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(a) Abstract

1. Objectives

There are accumulating evidence that free, sialylated complex-type glycans can be accumulated in the cytosol of mammalian cells. However, how these glycans were generated or, once formed, catabolized remains largely unknown.

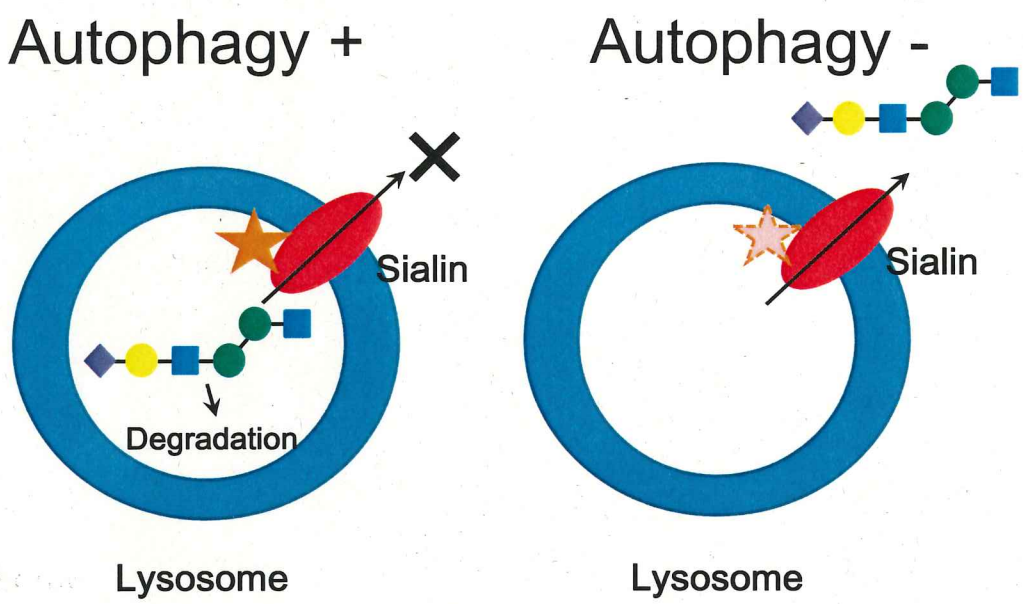
2. Methods

We utilized two distinct mammalian cell lines, *i.e.* human cancer-derived MKN45 cells and autophagy-defective mouse embryonic fibroblast cells (*Atg5*-/-), to analyze the formation/degradation mechanism of sialylated free glycans in the cytosol.

3. Results

In MKN45 cells, previously it was found that Neu2, a cytosolic sialidase, is involved in their degradation, and recently we also found a factor involved in the stabilization of Neu2 protein in the cytosol. Co-expression of this protein together with Neu2 resulted in efficient catabolism of sialyl free glycans. In *Atg*5-/- cells, Accumulation of these glycans was observed under non-starved conditions, suggesting that non-induced, basal autophagy is essential for their catabolism. Interestingly, once accumulated in the cytosol, sialyl glycans cannot be efficiently catabolized by resumption of the autophagic process, suggesting that functional autophagy is important for preventing sialyl oligosaccharides from accumulating in the cytosol.

4. Figures



Proposed mechanisms for the role of autophagy in catabolism of sialyl-fOSs. (Seino, *et al.* ***J. Biol. Chem.*** **288,** 26898-26907 (2013))
Left: in normal basal autophagy, the substrate specificity of sialin, a sialic acid transporter, was strictly maintained, possibly due to its modification or binding proteins (indicated by a *star*), for which the normal basal autophagy process is essential. As a result, sialyl-fOSs did not accumulate in the cytosol and instead properly catabolized in lysosomes.
Right: in the absence of functional autophagy, specific modifications or binding proteins were lost, and sialin lost strict substrate specificity; sialyl-fOSs were released into cytosol by the action of sialin.