Oxidative stress leads to D enrichment in microbial lipids

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Lipid D/H ratios are becoming useful environmental proxies for climate, environment, and metabolism. However, we are still trying to understand the biochemical effects that underlie the observed environmental variations. Here, we show how oxidative stress modulates the D/H ratios of microbial lipids. Oxidative stress is an unavoidable risk for organisms living in an aerobic environment. Highly toxic reactive oxygen species (ROS) are formed as a byproduct of aerobic respiration. To control ROS emission and counteract oxidative stress, organisms have developed strategies to maintain ROS at nontoxic levels. A first line of defense is the dismutation of superoxide ($O^{\cdot-}_2$) to H_2O_2 by superoxide dismutase. The resulting H_2O_2 is then reduced to water by a range of antioxidant enzymes and molecules including the important glutathione peroxidase and peroxiredoxin system that rely on the reducing power of NADPH. Thus, NADPH has to be regenerated constantly to maintain the antioxidant defense system and this also has to be considerably enhanced when oxidative stress is encountered.

In this study, we cultured a diverse set of aerobic heterotrophic bacteria on glucose and artificially induced different levels of oxidative stress. By analyzing their lipid δD values, we discovered significant more D-enriched lipids in cultures under oxidative stress than in the cultures without. In all investigated species, strong correlations were observed between the level of induced stress and the D/H fractionation between lipid and growth water. Quantitative metabolic flux analysis further revealed that oxidative stress induced flux-changes through NADPH-generating reactions, as well as the resulting overproduction of NADPH, were highly correlated with D/H fractionation.

Our results substantiate the hypothesis that differences in the kinetic isotope effects associated with different NADPH-generating dehydrogenases in central carbon metabolism and transhydrogenases are a key biochemical control on lipid δD. In addition, NADPH-consuming antioxidant enzymes that exhibit normal kinetic isotope effects seem to play an important role as well. Our results contribute to a better understanding of the biochemical mechanisms controlling D/H fractionation and may have numerous applications, including in marine phytoplankton, where we could learn more about how they are impacted by oxidative stress.