Yarrowia lipolytica adaptation to oxidative stress induced by increased air pressure

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Microorganisms in industrial scale reactors rarely encounter the physiologically optimum environment, and instead are frequently exposed to a variety of changes in their environment within the bioreactor. Cells in bioreactors are often exposed to O_2 partial pressures higher than 210 mbar (corresponding to air at 1 bar). In many cases, increased O_2 partial pressure (higher than approximately 1 bar) is toxic to aerobic cultures and inhibits microbial growth and product formation. During the reduction of molecular oxygen to water through acceptance of four electrons, reactive oxygen species (ROS) such as superoxide anion radical (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl radical (HO·) are generated. ROS can damage proteins by causing modifications of amino acid side chains, formation of cross-links between proteins and fragmentation of the polypeptide backbone. In addition, ROS can modify the bases and sugars in DNA, leading to DNA chain breaks, and cause lipid peroxidation in cell membranes.

Stress responses are designated as molecular mechanisms induced in the cells upon exposure to stress conditions. In the case of yeasts, stress conditions are broadly defined as those environmental factors that cause a reduction in growth rate and induction of hyphae formation. Stress responses aim to protect cells against detrimental effects of stress factors and repair damages that are already done. Antioxidant enzymes, such as catalase and superoxide dismutase (SOD), constitute the primary defenses of the cells because they are responsible for transforming these reactive oxygen species into nonreactive ones.

To examine eventual effects of oxygen toxicity on yeast cells, with the increase in oxygen partial pressure, the changes of intracellular antioxidant enzyme activities under different air pressures were determined for batch cultures of *Yarrowia lipolytica*. An increase of the SOD-specific activity at 6 bar (1.26 bar of oxygen partial pressure) of 53.4-fold was obtained compared with the experiments under 1 bar. However, no inhibition of cellular growth was observed and a 3.4-fold improvement in specific cellular growth rate under increased pressure was obtained compared to the growth at atmospheric pressure. This shows the ability of *Y. lipolytica* cells to respond to the increase of ROS formation caused by hyperoxygenation.

Thus increased pressure can be used to enhance oxygenation in bioprocesses involving this yeast as is the case of lipase production, with the concomitant effect of improving lipase productivity. An increase of 5 bar of total air pressure led to a 3.7-fold increase of lipase production by *Y. lipolytica*.