Lepur A, Carlsson MC, Novak R, Dumić J, Nilsson UJ, Leffler H. (2012). Galectin-3 endocytosis by carbohydrate independent and dependent pathways in different macrophage like cell types. *Biochim Biophys Acta.* Jul;1820(7):804-18. Epub 2012 Mar 17.

BACKGROUND:

Galectin-3 (the Mac-2 antigen) is abundantly expressed in both macrophage like cells and certain non-macrophage cells. We have studied endocytosis of galectin-3 as one important step relevant for its function, and compared it between variants of a macrophage like cell line, and non-macrophage cells.

METHODS:

Endocytosis of galectin-3 was observed by fluorescence microscopy and measured by flow cytometry. The endocytosis mechanism was analysed using galectin-3 mutants, galectin-3 inhibitors and endocytic pathways inhibitors in the human leukaemia THP-1 cell line differentiated into naïve (M0), classical (M1) or alternatively activated (M2) macrophage like cells, and the non-macrophage cell lines HFL-1 fibroblasts and SKBR3 breast carcinoma.

RESULTS:

Galectin-3 endocytosis in non-macrophage cells and M2 cells was blocked by lactose and a potent galectin-3 inhibitor TD139, and also by the R186S mutation in the galectin-3 carbohydrate recognition domain (CRD). In M1 cells galectin-3 endocytosis could be inhibited only by chlorpromazine and by interference with the non-CRD N-terminal part of galectin-3. In all the cell types galectin-3 entered early endosomes within 5-10min, to be subsequently targeted mainly to non-degradative vesicles, where it remained even after 24h.

CONCLUSIONS:

Galectin-3 endocytosis in M1 cells is receptor mediated and carbohydrate independent, while in M2 cells it is CRD mediated, although the non-CRD galectin-3 domain is also involved. General significance The demonstration that galectin-3 endocytosis in M1 macrophages is carbohydrate independent and different from M2 macrophages and non-macrophage cells, suggests novel, immunologically significant interactions between phagocytic cells, galectin-3 and its ligands.