P024 CinD (YtjD) of *Lactococcus lactis* is a copper-induced nitroreductase involved in the control of protein nitrosylation

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Lactococcus lactis IL1403 is a lactic acid bacterium widely used for the manufacture of food and dairy products. Among the different stresses this microorganism can be exposed to during industrial processes, copper challenge is common when fermentation is performed in copper vats. Although copper is an essential trace element, it is toxic when present in excess. To tightly control cytoplasmic copper levels, all living organisms have evolved homeostatic mechanisms. In *L. lactis*, eleven genes are under the control of the copper-inducible CopR repressor. The CopR regulon encompasses the CopR regulator, two copper ATPases, a copper chaperone, and seven additional genes of unknown function. We here addressed the function of one of these genes, *ytjD,* which we renamed *cinD* (copper-induced nitroreductase). Copper, cadmium and silver induced *cinD in vivo*, as shown by real time quantitative PCR. CinD was overexpressed, purified and was shown to encode a flavoprotein with nitroreductase activity. It catalyzed the reduction of nitrosylated glutathione and tyrosine *in vitro*, using NADH or NADPH as a reductant. When the *cinD* gene was inactivated, *L. lactis* became sensitive to S-nitrosoglutathione-induced nitrosative stress. Inactivation of *cinD* also increased intracellular levels of S-nitrosylated proteins. These findings suggest that the induction of CinD by copper represents a novel defense mechanism against nitrosative stress and indicate a connection between metal stress and nitrosative stress.