

## Synthesis, structure, modelling and interactions of GAG mimetics with proteins

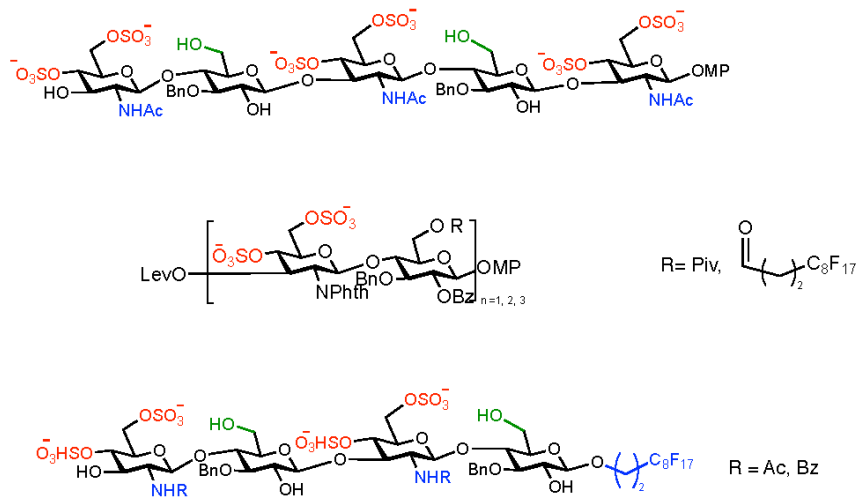
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Midkine (MK), together with Pleiotrophine (PTN or HB-GAM), constitutes the family of neurite growth-promoting factors (NEGF). They are involved in early neural growth and other physiological actions related to mitogenesis or inflammation. They interact with extracellular glycosaminoglycans (GAG) that are fundamental for their activity through interaction with specific membrane receptors. We have been exploring the synthesis, binding properties, and structure of synthetic canonical Chondroitin Sulfate tetrasaccharides, [1] and now we showed our results with GAG mimetics with variations on the basic skeleton's (see figure). Variations were the substitution of GlcA by Glc; [2] or GalN by Glc and the introduction of fluorinated aliphatic chains to improve the isolation, both in the anomeric or in primary alcohol positions. We used NMR to study the 3D shape of these new compounds concluding that they still have the same 3D pattern that the GAG homologs. [2]

After our analysis combining NMR and modeling, we can conclude that the shape of the mimetics studied is similar to that of GAG. Therefore they can be considered good mimetics of them in spite of drastic changes such as removing a negative charge, per disaccharide.



### Bibliographic references:

- [1] M. J. Garcia-Jimenez, S. Gil-Caballero, S. Maza, F. Corzana, F. Juarez-Vicente, J. R. Miles, K. Sakamoto, K. Kadomatsu, M. Garcia-Dominguez, J. L. de Paz and P. M. Nieto, *Chem. Eur. J.* (2021), 27, 12395-12409; M. Torres-Rico, S. Maza, J. L. de Paz and P. M. Nieto, (2021) *Org. Biomol. Chem.* 19, 5312-5326.  
 [2] M. J. García-Jiménez, M. Torres-Rico, J. L. De Paz and P. M. Nieto, (2022) *Int. J. Mol. Sci.*, 23, 3026.