

P015 Regulation of hyaluronan binding to the lymphatic receptor lyve-1

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The hyaluronan (HA) receptor LYVE-1 (lymphatic endothelial vessel hyaluronan receptor-1) is expressed primarily on lymphatic endothelial cells (LECs) where it is implicated in both lymph node trafficking and HA clearance. Curiously, although both full-length and soluble recombinant forms of LYVE-1 display specific saturable binding to HA *in vitro*, the endogenous receptor in LEC appears to be functionally silenced. Here we show that silencing is achieved by terminal sialylation of LYVE-1 N- and O-linked glycan chains in a manner akin to that of the related inflammatory leukocyte HA receptor CD44. Using glycosylation defective *lec/ldl-D* CHO mutants, lectin binding analyses and enzymatic deglycosylation we provide information on the likely nature and linkage of the inhibitory sialic acid modification. In addition, we provide evidence that the inhibition is reversible insofar as neuraminidase treatment of LYVE-1 Fc unmasks HA binding and agents such as PMA (phorbol 12-myristate 13-acetate) that induce de-sialylation of LYVE-1 in primary human LEC and transfected 293T cells, can enhance both HA-binding and ectodomain shedding. Such properties suggest that HA-binding is tightly regulated *in vivo* and that shed rather than membrane-bound LYVE-1 may be the physiologically active form of the receptor.