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ИНАКТИВАЦИЯ Ras1 В ДЕЛЯЩИХСЯ ДРОЖЖАХ УСИЛИВАЕТ ОТВЕТ НА ОКИСЛИТЕЛЬНЫЙ СТРЕСС, ИНДУЦИРУЕМЫЙ *трет*-БУТИЛГИДРОПЕРОКСИДОМ (tBHP)[1]

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Малые GTPазы Ras функционируют как молекулярные переключатели, регулирующие клеточный гомеостаз. Ras-зависимые сигнальные пути регулируют такие важные процессы, как прохождение клеточного цикла, апоптоз, миграция и старение клеток. Нарушение сигнального пути Ras связано с несколькими патологическими состояниями. Установлено, что белки Ras могут участвовать в регуляции окислительно-восстановительных сигнальных путей, включая влияние на уровень активных форм кислорода, создающих условия для канцерогенеза. Предполагается, что активные формы кислорода и разобщение митохондриальных функций являются главными факторами, воздействующими на физиологические процессы в клетках и вовлеченными в разные патологии. В настоящей работе изучена роль Ras1, *трет*-бутилгидропероксида (tBHP) и антимицина А в ответе клеток *Schizosaccharomyces pombe* на окислительный стресс. Обнаружено снижение выживаемости, более высокий уровень активных форм кислорода и нарушение функций митохондрий в клетках *ras1*Δ и в клетках дикого типа, обработанных tBHP, а также ингибитором дыхательной цепи антимицином А. Более того, эти эффекты сильнее выражены в обработанных антимицином или tBHP клетках *ras1*Δ. Показано также, что Ras1 регулирует экспрессию и активность таких антиоксидантных ферментов, как глутатионпероксидаза (GSH-Px), глутатион-S-трансфераза (GST) и каталаза. Эти результаты свидетельствуют о потенциальной роли Ras1 *S. pombe* в смягчении ответа на окислительный стресс.

Ключевые слова: *Schizosaccharomyces pombe*, Ras1, активные формы кислорода, ROS, *трет*-бутилгидропероксид tBHP, окислительный стресс

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Inactivation of Ras1 in Fission Yeast Aggravates the Oxidative Stress Response Induced by Tert Butyl Hydroperoxide (tBHP)

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Ras proteins are small GTPases and function as molecular switches to regulate cellular homeostasis. Ras-dependent signalling pathways regulate several essential processes such as cell cycle progression, growth, migration, apoptosis, and senescence. The dysregulation of Ras signaling pathway has been linked to several pathological outcomes. A potential role of RAS in regulating the redox signalling pathway has been established that includes the manipulation of ROS levels to provide a redox milieu that might be conducive to carcinogenesis. Reactive oxygen species (ROS) and mitochondrial impairment have been proposed as major factors affecting the physiology of cells and implicated in several pathologies. The present study was conducted to evaluate the role of Ras1, tert Butyl hydroperoxide (tBHP), and antimycin A in oxidative stress response in *Schizosaccharomyces pombe* cells**.** We observed decreased cell survival, higher levels of ROS, and mitochondrial dysfunctionality in *ras1*Δ cells and tBHP as well as respiratory inhibitor, antimycin A treated wild type cells. Furthermore, these defects were more profound in *ras1*Δ cells treated with tBHP or antimycin A. Additionally, Ras1 also has been shown to regulate the expression and activity of several antioxidant enzymes like glutathione peroxidase (GSH-Px), glutathione-S-transferase (GST), and catalase. Together, these results suggest the potential role of *S. pombe* Ras1 in mitigating oxidative stress response.

Keywords: *Schizosaccharomyces pombe*, Ras1, ROS, tBHP, oxidative stress