

) 24

<u>Roy Steneker</u>^a, Madouc D. Bergers^a, Tressie Chêne^a, Leonard de Paepe^a, Sofie Niggemeier^b, Jan-Hendrik Hehemann^b, Jeroen D.C. Codée^a, Hermen S. Overkleeft^a

^a Leiden Institute of Chemistry, Leiden University, 2333 CC Leiden, The Netherlands roysteneker@gmail.com ^b MARUM MPG Bridge Group Marine Glycobiology, Max Planck Institute for Marine

Microbiology, D-28359 Bremen, Germany

Marine glycans are vital biomolecules that play a pivotal role in the global carbon cycle, contributing to the fixation of approximately 50 gigatons of carbon by the oceans each year [1]. Glycans derived from marine organisms have gained significant attention due to their diverse biological activities and their potential applications across various industries. Among these, fucoidans - sulfated polysaccharides primarily composed of L-fucose residues - are of particular interest. Fucoidans display a high degree of structural heterogeneity, especially in their sulfation patterns, making it challenging to establish clear structure-function relationships [2]. This knowledge gap could potentially be narrowed by studying the enzymes that degrade these complex biopolymers, which may also serve as valuable tools for the consistent enzymatic extraction of well-defined fucoidan structures [3]. Fucoidans are typically broken down by marine microbes, yet their degradation pathways remain poorly understood and involve a wide array of enzymes classes, including sulfatases and glycosidases [4]. Among these are fucoidan hydrolases, or fucoidanases, which cleave the glycosidic linkages between sulfated fucose moieties [5]. Despite limited knowledge about these enzymes, studies suggest that they could operate via a retaining catalytic mechanism [6]. As this mechanism proceeds through a covalent enzyme-glycosyl intermediate, it presents the opportunity for covalent trapping of the active site residues using mechanism-based inhibitors and probes [7]. In this work, we designed, synthesized and applied new activity-based probes to selectively target fucoidan hydrolases from marine organisms.

References:

- 1. Mardhekar, S. et al. RSC Chem. Biol. 2025.
- 2. Jiao, G. et al. Mar. Drugs 2011, 9(2), 196-223.
- 3. Ale, M.T. RSC Adv., 2013, 3, 8131-8141.
- 4. Sichert, A. et al., Nat. Microbiol., 2020, 5, 1026–1039.
- 5. Zhao, Y. et al. Mar. Drugs 2025, 23, 97.
- 6. Vickers, C. et al. J. Biol. Chem. 2018, 293 (47), 18296–18308.
- 7. Artola, M. et al. J. Am. Chem. Soc. 2024, 146, 24729–24741.