Interactions between microbes and lysosome rich enterocytes impact protein absorption in the zebrafish gut

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Lysosome rich enterocytes (LREs) are a specialized population of intestinal cells that is critical for dietary protein absorption. Recent work from our lab has uncovered components of the endocytic machinery that allow for luminal protein uptake. Previous work has shown that the gut microbiome regulates metabolic processes such as fat absorption and that dietary fat content affects the microbiome. Therefore, we used custom diets and gnotobiology to test whether LRE protein uptake and degradation activity is regulated by microbes and if mutations in LRE endocytic machinery affect the gut microbiome. Using microscopy-based quantitative gavage assays, we observed that protein uptake and degradation activity is higher in germ free (GF) zebrafish compared to conventionalized (CV) larvae. We then performed HCR™ RNA-FISH and found that expression of key endocytic genes is upregulated in germ free larvae. Furthermore, we also found that mutations in LRE endocytic machinery cause significant perturbations in the gut microbiome. Moreover, using custom diets, we found that the dietary protein content strongly affects the microbiome and larval growth. Together, these results show that there are interactions between the gut microbiome, diet, and LREs that affect both protein absorption and organismal development.