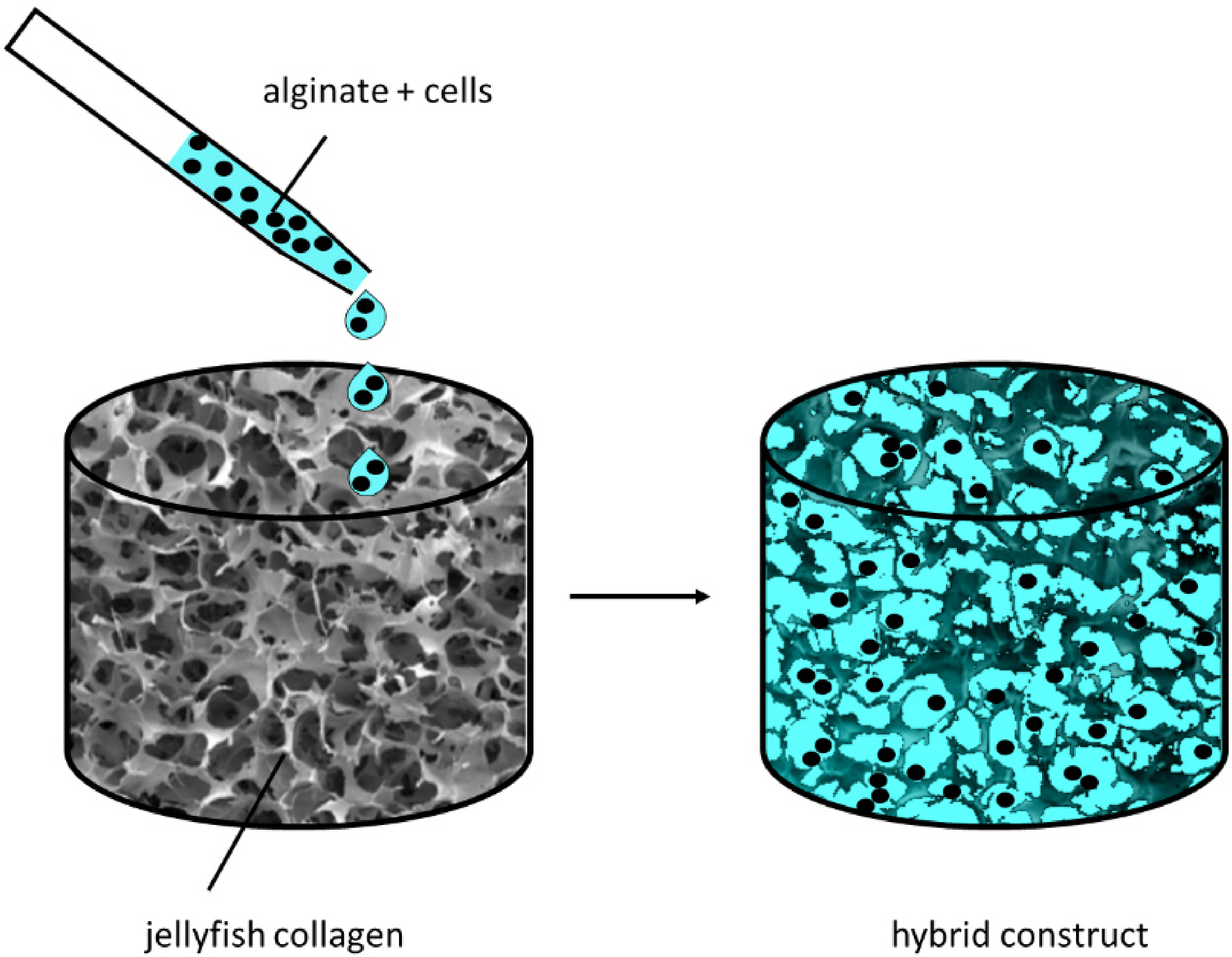

Fig. 1. Combining sponges of jellyfish collagen with alginate derived from brown algae and stem cells from the bone marrow of adult humans.

Collagen is the main structural protein in the human body and its different types are found in nearly all tissues. For example, collagen type I is mainly abundant in skin and bone, while collagen type II is the main component of cartilage. Interestingly, also jellyfish contains a lot of collagen, its structure being quite similar to human collagen. Especially collagen extracted from the jellyfish *Rhopilema esculentum,* equals human collagen II.

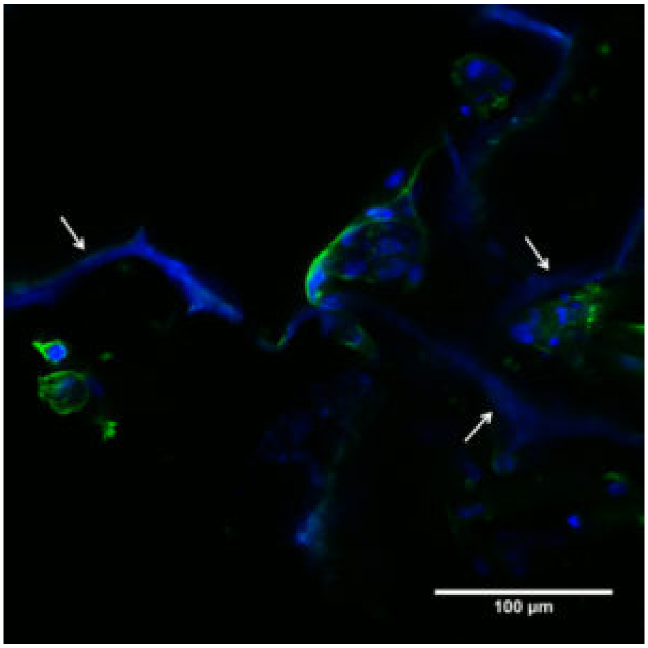

Fig. 2. Fluorescence staining of collagen sponges infiltrated with alginate and stem cells from the bone marrow of adult humans after 21 days of cultivation. Groups of cells were loosely connected to the collagen structure, while cells are entrapped in the alginate gel that fills up the pores of the collagen sponge. Cells show the typical round shape of cartilage cells. Structural components of the cells are stained green; round cell nuclei stained blue. Furthermore, blue autofluorescence of the porous scaffold structure is visible (arrows).

We have developed marine hybrid structures consisting of porous sponges from jellyfish collagen, which mimic the fibrous network of collagen, and the soft hydrogel alginate. Derived from brown algae, alginate forms gels in the presence of different salts, mimicking the water rich carbohydrates of cartilage. To combine both materials, collagen sponges were infiltrated with stem cells from the bone marrow of adult humans together with an alginate solution (Fig. 1). Afterwards, the latter was transformed into a gel by addition of calcium salt.
Constructs were cultivated for 21 days in culture dishes under addition of growth factors. During this time the stem cells developed into cartilage cells. This was shown by the typical round shape of the cells (Fig. 2) and by the secretion of cartilage carbohydrates, steadily increasing from day 12

on. Furthermore, genes which are important for cartilage formation were more frequently translated. Especially the translation of collagen II was enhanced compared to collagen I, thus indicating development of the stem cells towards cartilage forming chondrocytes.

In addition to these promising results, combining jellyfish collagen and alginate has further advantages. Collagen for medical devices is normally isolated from cows or pigs. This may bear the risk of infection for instance with bovine spongiform encephalopathy (BSE) and some people might refuse pig derived collagen for religious reasons. Jellyfish collagen bears no risk of disease transmission, since evolutionary separation between jellyfish and mammals dates back long time ago. Combining jellyfish collagen sponges with alginate, allows it to entrap cells in a gel which forms a similar water-rich environment as in native cartilage. Meanwhile the collagen sponge stabilizes the construct, making it easier to handle compared to a pure gel. Thus, giving cells the opportunity to recognize both structures creates a superior environment for the development of cartilage.

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