A Diverse Range of Bacterial and Eukaryotic Chitinases Hydrolyzes the LacNAc (Galβ1-4GlcNAc) and LacdiNAc (GalNAcβ1-4GlcNAc) Motifs Found on Vertebrate and Insect Cells

There is emerging evidence that chitinases have additional functions beyond degrading environmental chitin, such as involvement in innate and acquired immune responses, tissue remodeling, fibrosis, and serving as virulence factors of bacterial pathogens. We have recently shown that both the human chitotriosidase and a chitinase from Salmonella enterica serovar Typhimurium hydrolyze LacNAc from Gal beta 1-4GlcNAc beta-tetramethylrhodamine (LacNAc-TMR (Gal beta 1-GlcNAc beta (CH2)(8)-CONH(CH2)(2)NHCO-TMR)), a fluorescently labeled model substrate for glycans found in mammals. In this study we have examined the binding affinities of the Salmonella chitinase by carbohydrate microarray screening and found that it binds to a range of compounds, including five that contain LacNAc structures. We have further examined the hydrolytic specificity of this enzyme and chitinases from Sodalis glossinidius and Polysphondylium pallidum, which are phylogenetically related to the Salmonella chitinase, as well as unrelated chitinases from Listeria monocytogenes using the fluorescently labeled substrate analogs LacdiNAc-TMR (GalNAc beta 1-4GlcNAc beta-TMR), LacNAc-TMR, and LacNAc beta 1-6LacNAc beta-TMR. We found that all chitinases examined hydrolyzed LacdiNAc from the TMR aglycone to various degrees, whereas they were less active toward LacNAc-TMR conjugates. LacdiNAc is found in the mammalian glycome and is a common motif in invertebrate glycans. This substrate specificity was evident for chitinases of different phylogenetic origins. Three of the chitinases also hydrolyzed the beta 1-6 bond in LacNAc beta 1-6LacNAc beta-TMR, an activity that is of potential importance in relation to mammalian glycans. The enzymatic affinities for these mammalian-like structures suggest additional functional roles of chitinases beyond chitin hydrolysis.

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