

COVER SHEET

TITLE: Pleiotropic Drug Resistance Activation via Over Expression  
of Zv01

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ABSTRACT

**Pleiotropic Drug Resistance Activation Via Over Expression of Zuo1**

Pleiotropic drug resistance (PDR) is the resistance to multiple drugs that occurs by upregulating gene expression of ABC (ATP-binding cassette) transporters that transport drug out of the cell. Thakur et al. (2008) demonstrated that in *Saccharomyces cerevisiae* the nuclear transcription factor Pdr1 is bound directly by drugs to induce expression of these drug efflux pumps. In addition, two chaperone proteins that function in the folding of nascent polypeptide chains have also been found to induce the PDR pathway when free from ribosomes. Zuo1 and Ssz1 form a heterodimer and are tethered to the ribosome via Zuo1's ribosome-binding domain. Ssz1 induces PDR when expressed at levels in which some Ssz1 is free from ribosomes (Hallstrom *et al.*, 1998). Zuo1 lacking its charged ribosome binding domain (Zuo1 $\Delta$ chg) also upregulates the pathway in a Pdr1-dependent manner (Eisenman 2004). Since Zuo1 and Ssz1 are expressed at similar levels and form a heterodimer, we investigated whether over expression of Zuo1 could also induce PDR and if ribosome dissociation is sufficient for this induction. Here we show that over expression of Zuo1 does not induce PDR even though Zuo1 is free from ribosomes at levels equal to or higher than that of Zuo1 $\Delta$ chg. Our results suggest that ribosome dissociation, though it may be a requirement, is not sufficient for induction of PDR by Zuo1.

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