

Genomic analysis of glutathione biosynthesis and metabolism in the invertebrate chordate *Ciona intestinalis*
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The thiol-containing tripeptide glutathione (GSH) provides the most abundant redox buffer in eukaryotic cells. Glutathione homeostasis reflects a complex interplay of synthesis, transport, storage, oxidation/reduction, further metabolism, and catabolism. To identify molecular mechanisms that coordinate these poorly understood processes, we are using a comparative genomic approach focused on *Ciona intestinalis*. Adult animals are sessile filter feeders and routinely encounter natural marine toxins chemically similar to known inducers of human detoxification genes. We hypothesize that functional, noncoding elements in the *Ciona* genome, which regulate glutathione homeostasis *that are conserved* with higher vertebrates may be useful for the identification of novel transcriptional networks underlying genetic susceptibility to environmentally triggered diseases. Initial efforts to annotate genes contributing to GSH homeostasis have identified *Ciona* homologs of *GCLC*, *GCLM*, *GSS*, *GGT*, the dipeptidases (*ANPEP*, *DPEP1*, *LAP3*), *GPX1*, *GSR*, *GSTA1*, *GSTM1*, *GSTP1*, *GLRX*, *xCT*, *OATP1B1*, and *MRP2* and known regulators including *Nrf2*, *KEAP1*, small MAF, *NFkB*, AP-1, *AHR*, *FXR*, *PXR*, *RXR*, and *VDR*. In addition, RT-PCR data demonstrate constitutive expression of *GCLC*, *GCLM*, and *GSTM1* in the branchial basket, GI tract and heart as well as upregulation of *GCLC* and *GCLM* by the prototypical antioxidant TBHQ in these tissues.