

MUC1 GLYCOPEPTIDES INCORPORATING Tn ANTIGEN MIMETICS

C. Breton, M. Torres, P. Oroz, I. Compañón, A. Avenzoza, M. M. Zurbano, J. H. Busto, F. Corzana, and J. M. Peregrina

Departamento de Química, Centro de Investigación en Síntesis Química, Universidad de La Rioja, 26006 Logroño, La Rioja, Spain.

e-mail: carmen.breton@unirioja.es

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Immunotherapy, one of the most modern methods for treating cancer, relies on patients' immune system to identify and successfully destroy cancer cells. The development of this immunotherapy requires the study of new biomarkers, as in the case of the MUC1 mucin. In cancer cells, unlike healthy cells, alterations in its glycosylation occur, exposing different antigens that can trigger an immune response, such as the Tn antigen (GalNAc- α -O-Ser/Thr). Consequently, therapeutic cancer vaccines have been developed using peptides that include the Tn antigen. However, because O-glycopeptides are quickly degraded in biological systems, their therapeutic utility is occasionally limited. Therefore, different mimetics of the Tn antigen are currently being developed, including those that involve changes in the O-glycosidic bond^[1].

As shown in **Figure 1**, several mimetics of the Tn antigen have been synthesized and incorporated into different positions of the MUC1 tandem repeat peptide sequence using the solid-phase peptide synthesis (SPPS) methodology^[2]. Experimental analysis using surface plasmon resonance (SPR) and ELISA techniques were developed to determine the affinity (K_D) of each non-natural glycopeptide to various anti-MUC1 antibodies. The best surrogates in terms of affinity will be the selected candidates to develop cancer therapeutic approaches in the future.

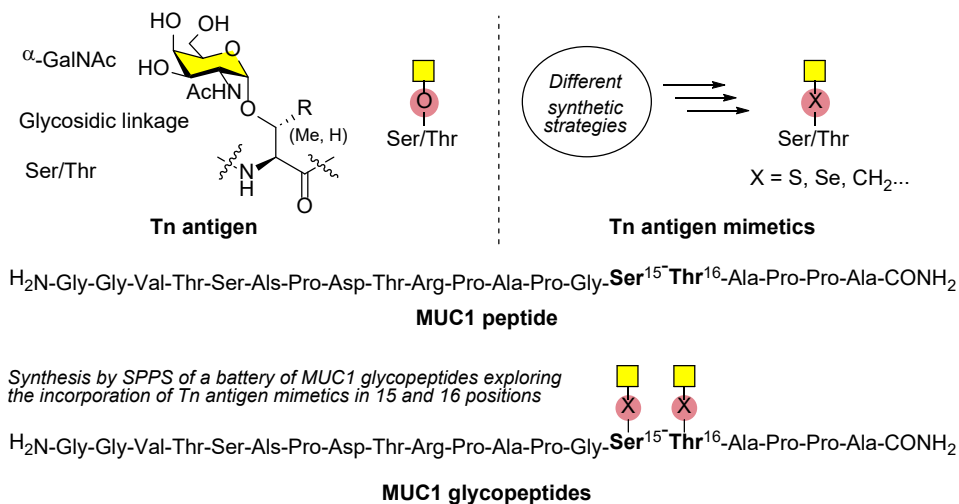


Figure 1: Tn antigen mimetics and glycopeptides synthesized in this work.

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References

- [1] I. Compañón, et al. *J. Am. Chem. Soc.* **2019**, 141, 4063-4072.
- [2] I. A. Bermejo, C. D. Navo, et al. *Chem. Sci.* **2020**, 11, 3996–4006.