

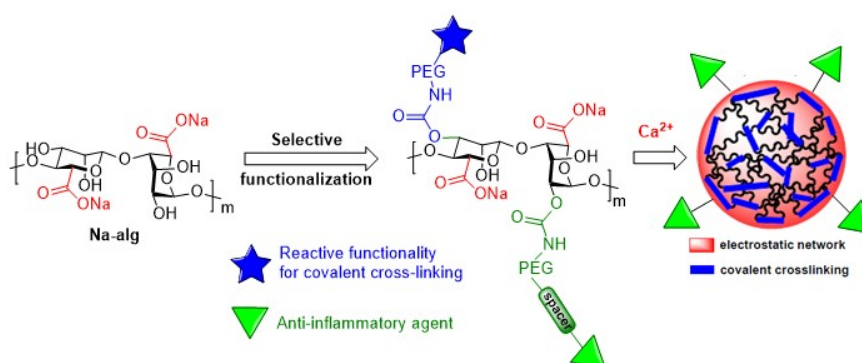
Improving the properties of alginate-based hydrogels by functionalization with bioactive ingredients

E. Noverraz¹, L. Szabó¹, S. Passemard¹, C. Wandrey¹, S. Gerber-Lemaire^{1*}

¹EPFL / Institute of chemical sciences & engineering

The progress of medical therapies relying on the transplantation of immobilized cells relies on both the quality of cells and the properties of the encapsulation materials. Such material has to be biocompatible, its physical characteristics have to be adjustable, and the microencapsulation process should be simple to avoid any damages to the cells. The biopolymer sodium alginate (Na-alg) presents several favorable properties for cell transplantation applications.¹ However, long term *in vivo* durability and selective permeability of alginate-based microspheres are still not optimal.²

The strategy that we developed to improve the performance of alginate-based hydrogels relies on the combination with other polymers such as poly(ethylene glycol) (PEG) to produce microspheres by ionotropic gelation and further reinforcement by covalent cross-linking.²⁻⁶ Following this concept, additional bioactive ingredients can be conjugated to the hydrogel matrix to reduce inflammation response and fibrotic overgrowth which are commonly observed after transplantation, leading to cell asphyxia.⁷ We report herein synthetic pathways for the functionalization of the polymeric components involved in hydrogel formation allowing conjugation of anti-inflammatory agents at the surface of the resulting microspheres for controlled release around the transplantation site. Depending on the chemical linkage envisaged for the conjugation process, different time scales for local delivery are expected.



[1] Smidsrød, O.; Skjåk-Braek, G. Alginate as immobilization matrix for cells. *Trends Biotechnol.* **1990**, *8*, 71-78.

[2] Moya, M. L.; Morley, M.; Khanna, O.; Opara, E. C.; Brey, E. M. Stability of alginate microbead properties *in vitro*. *J. Mater. Sci.: Mater. Med.* **2012**, *23*, 903–912.

[3] R. Mahou, C. Wandrey, *Macromolecules*, **2010**, *43*, 1371-1378.

[4] R. Mahou, G. Kollarikova, C. Gonelle-Gispert, R. Meier, F. Schmitt, N.M. Tran, M. Dufresne, I. Altimari, I. Lacik, L. Bühler, L. Juillerat-Jeanneret, C. Legallais, C. Wandrey, *Macromol. Symp.*, **2013**, *329*, 49-57.

[5] R. Mahou, R. Meier, L. Bühler, C. Wandrey, *Materials*, **2014**, *7*(1), 275-286.

[6] R. Mahou, F. Borcard, V. Crivelli, E. Montanari, S. Passemard, F. Noverraz, S. Gerber-Lemaire, L. Bühler, C. Wandrey, *Chem. Mater.* **2015**, *27*, 4380-4389.

[7]. Vériter, S.; Mergen, J.; Goebels, R.-M.; Aouassar, N.; Grégoire, C.; Jordan, B.; Levêque, P.; Gallez, B.; Gianello, P.; Dufrane, D. *Tissue Engineering Part A* **2009**, *16*, 1503-1513.