The regulatory redundancy of Na^+ absorption in zebrafish

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For maintaining the internal Na^+ homeostasis, freshwater fish have to actively absorb Na^+ through skin/gill ionocytes from environment. In zebrafish, three distinct subtypes of ionocytes, Na^+-K^+-ATPase rich cells, H^+-ATPase rich (HR) cells and Na^+-Cl^- cotranspoter (NCC) expressing cells, were recently identiifed. HR cells, apically expressing Na^+/H^+ exchangers, are the main type of ioncoytes for Na^+ absorption function while NCC cells play a minor role in Na^+ uptake. The present study aimed to explore the physiological synergy of HR cells and NCC cells on Na^+ absorption mechanism.

The differentiation of HR cell is regulated by the homologous of *Drosophila glial cell missing* transcription factor, *gcm2*. Knock-down the expression of GCM2 caused complete loss of HR cells; however, both Na^+ influx and NCC cell number were increased in the *gcm2* morphants. Metolazone, a specific inhibitor of NCC, impaired Na^+ influx in zebrafish, while knocking down NCC expression caused an increase of HR cell number that resulted in augments in both Na^+ influx and Na^+ content. These results provide the evidence that HR cells and NCC cells have functional redundancy in Na^+ absorption, and suggest this functional redundancy as a critical strategy for freshwater fish to cope with ion-deficient environments.