Title:	Yeast glutaredoxin, GRX4, functions as a glutathione S-transferase required for red ade pigment formation in Saccharomyces cerevisiae
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Abstract:	The adenine biosynthetic mutants ade1 and ade2 of Saccharomyces cerevisiae accumulate a characteristic red pigment in their vacuoles under adenine limiting conditions. This red pigmentation phenotype, widely used in a variety of genetic screens and assays, is the end product of a glutathione-mediated detoxification pathway, where the glutathione conjugates are transported into the vacuole. The glutathione conjugation step, however, has still remained unsolved. We show here, following a detailed analysis of all the members of the thioredoxin- fold superfamily, the involvement of the monothiol glutaredoxin GRX4 as essential for pigmentation. GRX4 plays multiple roles in the cell, and we show that the role in ade pigmentation does not derive from its regulatory role of the iron transcription factor, Aft1p, but a newly identified GST activity of the protein that we could demonstrate using purified Grx4p. Further, we demonstrate that the GRX domain of GRX4 and its active site cysteine C171 is critical for this activity. The findings thus solve a decades old enigma on a critical step in the formation of this red pigmentation
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