

Abstract

The Magadi tilapia (*Alcolapia grahami*) is a cichlid fish that inhabits one of the Earth's most extreme aquatic environments, with high pH (~10), salinity (~60 % of seawater), high temperatures (~40 C), and fluctuating oxygen regimes. The Magadi tilapia evolved several unique behavioral, physiological, and anatomical adaptations, some of which are constituents and thus retained in freshwater conditions. We conducted a transcriptomic analysis on *A. grahami* to study the evolutionary basis of tolerance to multiple stressors. To identify the adaptive regulatory changes associated with stress responses, we massively sequenced gill transcriptomes (RNAseq) from wild and freshwater-acclimated specimens of *A. grahami*. As a control, corresponding transcriptome data from *Oreochromis leucostictus*, a closely related freshwater species, were generated. We found expression differences in a large number of genes with known functions related to osmoregulation, energy metabolism, ion transport, and chemical detoxification. Over-representation of metabolism-related gene ontology terms in wild individuals compared to laboratory-acclimated specimens suggested that freshwater conditions greatly decrease the metabolic requirements of this species. Twenty-five genes with diverse physiological functions related to responses to water stress showed signs of divergent natural selection between the Magadi tilapia and its freshwater relative, which shared a most recent common ancestor only about four million years ago. The complete set of genes responsible for urea excretion was identified in the gill transcriptome of *A. grahami*, making it the only fish species to have a functional ornithine-urea cycle pathway in the gills—a major innovation for increasing nitrogenous waste efficiency.