Mechanisms and regulation of Na^+ uptake by zebrafish (*Danio rerio*) in acidic water

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Unlike the majority of freshwater fish investigated to date, zebrafish*, Danio rerio*, markedly increase the Na^+ uptake when exposed to extremely acidic (pH 4.0) water. The goal of the present study was to identify Na^+ transporters involved in Na^+ uptake in acidic water and to provide insight into the regulatory mechanism underlying its stimulation. Pharmacological manipulation indicated that both Na^+/H^+ exchanger (NHE) and H^+-ATPase are required. Experimentally limiting ammonia excretion by exposing fish to high external ammonia or by increasing water buffer capacity decreased Na^+ uptake. Furthermore, translational knockdown of the apical ammonia-conducting channel, Rhcg1, prevented the inhibition of Na^+ uptake by pharmacological blockade of NHE, suggesting the critical importance of Rhcg1 in facilitating the function of NHE. Given the well-known regulation of NHE via cortisol and the likelihood of acid water exposure triggering a stress response, we tested whether cortisol is involved in stimulating Na^+ uptake in acidic water. Pharmacologically blocking or activating glucocorticoid (GR) and mineralocorticoid receptors suggested a GR-mediated Na^+ uptake mechanism in zebrafish. Furthermore, acid-exposing the zebrafish pre-treated with a GR-inhibitor significantly reduced Na^+ uptake. These observations suggest the potential hormonal regulation by cortisol mediated by GR of Na^+ uptake in zebrafish exposed to acidic water.