



Supplementary Figure 1. Simplified diagram of the cAMP signaling pathway showing a potential scenario for the activation of PKA signaling pathway caused by the nonsense mutation in *MTH1* present in the M1 adaptive strain. *Mth1* normally represses *HXT* transcription via *Rgt1*. The log base 2 gene expression data for the components of the signaling pathway are shown below or next to each gene. The tables labeled “induced” or “repressed” are significantly perturbed genes (see Methods) in our dataset that are either induced or repressed in the activated *Gpa2* and *Ras* experiments in Wang et al. The genes whose expression was significantly induced in M1 are highlighted in red, while significantly repressed genes are highlighted in green. Only one gene in the “induced” and two genes in the “repressed” set differ between our data and Wang et al data. The consistency between the datasets suggests that the PKA signaling pathway is increased in M1 relative to the original parent.