# Study on yeast response to vanillin, a fermentation inhibitor derived from lignocellulosic biomass

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## Abstract

Vanillin is a phenolic aldehyde compound generated during the saccharification pretreatment of the lignocellulosic biomass in bioethanol production. It has been reported that vanillin inhibits yeast growth, represses translation and induces the formation of ribonucleoprotein granules such as P-bodies and stress granules in *Saccharomyces cerevisisae.* I herein demonstrated that vanillin causes oxidative stress and induces mitochondrial fragmentation in yeast cells, providing some new information regarding the effects of vanillin on yeast. Additionally, I found that the null mutant of glucose-6-phosphate dehydrogenase (G6PDH), which catalyzes the rate-limiting NADPH-producing step in the pentose phosphate pathway (PPP), was more susceptible to vanillin than the wild-type, suggesting the importance of G6PDH and PPP in vanillin tolerance. It has been known that vanillin can be reduced to its less toxic form, vanillyl alcohol, by the yeast NADPH-dependent medium chain alcohol dehydrogenases, Adh6 and Adh7 *in vitro*. In this study, I verified the roles of these proteins in vanillin tolerance *in vivo*. I also showed that although both the *ADH6* and *ADH7* genes were transcriptionally upregulated, the protein levels of Adh7 but not Adh6 were significantly increased in the presence of high concentration of vanillin, indicating that the *ADH7* mRNA was preferentially translated under severe vanillin stress. In addition to the *ADH7* gene, we found that the expression of *VIE1* gene, coding an unknown protein, was also significantly induced upon vanillin treatment. Both the *ADH7* and *VIE1* promoter can drive the expression of non-native genes under severe vanillin stress despite the overall translation repression, suggesting that these promoters are useful to overexpress genes in bioethanol production. Importantly, the *VIE1* promoter also enabled the increased expression of genes in the presence of furfural and 2-hydroxymethylfurfural, other fermentation inhibitors derived from lignocellulosic biomass. Therefore, the *VIE1* promoter would be more practical in modification of gene expression in order to improve the efficiency of ethanol production from lignocellulosic biomass.