## Characterizing the roles of endo-lysosomal proteins in regulating EGFR localization and function

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**Objective:** Epidermal growth factor receptor (EGFR) is one of the drivers of tumorigenesis in head and neck cancers (HNC). Localization of EGFR to the plasma membrane (PM) and signaling is dependent on the PM cholesterol. In a previous study, correlation analysis of EGFR expression in tumors in The Cancer Genome Atlas (TCGA) HNC database with the expression of 115 endo-lysosomal genes involved in cholesterol trafficking to the PM, and Kaplan-Meier plots for low and high expressers of the same genes identified 8 genes, expression of which either positively or negatively correlated with EGFR expression in HNC and survival duration of patients. Goal of this study was to determine if knock down of orthologs of those 8 genes in *C. elegans* could either promote or suppress the *let-23* (EGFR ortholog)-driven multivulva phenotype of worms expressing constitutively active *let-23*.

**Experimental Methods:** *vha-8*, *vha-16*, *vha-17, tsp-7*, *gana-1*, *vps-26, vps-35, sulp-8* and *clh-6* were knockdown in *let-23* mutant worms using RNAi. Thereafter, worms were anesthetized and imaged using a C2 confocal laser scanning microscope to quantify the multivulva phenotype.

**Results:** Significant enhanced multivulva phenotype was observed with *tsp-7*, *sulp-8, gana-1* and *vha-17* knockdown relative to the vector control, which corresponds to the previous finding that their human orthologs negatively correlate with EGFR expression. A trend in decrease of multivulva phenotype was observed *vps-26* and *vps-35* knockdown, whose human orthologs show positive correlation with EGFR expression. Interestingly, *clh-6* knockdown worms also showed a decrease in multivulva phenotype, while expression of its human ortholog shows a negative correlation with EGFR expression. All other knockdowns produced a lethal phenotype.

**Conclusion:** Our data suggest that modulation of endo-lysosomal proteins can alter the function of *let-23* in *C. elegans* worms and hence potentially could be used as therapeutic targets in inhibiting EGFR in human cancers.

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