Study of the Role of RTG-dependent Retrograde Signaling in Mitochondrial Activity Maintenance of *S. cerevisiae*

Nicole Quesada Torelli[1], Fernanda M. da Cunha[2], Alicia J. Kowaltowski[1]

[1] Departamento de Bioquímica, Instituto de Química, Universidade de São Paulo, São Paulo, Brasil, [2] Escola de Artes, Ciências e Humanidades, Universidade de São Paulo, São Paulo, Brasil

Introduction: RTG-dependent retrograde signaling is a communication pathway between the mitochondrion and the nucleus. Through a mechanism still being elucidated, the protein complex Rtg1/3p is translocated from the cytoplasm to the nucleus, where it acts as a transcription factor. The Msk1/Bmh1/2p complex is a negative regulator of retrograde signaling and is inactivated by Rtg2p. While many studies have been focusing on which genes are activated by this pathway, little is known about its implications in the metabolism. **Material and methods:** WT, *rtg*Δ cells were grown in YPD medium and assayed for respiration rates (oxygraph), citrate synthase activity (CoA-SH reaction with DNTB), membrane potential (Safranin-O fluorescence), hydrogen peroxide production (Amplex Red fluorescence) and viability in SD medium (spot test). **Results and Discussion:** After 7 days of growth in fermentative medium, WT cells present lower respiratory rates than *rtg1Δ* and *rtg2Δ* cells, indicating that cells lacking the retrograde signaling pathway are unable to react to a substrate shift. We confirmed higher mitochondrial activity in *rtgΔ* cells by measuring citrate synthase activity. By using isolated mitochondria, we identified that not only *rtgΔ* cells have more mitochondria than WT, but also each mitochondrion has a higher respiratory rate, though similar membrane potentials. Measurements of hydrogen peroxide production show that WT cells produce more oxidants, indicating that the signaling pathway is not acting to remove defective mitochondria. Life span assays of cells grown in minimum medium presented no differences between WT and *rtg1Δ* cells, showing that the pathway is not stimulating mitophagy as a nutrient source. **Conclusion:** RTG-dependent retrograde signaling seems to be important for mitochondrial mass and activity adaptation to substrate shift. We believe that mitophagy promoted by retrograde signaling, and even higher hydrogen peroxide production, may be important to extend chronological life span.

Keywords: RTG, retrograde signaling, mitochondria
Financial support: CNPq, FAPESP, CEPID Redoxoma