

von Mach T, Carlsson MC, Straube T, Nilsson U, Leffler H, Jacob R. (2014) Ligand binding and complex formation of galectin-3 is modulated by pH variations. *Biochem J.* 457(1):107-115.

Galectin-3-dependent clusters or lattices are formed at the surface as well as in distinct organelles of eukaryotic cells. Incorporation into membrane proximal networks can fix glycoproteins within subcellular domains or sort them into distinct transport pathways. In the present paper we analysed the effect of acidification on the sugar binding and self-oligomerization of galectin-3. Using a fluorescence anisotropy assay we measured decreasing galectin-3 affinities to the blood group antigen GalNAc α 1-3(Fuc α 1-2)Gal β 1-4Glc under low pH conditions. Binding to the strong interaction partner N-acetyl-D-lactosamine was also lost at pH 5.0, whereas the less efficient ligand lactose was still able to bind. This indicates that variations in the binding specificity to distinct glycans can be observed by altering the pH. The formation of galectin-3-based complexes by interaction with the multivalent glycoproteins asialofetuin or transferrin was also obliterated at acidic pH and the ligand-binding affinity itself was modulated by oligomerization of the lectin. When galectin-3 was added to giant plasma membrane vesicles from the apical surface of epithelial cells, pH modulation could generate or eliminate the formation of membrane domains enriched with p75(NTR) (neurotrophin receptor p75). In conclusion, the results of the present study suggest that the formation and composition of galectin-3 networks can be fine-tuned by changes in the environmental pH.