Avery, S. V., N. G. Howlett, and S. Radice. 1996. Copper toxicity towards Saccharomyces cerevisiae: dependence on plasma membrane fatty acid composition. *Appl.Environ.Microbiol.* 62:3960-3966.

Abstract: One major mechanism of copper toxicity towards microorganisms is disruption of plasma membrane integrity. In this study, the influence of plasma membrane fatty acid composition on the susceptibility of Saccharomyces cerevisiae to Cu2+ toxicity was investigated. Microbial fatty acid composition is highly variable, depending on both intrinsic and environmental factors. Manipulation was achieved in this study by growth in fatty acid-supplemented medium. Whereas cells grown under standard conditions contained only saturated and monounsaturated fatty acids, considerable incorporation of the diunsaturated fatty acid linoleate (18:2) (to more than 65% of the total fatty acids) was observed in both whole-cell homogenates and plasma membrane-enriched fractions from cells grown in linoleate-supplemented medium. Linoleate enrichment had no discernible effect on the growth of S. cerevisiae. However, linoleate-enriched cells were markedly more susceptible to copper-induced plasma membrane permeabilization. Thus, after addition of Cu(NO3)2, rates of cellular K+ release (loss of membrane integrity) were at least twofold higher from linoleate-supplemented cells than from unsupplemented cells; this difference increased with reductions in the Cu2+ concentration supplied. Levels of cellular Cu accumulation were also higher in linoleate-supplemented cells. These results were correlated with a very marked dependence of whole-cell Cu2+ toxicity on cellular fatty acid unsaturation. For example, within 10 min of exposure to 5 microM Cu2+, only 3% of linoleate-enriched cells remained viable (capable of colony formation). In contrast, 100% viability was maintained in cells previously grown in the absence of a fatty acid supplement. Cells displaying intermediate levels of linoleate incorporation showed intermediate Cu2+ sensitivity, while cells enriched with the triunsaturated fatty acid linolenate (18:3) were most sensitive to Cu2+. These results demonstrate for the first time that changes in cellular and plasma membrane fatty acid compositions can dramatically alter microbial sensitivity to copper.