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CHAPERONE-MEDIATED AUTOPHAGY IN FISH: A KEY FUNCTION IN THE MIDST OF A STRESSFUL ENVIRONMENT

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Chaperone-mediated Autophagy (CMA) is a protein degradation pathway that helps maintain cellular proteostasis in response to various stressors such as starvation, oxidative stress, and hypoxia. While CMA has been well described in mammals, it was only recently evidenced in fish. This discovery has provided new and exciting insights into the role of CMA in these species, which are facing increasingly stressful environmental events. In the present study, we first show that CMA-related factors are ubiquitously expressed during early development as well as in several adult tissues of rainbow trout (*Oncorhynchus mykiss*), a major aquaculture species. An in vitro CMA activity assay using isolated lysosomes confirmed that rainbow trout also exhibits CMA activity, which increases 21-fold during nutrient deprivation, a known CMA inducer. To understand the physiological role of CMA in trout, we generated a knock-out (KO) line lacking a key CMA rate-limiting gene, the lysosomal-associated membrane protein 2a (lamp2a), using CRISPR-Cas9 genome editing. Our findings showed that the deficient fish experienced significant disruptions in both carbohydrate and fat metabolisms. In addition, key enzymes and components of pathways involved in the defense against oxidative stress were upregulated. Taken together, these findings show that CMA is a critical pathway that shapes a distinct part of the proteome related to major metabolic pathways and plays a pivotal role in protecting against environmental threats by maintaining cellular homeostasis.