IUPAC 23

chains

The Hague | The Netherlands
20-25 August 2023

# Book of abstracts

## CONNECTING CHEMICAL WORLDS

www.iupac2023.org

# P2-B0685

## Incorporation of Tn Antigen Mimetics into the MUC1

*Carmen Breton*[*1], *Jesús Manuel Peregrina*[1], *Francisco Corzana*[1], *Paula Oroz*[1], *Ismael Compañon*[1]
[1] *Universidad De La Rioja, Logroño, Spain*

One of the most recent approaches to treating cancer is immunotherapy, which is based on the patient's immune system's ability to recognize and effectively eradicate malignant cells. The development of immunotherapy requires the study of new biomarkers, as in the case of the glycoprotein MUC1 mucin. In cancer cells, unlike in healthy cells, alterations occur in its glycosylation, exposing different antigens that can trigger an immune response, such as the Tn antigen (GalNAc-α-O-Ser/Thr). Thus, the Tn antigen has been incorporated into peptides and used to generate therapeutic vaccines against cancer. However, the therapeutic use of O-glycopeptides is sometimes limited since they are easily hydrolyzed in biological systems. Therefore, different mimetics of the Tn antigen are being developed, including those that involve changes in the O-glycosidic bond[1].
In this work, the oxygen atom of this bond has been replaced by a sulfur or selenium atom. These Tn antigen mimetics have been incorporated into MUC1 tandem repeat peptide sequence using SPPS (Solid-Phase Peptide Synthesis) methodology[2]. Affinities (KD) of all glycopeptides incorporating unnatural Tn mimetics to different anti-MUC1 antibodies were determined experimentally. The results obtained were explained in base of the conformational preferences deduced from NMR experiments combined to MD simulations. The best surrogates in terms of affinity will be the selected candidates to develop cancer therapy approaches in the future.

References
[1] I. Compañón, et al. J. Am. Chem. Soc. 2019, 141, 4063-4072.
[2] J. Macías-León, et al. Chem. Commun. 2020, 56, 15137-15140.

Acknowledgments
We thank the Ministerio de Ciencia, Innovación y Universidades (AEI PID2021-127622OB-I00 & PDC2022-133725-C21 Projects) and the Asociación Española Contra el Cáncer for the predoctoral fellowship of C.B.