

PNC DI III - Programul 3 Subprogramul 3.1 – Proiecte de mobilități România - Belgia 2016

Project: **Multifunctional Dynamic Nanoplatfoms for Targeted Biomedical Applications**

Acronym: **DyNAp**

Project director: **Dr. Lilia CLIMA**

The *main objective* of DyNAp project is establishing the successful scientific bilateral cooperation in the field of adaptive nanoplatfoms between the PPIMC and UNamur for the sustainable collaboration and applications to competitions within the European Framework.

- **Description of the partners involved in the project and their institutions; Complementarity project research teams participating in bilateral / multilateral.**

Unit of Organic Chemistry, UNamur. Founded in 1831, the University of Namur (UNamur) carries on the values of the humanistic tradition through teaching and research: universality, quality, ethical commitment and solidarity. Its priority is to educate students and researchers as responsible and active members of society. Within the University of Namur, **the Department of Organic Chemistry** (Unité de Chimie Organique, UCO, headed by Professor Stéphane Vincent) is constituted of three distinct laboratories, Organic Chemistry and Synthesis Lab (laboratoire de Chimie Organique de Synthèse, COS), Bio-Organic Chemistry Lab (laboratoire de Chimie Bio-Organique, CBO, **Leader Professeur Stéphane Vincent**) and Organic Chemistry of Supramolecular materials (laboratoire de Chimie Organiques des Matériaux Supramoléculaire, COMS). Overall, UCO department is the UNamur's new centre of excellence in organic chemistry for fundamental and applied research where all three units are closely related to each other.

The CBO laboratory is specialized in bio-organic chemistry, with a special emphasis in glycosciences. In particular, the laboratory is interested in the mechanistic and inhibition studies of essential enzymes involved in the bacterial cell wall biosynthesis and the colonization processes by important human pathogens. CBO particularly specialized in the multi-step organic synthesis of complex glycoconjugates: nucleotide-sugars, glycofullerenes, glycolipids and functionalized carbohydrates. ***Three main research axes are currently developed in CBO research group:***

- a. Synthesis of inhibitors of the LPS (LypoPolySaccharide) biosynthetic pathway (antivirulence molecules, *Chem. Eur. J.* 2011, 17, 11305-13).

- b. Glycosylated nanoplateforms as bacterial antiadhesive molecules and glycosyltransferase inhibitors (*Nature Chem.* 2016, 8, 50-57, *Nanoscale*, 2015, 7, 1760–1767, *Chem. Commun.* 2011, 47, 1321-3, *Chem. Commun.* 2010, 46, 3860-3862).
- c. Novel strategies to fight tuberculosis: inhibition and mechanistic study of the galactofuranose biosynthesis (*Chem. Eur. J.* 2014, 20, 106-12, *J. Am. Chem. Soc.* 2015, 37, 1230–1244).

In particular, the CBO laboratory has so far developed novel synthetic procedures to prepare multimeric glycosylated nanostructures with a defined topology of ligand presentation. Thus, novel glyconanoplateforms based on fullerenes and pillar-arenes have been successfully prepared and assayed against bacteria or therapeutically relevant bacterial proteins.

“P. Poni” Institute of Macromolecular Chemistry (PPIMC), Centre of Advanced Research in Bionanoconjugates and Biopolymers (IntelCentru).

PPIMC is an Institute of Excellence of the Romanian Academy and, based on annual evaluations and during the last five years it was ranked in the first/second position among the 65 institutes/centres of the Romanian Academy. This leading position is internationally recognized by the Institute for Scientific Information (ISI), Philadelphia, USA who lists the PPIMC among the “main Romanian actors on the international scientific scene”; in fact, the Institute holds the first position in Romania in the ISI classification as a research institute. PPIMC functions as a coordinator for joint national and international projects and was appointed by the Romanian Ministry of Education, Research and Innovation as a Regional Contact Point for FP6/FP7 projects and National Contact Point for NMP Priority. Since 2007 the Institute also hosts the NE Romanian Regional centre for EURAXESS. Within PPIMC, **the Centre of Advanced Research in Bionanoconjugates and Biopolymers** department (*IntelCentru*) led by **dr. Mariana Pinteala** is a young and truly interdisciplinary centre of excellence with the main focus on the design, preparation and characterization of biologically inspired nanostructures as potential drug carriers and the interaction of such artificial structures with living systems. In the recent years, *IntelCentru* department have turned its attention toward the exploitation of the dynamic constitutional networks as adaptable gene delivery systems. Extensive organic synthesis was employed to prepare combinatorial libraries of building blocks, together with the development of analytical methods to study their interaction and self-organization in the presence of a target biomolecule (synthetic or natural double-stranded DNA). Also, specific analytical methods have been

developed to determine the capacity of the dynamic platform to complex DNA and to determine the optimum space organization of the final polyplexes using surface techniques (TEM and AFM). The *PPIMC* and *IntelCentru* provide equipment for the characterization of small organic molecules, polymers or nanostructures, together with biochemical and biophysical investigations, including cell culturing and molecular biology (the integral list of equipment is available on the websites: <http://www.icmpp.ro/> and <http://www.intelcentru.ro/>). Some of the biological applications (antimicrobial activities, inhibition of the host/pathogen interaction, and visualization of the nanoparticles' internalization into bacteria) will be realized in UNamur.

The current proposal creates an unique complementary team of two academic research groups focused on *glycochemistry for chemical biology applications (UNamur)* on one hand, and bioconjugates synthesis and characterization (**PPIMC, IntelCentru**) on the other hand. The combination of specialists in glycochemistry with specific biological applications and specialists in structure-function analyses would not only create a synergetic effect to the proposed research field, but also help in sharing the unique knowledge of the involved groups among each other. We are confident that our multi-disciplinary collaboration will contribute to translational research having the potential to advance the applied nanomedical sciences. Our primary middle and long-term objective is to create a fruitful result-oriented collaboration in order to successfully apply to competitions within the European Framework (H2020, Era-Net, Euronanomed, etc.).

Dissemination

1. B. F. Craciun, M. Pinteala, L. Clima. Non-viral vectors based on PEGylated Squalene. Oral presentation: 4th French-Romanian Colloquium on Medicinal Chemistry, Iasi, Romania, October 5-7 **2017**.
2. Dynamic Self-Organizing systems for DNA delivery; G. Pricope, M. Pinteala, L. Clima, submitted to *Rev. Roum. Chim.*, **2018**, 63(7-8), 613-619.