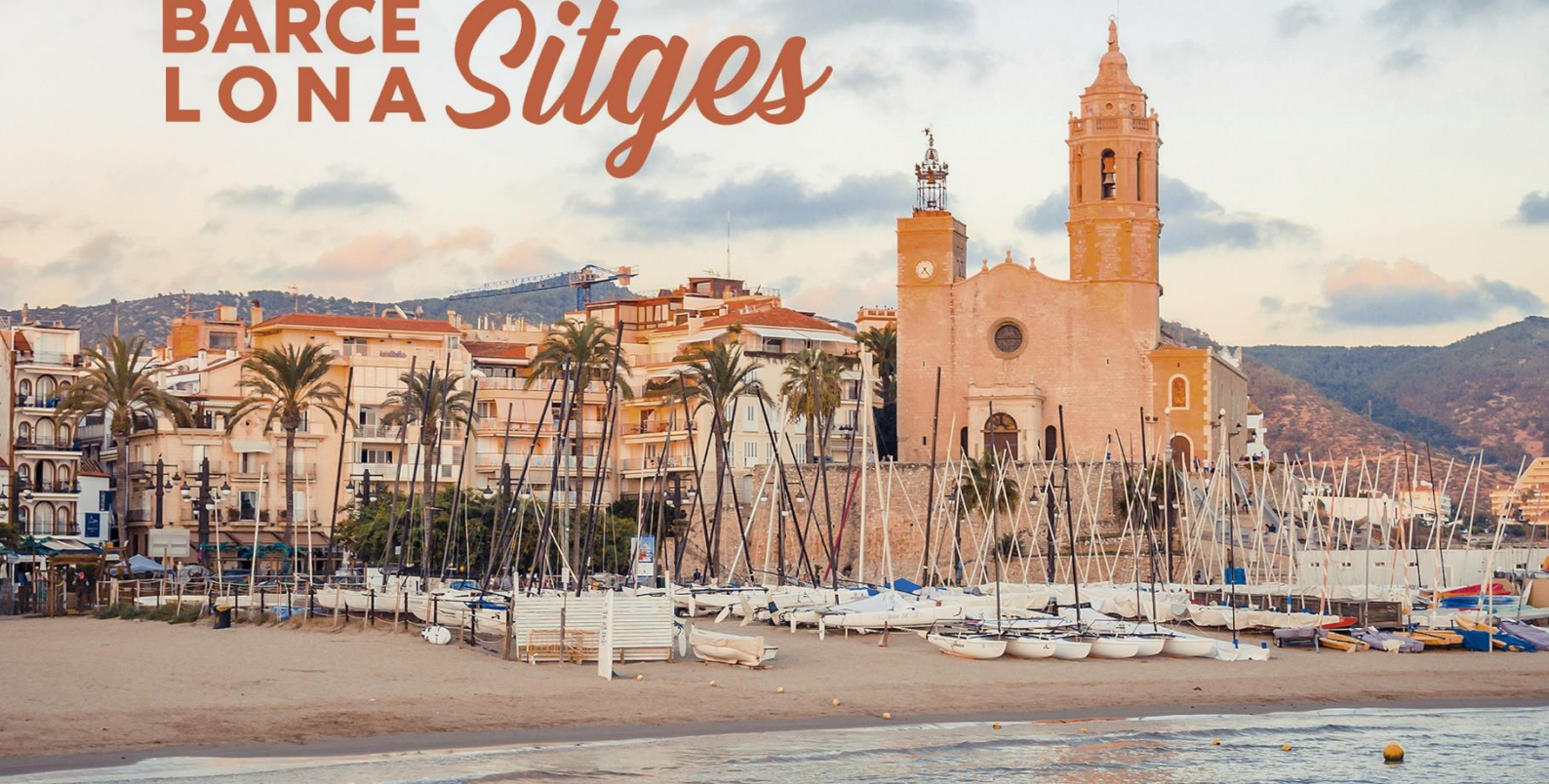
# 7th IBERIAN CARBOHYDRATE MEETING

January 15-17 2024

BARCELONA Sitges



# ABSTRACT BOOK

GRUPO ESPECIALIZADO HIDRATOS DE CARBONO

RSEQ Real Sociedad Española de Química

Sociedade Portuguesa de Química

**OC-26**

# MULTIVALENT CARBOHYDRATES SYSTEMS AS ANTIVIRAL THERAPEUTICS

Fayna García-Martín,[a] Óscar Suárez,[a] Gonzalo Millán,[a] Ester Jiménez-Moreno,[a] Filipa Marcelo,[b] Mónica Martínez-Orts,[c] Silvia Pujals,[c] Elena Lalinde,[a] Jesús R. Berenguer,[a] Héctor Busto,[a] Jesús M. Peregrina,[a] Asuka Nanbo,[d] and Francisco Corzana[a]

[a] *University of La Rioja (Spain),* [b] *Universidade Nova de Lisboa (Portugal),* [c] *Institute for Advanced Chemistry of Catalonia (IQAC)-CSIC (Spain),* [d] *University of Nagasaki (Japan)*

*e-mail: fayna.garcia@unirioja.es*

**Keywords:** *multivalent glycan presentation, synthesis of multivalency scaffolds, antiviral research, glycan-based therapeutics*

This proposal is centered on the development of various platforms that present glycans as potential therapeutics for Ebola virus disease. In the search for novel therapeutics for today's infectious diseases, it is essential to target molecular-level elements and utilize innovative tools to enhance antiviral efficacy and bioavailability. The Ebola virus initially targets dendritic cells and macrophages by fusing with receptor targets through its surface viral glycoprotein. A crucial entry point for the virus is the macrophage galactose lectin (MGL) receptor, whose main ligand is the alpha linked *N*-acetylgalactosamine glycan (α-GalNAc).[1] We hypothesize that effectively presenting this ligand can block the Ebola virus's entry and infection.

We have devised three distinct multipresentation strategies. First, we employed a multiantenna glycan, developed by multiple antigen presentation dendrimer scaffold with a terminal Ser/Thr linked to α-GalNAc at the lateral side (Thr/Ser(α-GalNAc)), a small library featuring various glycan repetitions.

Our second approach involves mesoporous silica nanoparticles (siNPs)[2] linked with a spacer terminating in Thr/Ser(α-GalNAc). The conjugation has been performed through copper-free *click chemistry*. The SiNPs serve as a vehicle to display the inhibitors, mimicking the viral envelope.

The third strategy entails developing self-assembling peptides containing GalNac. Self-assembled peptide structures are an evolving field for creating innovative therapeutics. In this context, our objective is to mimic the fibril structure of the Ebola virus by designing self-assembled fibrils containing *disks* with diverse functionalization. One of these functionalized disks contains an exposed Ser(α-GalNAc), the others contain the structural feature and a chromophore.

These multiGalNAc scaffolds and linkers have been synthesized by solid-phase synthesis and characterized using different techniques as RP-HPLC, MS and NMR. Additionally, the supramolecular inhibitors are characterized by microscopy. Further, STD-NMR can elucidate binding interactions between the GalNAc-presenting scaffolds and MGL proteins. Then, *in vitro* inhibitory assays provide crucial insights into their potential as therapeutics.

Our developed scaffolds hold promise as effective viral inhibitors while providing essential information to advance in the field of antiviral research.

Acknowledgments: We acknowledge financial support by AEI (PID2020-120099RA-I00). F. G.-M. acknowledges the contract *Beatriz Galindo* from the Ministry of Universities of Spain.

## References

[1] (a) A. Takada, et al. *J. Virol*., **2004**, *78*, 2943; (b) S. Van Vliet, et al. *Trends in Immun.*, **2008**, *29*, 83.

[2] C. Ezquerro, et al. *J. Mater. Chem. C.* **2017**, 5, 9721.

[3] E. Fuentes, et al., *J. Am. Chem. Soc.* **2020**, *142*, 10069.