Detailed Investigation of Human Galectins -1 and -3 by employing selectively deoxyfluorinated *N*-acetyllactosamines

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Human galectins (hGals) are carbohydrate-binding proteins playing key roles in a plethora of physiological processes. They are able to modulate immune responses and neoplastic transformation processes via the molecular recognition of galactoside-containing glycans.[1] As a result, the development of their selective inhibitors has become a focus of pharmaceutical research. However, the preparation of inhibitors targeting individual hGals remains challenging as 12 hGals featuring similar substrate specifications have been identified. A deeper understanding of the differences between individual hGals could facilitate the development of galectin inhibitors, and deoxyfluorinated carbohydrates are established tools capable of providing such valuable information.[2]

This work is focused on a detailed investigation of supramolecular recognition events between human galectins -1 and -3 and monodeoxyfluorinated *N*-acetyllactosamine probes, which were previously prepared in our laboratory.[3] The recognition was studied using a combination of X-ray crystallography, isothermal titration calorimetry and several advanced NMR techniques, such as ^{19}F T2-filter, ^{1}H–^{1}H STD, ^{1}H–^{15}N CSP or ^{19}F EXSY. These techniques provided insight into the thermodynamics and kinetics of recognition and enabled us to uncover of subtle differences between both investigated galectins. Such differences could be potentially exploited in the selective targeting of individual galectins with important implications for the galectins-focused pharmaceutic industry.

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References

1. Dings, R. P. M.; Miller, M. C.; Griffin, R. J.; Mayo, K. H. *Int. J. Mol. Sci.* **2018**, *19*, 905–926.
2. Linclau, B; Ardá, A.; Reichard, N.; Sollogoub, M.; Unione, L.; Vincent, S. P.; Jiménez-Barbero, J. *Chem. Soc. Rev. J.* **2020**, *49*, 3863–3888.
3. Kurfiřt, M.; Dračínský, M.; Červenková Šťastná L., Cuřínová, P.; Hamala, V.; Hovorková, M.; Bojarová, P.; Karban, J. *Chem. Eur. J.* **2021**, *27*, 13040–13051.