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Masters Defense Announcement

"ROLES OF PROTEIN KINASE A, STRESS-RESPONSIVE MAP KINASES, AND TARGET OF RAPAMYCIN (TOR) IN ROTENONE AND PARAQAUT RESISTANCE IN SCHIZOSACCHAROMYCES POMBE"

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2:00 PM Nott Hall RM 151

Some pesticides and herbicides have been extensively used without a thorough investigation of the potential harm they may have on those who are exposed to them. Rotenone is a widely used pesticide that has been shown to induce Parkinson's disease like symptoms in rats and death of dopaminergic neurons in culture. Paraquat similarly has been implicated in the manifestation of Parkinson's disease like symptoms. Both rotenone and paraquat have been shown to have negative effects via the inhibition of complex I of the mitochondria and production of oxidative stress. However, in mouse embryos lacking functional complex I activity neuron death still occurs following rotenone or paraquat treatment. In this study we use the model organism Schizosaccharomyces pombe, which lacks complex I, to further explore complex I independent targets of both rotenone and paraquat. Our lab had previously discovered that rotenone results in the drastic reduction of growth in cells lacking ERK-type MAP kinase, pmk1Δ and cells lacking protein kinase A (PKA) (pka1Δ). However loss of the p38 MAP kinase Spc1 (spc1Δ) leads to resistance to rotenone. Additionally, loss of Spc1 in a pka1Δ background rescued the previously observed hypersensitivity. The elimination of Spc1 in a pka1Δ background improved the clearance of reactive oxygen species (ROS), while loss of Spc1 in a pmk1Δ mutant background results in less ROS without rescue of growth defects. However, elimination of Spc1 in a pmk1Δ background does not produce rescue. Autophagy is a process of degradation that typically is responsible for the degradation of organelles that do not function properly or have been damaged. The mammalian target of rapamycin (mTOR) has been implicated as a negative regulator of autophagy. Interestingly, TOR activity was perturbed following the treatment of cells with rotenone. Additionally, we observed an increase in TOR-dependent phosphorylation in pka1Δ cells. Also, rotenone or paraquat treatment of cells caused a decrease in TOR dependent phosphorylation. Since TOR and PKA have both been implicated in the control of the process of autophagy and more recently p38 has been implicated in regulation of autophagy, we sought to investigate the relationship between these three signaling pathways. This study collectively implicates multiple signaling pathways in the resistance to oxidative stress-inducing agents such as rotenone and paraquat.