# NEW HYBRID POLYMER / PEPTIDE HYDROGELS AS INNOVATIVE PLATFORMS DESIGNED FOR CELL CULTURE APPLICATIONS

throughout the execution period until the present

## Stage I/2020

## Study of the self-assembly phenomenon of peptides in solution as low molecular weight gelators (LMWGs)

**A1: Study of the self-assembly capacity of peptides in suitable solvents for culture media (water, saline or glucose solution, etc.).**

**A2: Study of the co-assembly capacity of peptides - preliminary results**

**A3: Study of the influence of specific factors on the ability of peptides to form supramolecular stuctures- preliminary results**

**A4: Characterisation of the supramolecular assemblies obtained inside of activities l.1-l.3**

**Results delivered on stage:**

(1) self-assembled peptide-based structures as LMWGs, (2) Library of self-assembled peptides according to different specific factor

Project manager,
C.S.I Dr. Loredana E. Nita

## Summary of the stage

Low molecular weight gelling agents (LMWGs) are small molecules (<3kDa) that can associate following a hierarchical process of self-assembly in an anisotropic one-dimensional structure and that can subsequently form a 3D network generated by non-covalent interactions. Different molecular entities such as organic molecules, proteins, peptides and DNA have the capacity to create structurally complexe systems through spontaneous diffusion and specific association between molecules, dictated by non-covalent interactions. Peptides, ubiquitous in nature, are composed of a short amino acids chain that are classified according to their physico-chemical properties, into different groups, based on the nature of the lateral radical R. The peptide chain is based on covalent amide bonds resulting from the reaction between the carboxylic group of an amino acid with the amino group of the same or another amino acids. The versatility of the amino acids composition offers flexibility in the design of peptides chain. Peptides can perform specific biological functions due to their structure and assembly capacity. Self-assembly in ordered structures is governed by the type and order of the constituent blocks of amino acids used and is driven thermodynamically by non-covalent interactions. The secondary structure of the polypeptides describes the three-dimensional arragement of the local segments which are largely stabilized by hydrogen bonds. Generally, in the studies, dipeptides are functionalized at the N-terminal with a hydrophobic group, often a large voluminous aromatic group, such as as 9-fluorenylmethoxycarbonyl (FMOC), naphthalene, cinnamoyl, anthracene, carbazole or pyrene. The FMOC group is used, in particular, as a base-sensitive protection group. Self-assembly is governed by physical interactions, hydrogen bonds, Van der Waals, hydrophobic and electrostatic interactions.The non-covalent nature of the aggregation process allows a very fast response to external stimuli and a more efficient regulation of the macroscopic properties than in the case of polymeric hydrogels covalently assembled by crosslinking processes. For these reasons, the use of self-assembly for the engineering of functional biomaterials is a promising field of research with great potential for the treatment of injuries or diseases. Hydrogels have a water content >99%, giving them similarities to the extracellular matrix due to their high hydration. As a result, they have been used for applications in regenerative tissue engineering, cell culture, drug delivery, enzyme immobilization, and sensitiveilisation systems. They are considered ''smart'' materials due to their ability to react to stimuli, respond and adapt to mechanical and biological changes in the extracellular matrix, to control the release of drugs and biological products in advantageous spatiotemporal models. In addition to the chemistry of materials, cell adhesion is essential for cell infiltration and therefore, for tissue integration a goal for many tissue engineering construction.

Considering these aspects in the present stage, the ability of self-assembly of FMOC-phenylalanine as well as of co-assembly of FMOC-phenylalanine (FMOC-F) with other peptides was studied. The ability to form supramolecular structures was assessed by

combining different characterization techniques: FTIR, SEM microscopy, degree of swelling and adhesion tests.

## Conclusions

- The ability of self-assembly of FMOC-F as well as co-assembly of FMOC-F with other peptides was assessed by combining different characterizations techniques: FTIR, SEM microscopy, degree of swelling and adhesion tests.
- It was found that FMOC-F forms gels both in water and in suitable solutions for culture media (glucose or saline solution, DMSO).
- The co-assembly of FMOC-F with FMOC-Ala and FMOC-Leu, also was performed successfully.
- FTIR spectroscopy and SEM microscopy data support the formation of inter- and intra-molecular physical bonds that ensure the formation of fibrils and their organization in the 3D network. This observation is also confirmed by swelling studies that illustrate the superabsorbant character of prepared hydrogels (although the compounds are hydrophobic). This behavior of swelling at physiological pH will allow the subsequent incorporation of cell media nutrients, by diffusion, in the network matrix.

## Dissemination

### One paper sent for publication

L. E. Nita, A. P. Chiriac, A. Ghilan, A. G. Rusu, N. Tudorachi, D. Timpu, Alginate enriched with phytic acid for hydrogels preparation, sent for evaluation to Biochemica Engineering Journal.

### One patent application filed

A. P. Chiriac, A. G. Rusu, N. Tudorachi, L. E. Nita, A. Ghilan, I. Neamtu, C. Munteanu, Process for obtaining an amphihilic copolymer based on ethylene brasilate and squaric acid using triphenyl bismuth catalyst, A623/2020.