Scientific report

Project: Engineered glycopeptide-based micro/nanomotors for anti-tumoral co-drug release
Acronym: GlyPepTum
Code: PN-III-P1-1.1-PD-2019-0271, **No**. 149/2020

Stage no. 1 / 2020

Preparation and characterization of new amphiphile derivates of polysaccharides by grafting polypeptides with antitumoral activity

A1.1 Synthesis of functionalized polysaccharides grafted with polypeptide with potential antitumoral activity

Summary of the scientific report

In the first stage, the design and synthesis of amphiphilic glycopeptide derivatives was followed according to the project plan by grafting polypeptides containing amino acid sequences with antitumor activity on functionalized polysaccharide soluble in organic solvents. To obtain polypeptides, mainly leucine / lysine / cysteine (amino acids involved in the biochemical signaling pathways of tumors) were used, which can confer controlled biological properties.
Compared to typical polymers, polypeptides have a high chemical diversity of side chains, with a library of twenty-one natural amino acids. Functional groups, including charged species, carbohydrate residues, and moieties that respond to chemical, physical, mechanical, or biological stimuli can be readily incorporated into polypeptide materials. The formation of these structures allows interesting self-assembly behavior specific to the conformation and bioactivity of polypeptides. Polypeptides are obtained mainly by three methods: microbial synthesis, solid phase peptide synthesis (SPPS) and ring-opening polymerization (ROP) of N-carboxyhydrides (NCA). Two main methods have been widely used for the preparation of N-carboxyhydrides: the "Leuchs" method which involves the cyclization of N-alkoxycarbonyl-amino acids and the "Fuchs-Farthing" method. The second reaction, which is currently widely used for the preparation of NCAs, allows the synthesis of pure NCA monomers in good yield and without racemization. The proposed mechanism for the synthesis of NCAs involves the direct phosgenation of free α-amino acids (unprotected α-N-amino acids).

Obtaining chitosan derivatives grafted with polypeptides

The process of preparing the polypeptides consisted of ring-opening polymerization (ROP) of N-carboxyanhydrides of amino acids such as leucine, cysteine and lysine, in the presence of maleoyl-chitosan, used as a macroinitiator. N-carboxyanhydrides of leucine, cysteine and lysine (Leu-NCA, Cys-NCA and CBZ-Lyz-NCA) were prepared by the Fuchs-Farthing method. To obtain the glycopeptides, the N-carboxy anhydrides (Leu-NCA, Cys-NCA and CBZ-Lys-NCA) and the macro-initiator (MAC) were dissolved in DMSO (MAC-p$Leu_{1:50}$, MAC-p$Leu_{1:75}$, MAC-p$Lys_{1:25}$ si MAC-p$Cys_{1:50}$).

After 20 hours at 50 ° C, the resulting viscous liquid was precipitated by the addition of acetone and then washed with acetone three times.

Structural characterization of the functionalized polysaccharide grafted with polypeptides

Their obtaining was confirmed by structural analyzes (FT-IR and ^{1}H-NMR), and the gravimetric molecular masses were determined by the Static Light Scattering (SLS) technique.

Dissemination

Scientific results – Research Articles:

1. Alina Gabriela Rusu, Aurica P. Chiriac, Loredana Elena Nita, Irina Rosca, Daniela Rusu, Iordana Neamtu. Self-Assembled Nanocarriers Based on Modified Chitosan for Biomedical Applications: Preparation and Characterization. Polymers 2020, 12 (11), 2593, **IF 3.426.**