

# About OMICS Group

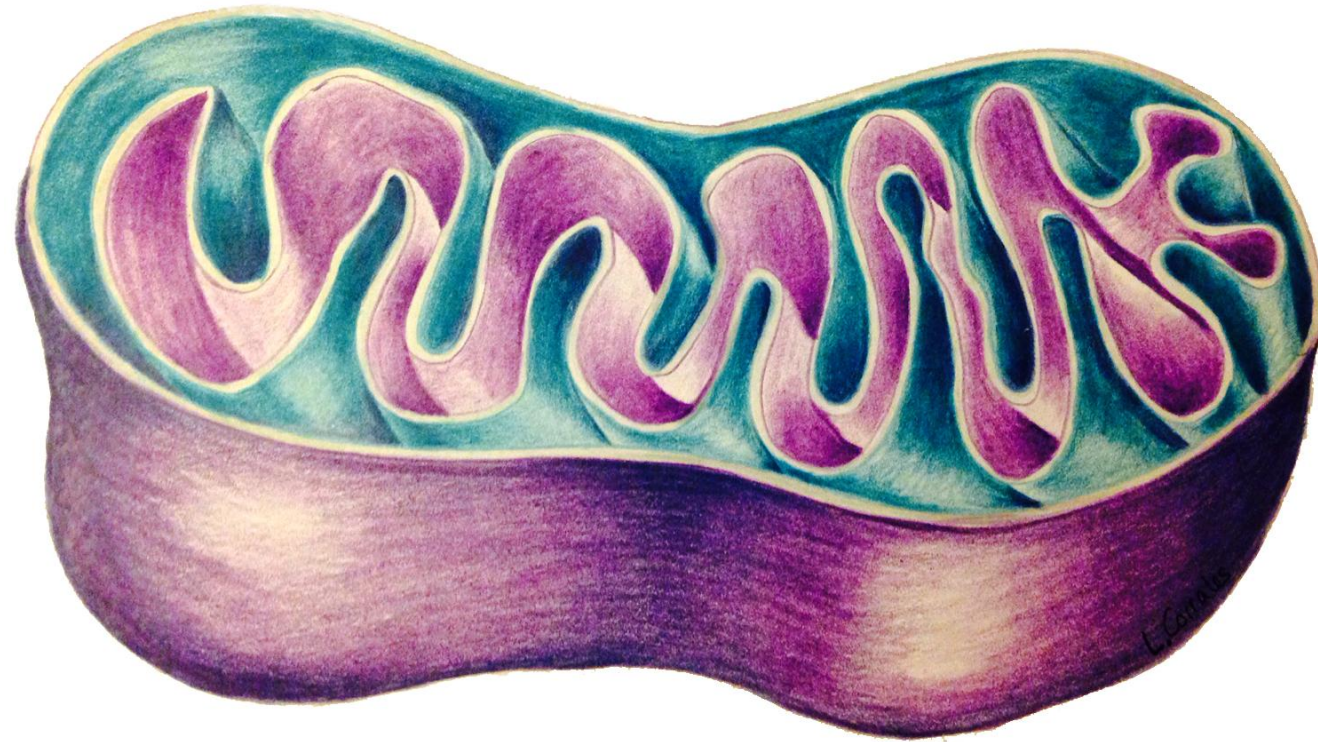
OMICS Group International is an amalgamation of [Open Access publications](#) and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 500 online open access [scholarly journals](#) in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS International also organizes 500 [International conferences](#) annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

# About OMICS International Conferences

OMICS International is a pioneer and leading science event organizer, which publishes around 500 open access journals and conducts over 300 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS International has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

# Dissecting the distinct functions of mitochondria

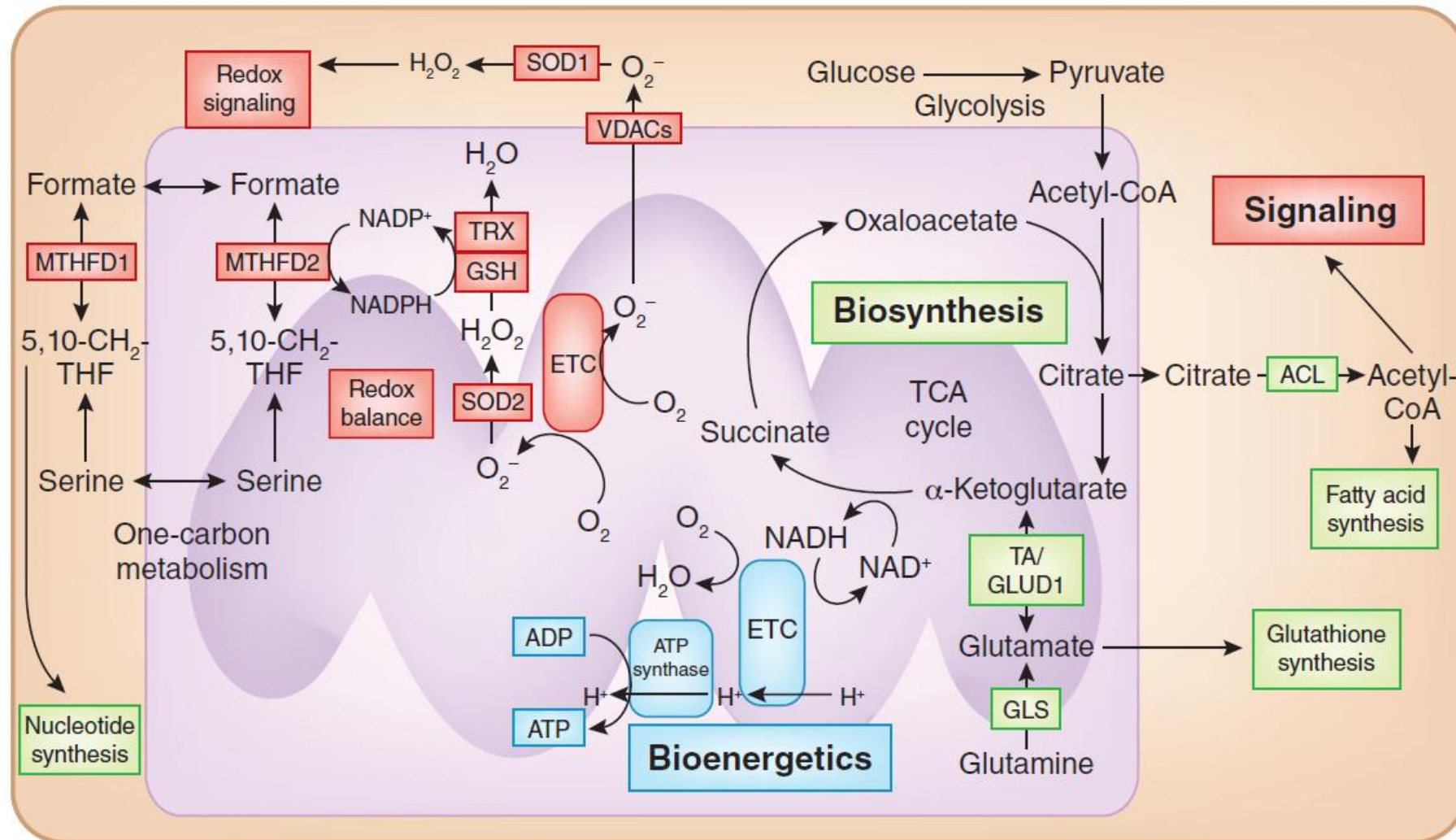


**4th International Conference and Exhibition on Metabolomics & Systems Biology**

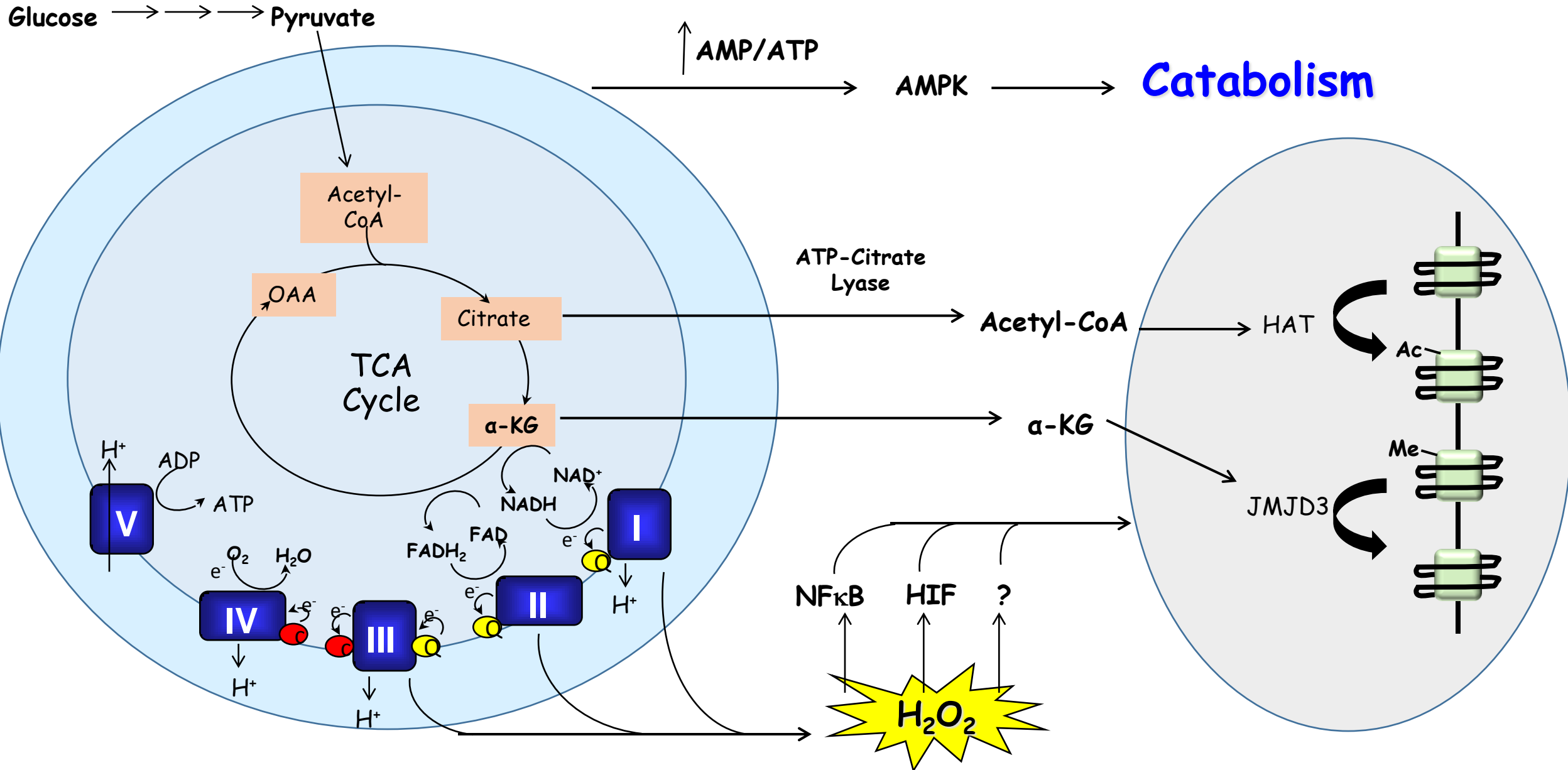
**April 29, 2015 – Philadelphia, USA**

**Inmaculada Martinez-Reyes – Dr. Navdeep Chandel Lab – Northwestern University, Chicago**

# Mitochondrial metabolism is necessary for tumorigenesis.

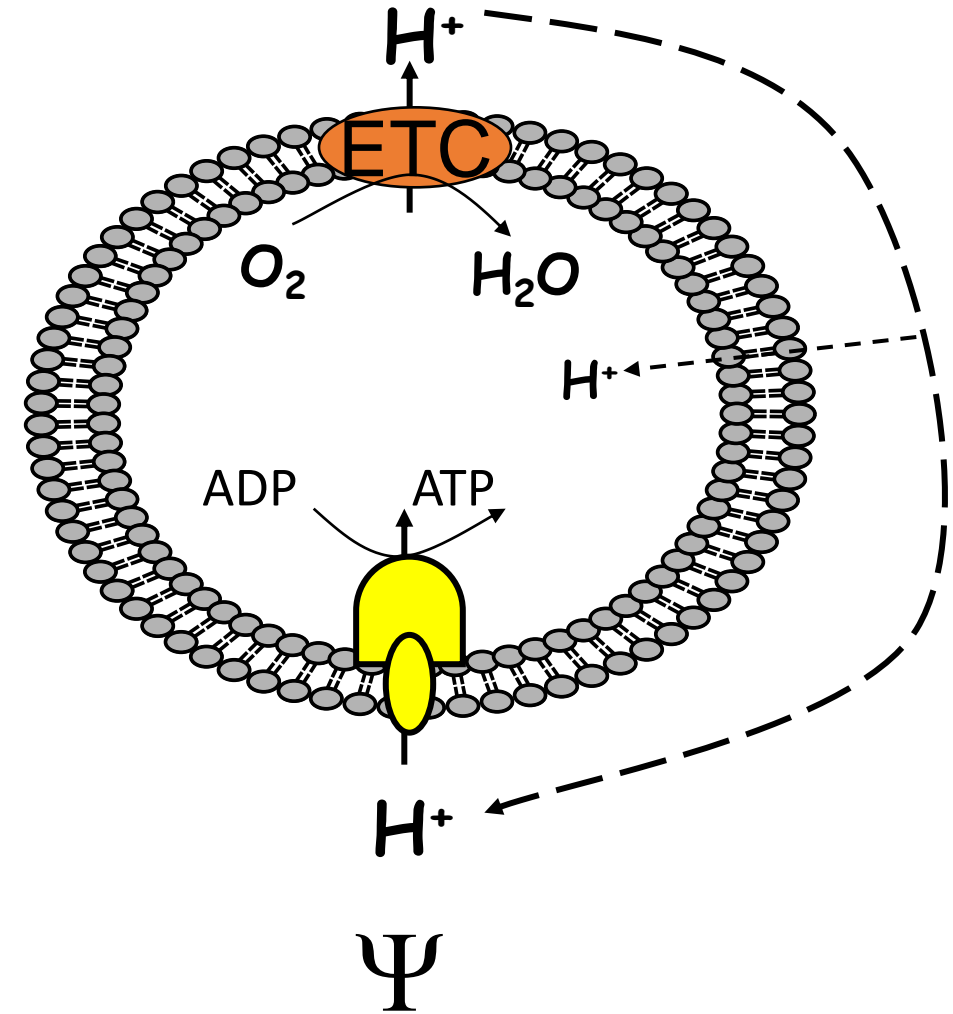
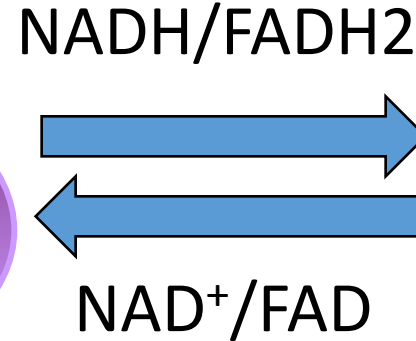
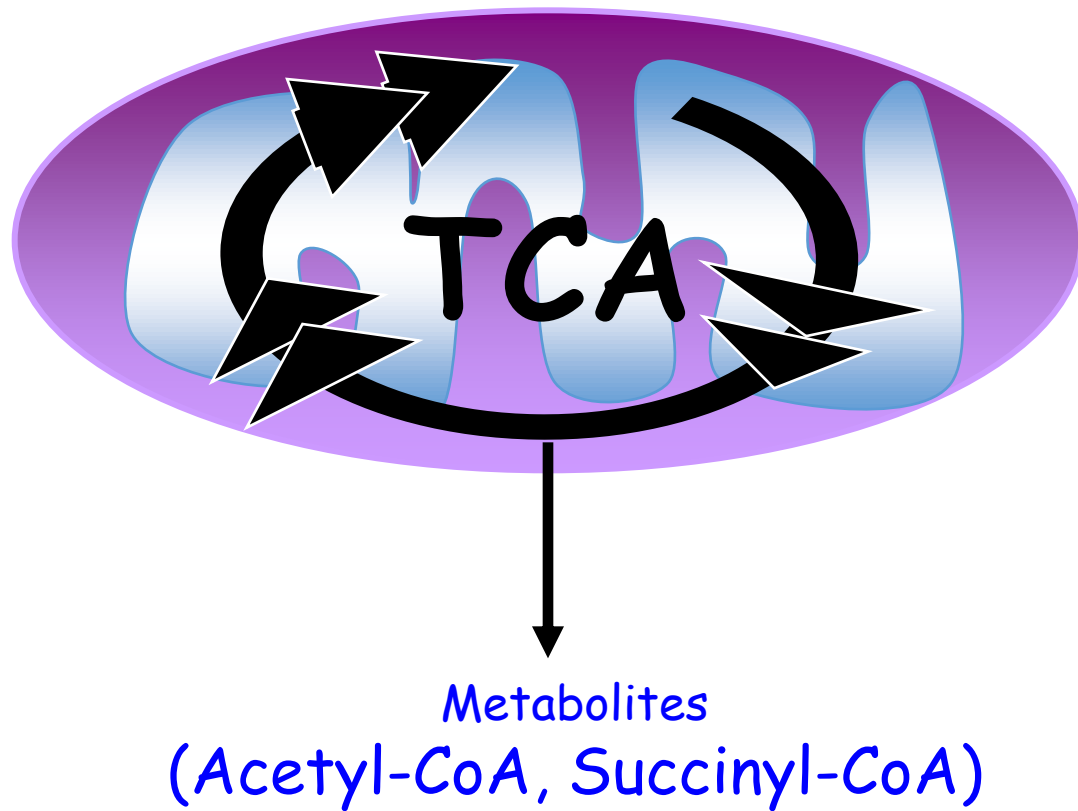


# Mitochondria as signaling organelles.



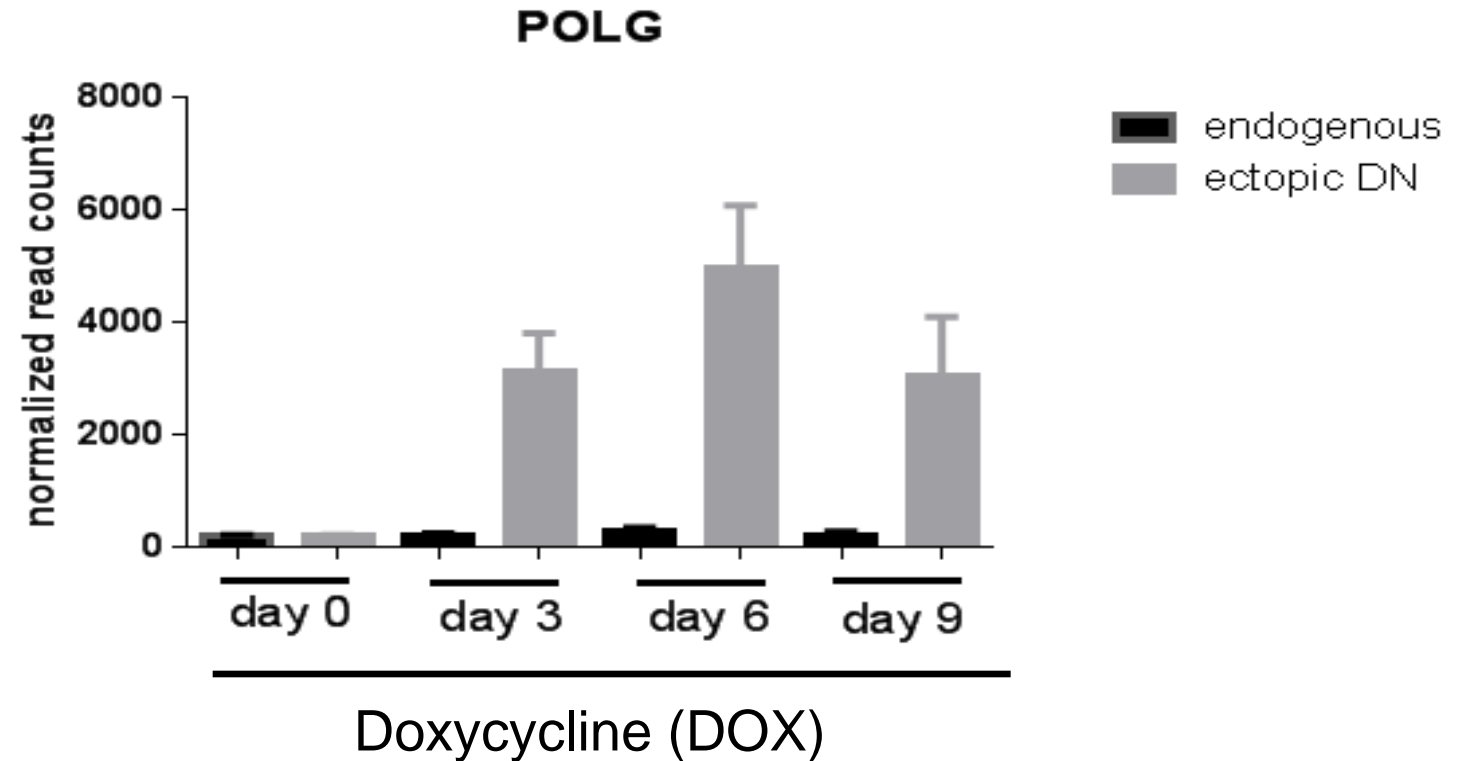
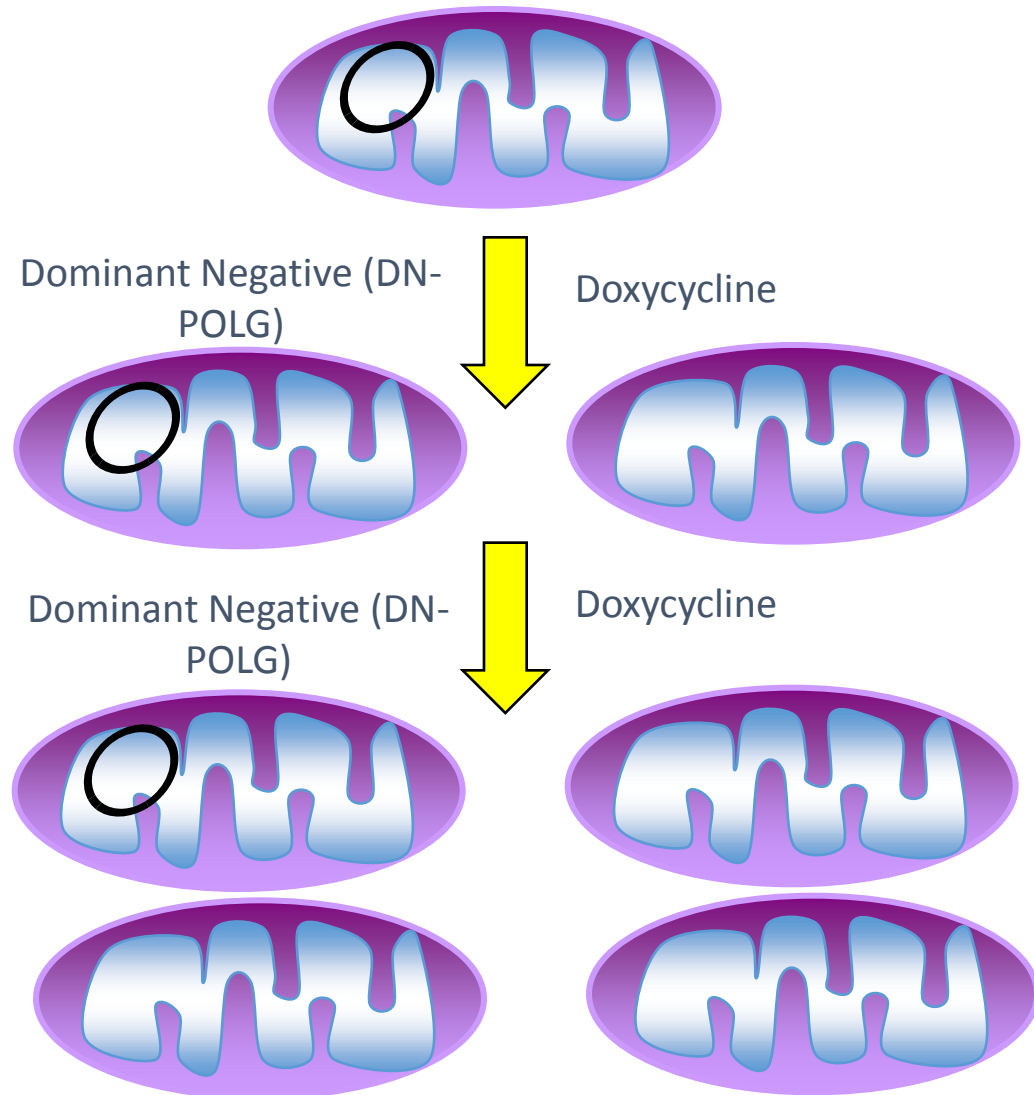
What functions of mitochondrial metabolism are necessary for cell proliferation and epigenetics?

# Two functions of mitochondria: TCA cycle metabolites and membrane potential.



(ATP, ROS, Iron-sulfur clusters)

# DNA polymerase gamma (POLG) is necessary for mitochondrial DNA (mtDNA) replication.





# Dominant negative PLOG depletes mtDNA encoded RNA transcripts.

## WT PLOG + DOX

Day 9

RNAseq normalized reads: DN-day0

## DN PLOG + DOX

Day 0

RNAseq normalized reads: DN-day0

Day 3

RNAseq normalized reads: DN-day3

Day 6

RNAseq normalized reads: DN-day6

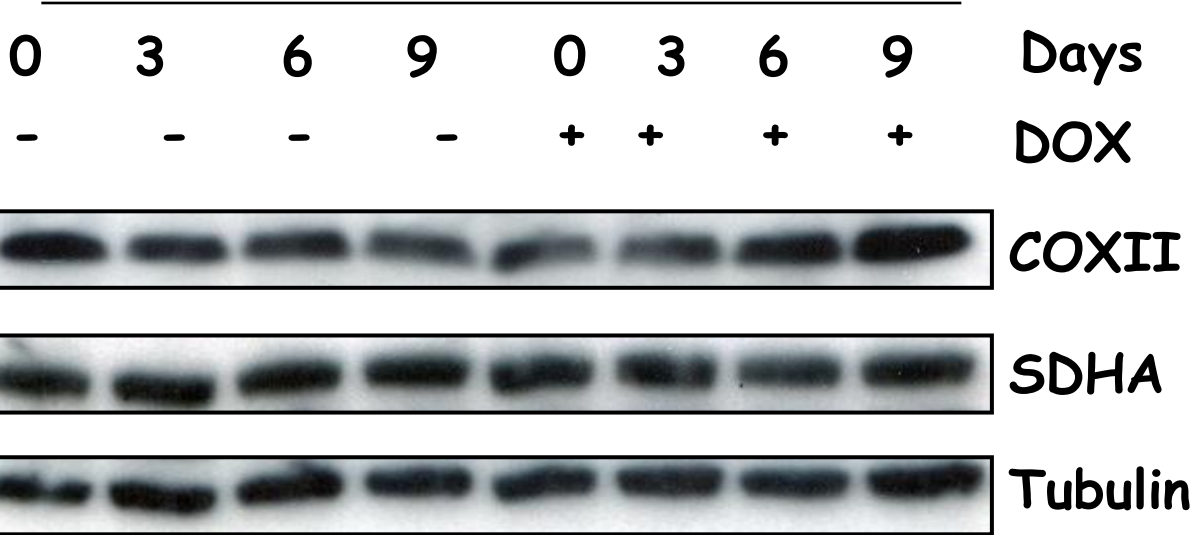
Day 9

RNAseq normalized reads: DN-day9

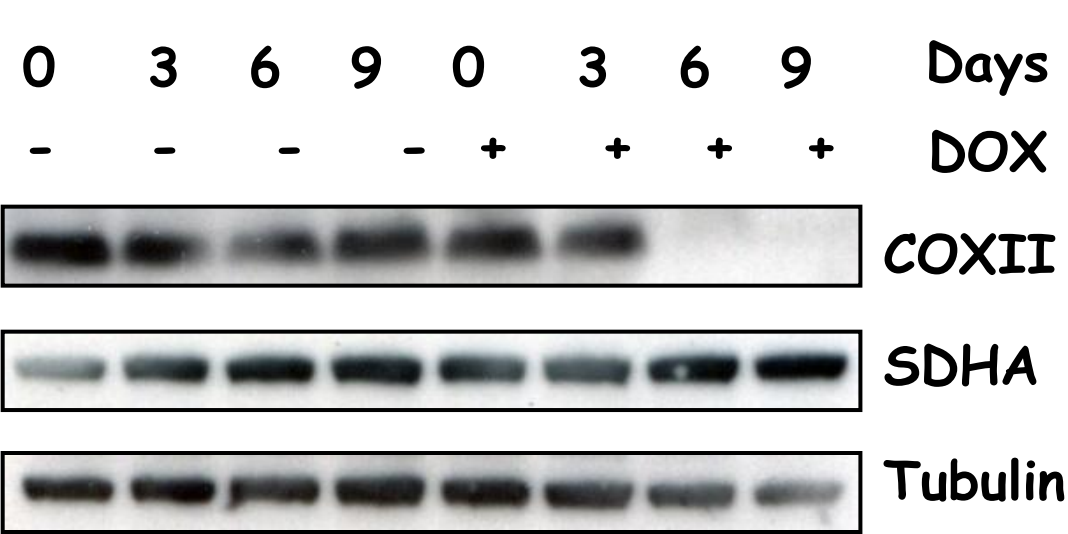
UCSC Genes (RefSeq, UniProt, CCDS, Rfam, tRNAs & Comparative Genomics)

# Dominant negative POLG depletes mtDNA encoded proteins.

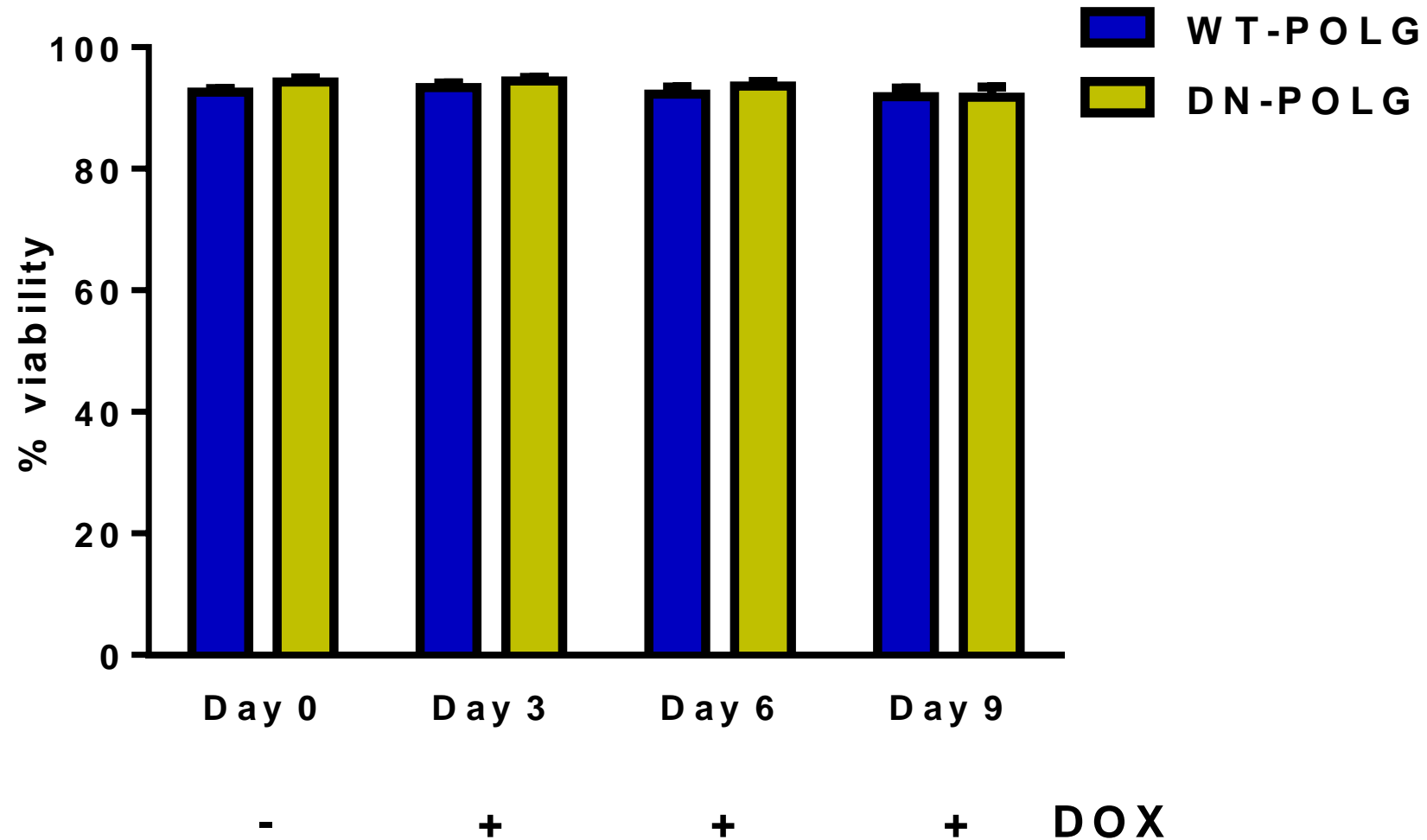
WT-POLG



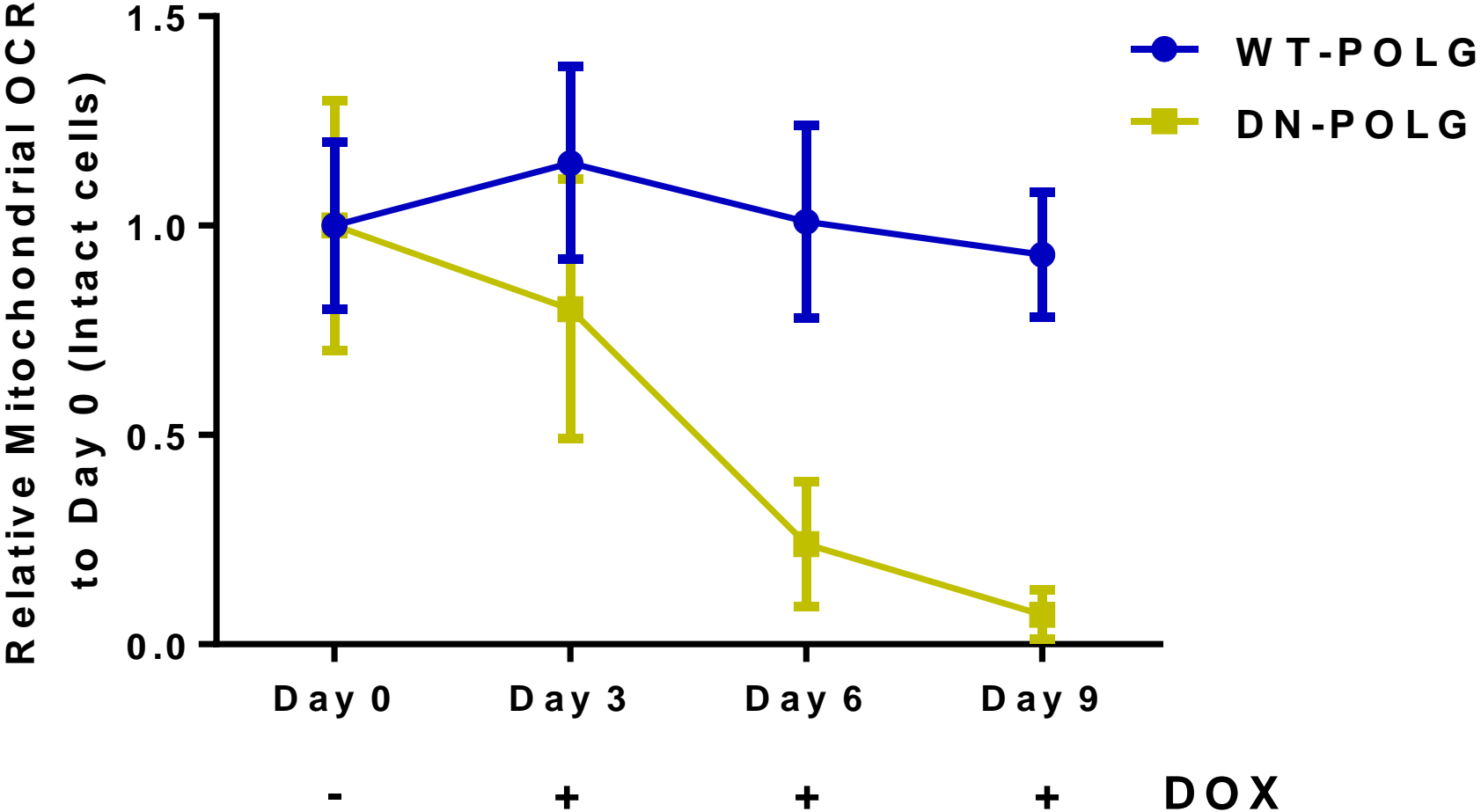
DN-POLG



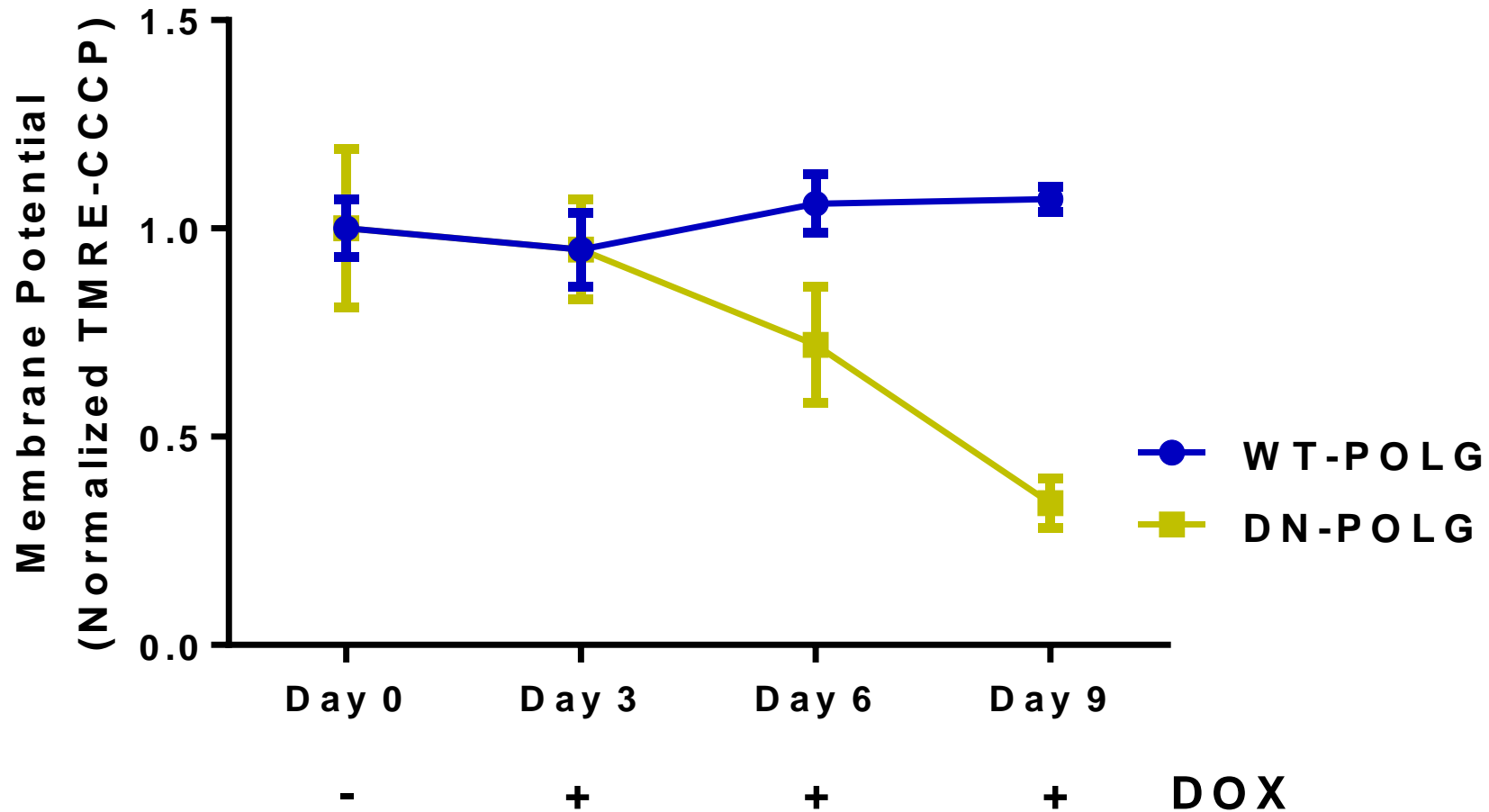
# Loss of mitochondrial DNA does not induce cell death.



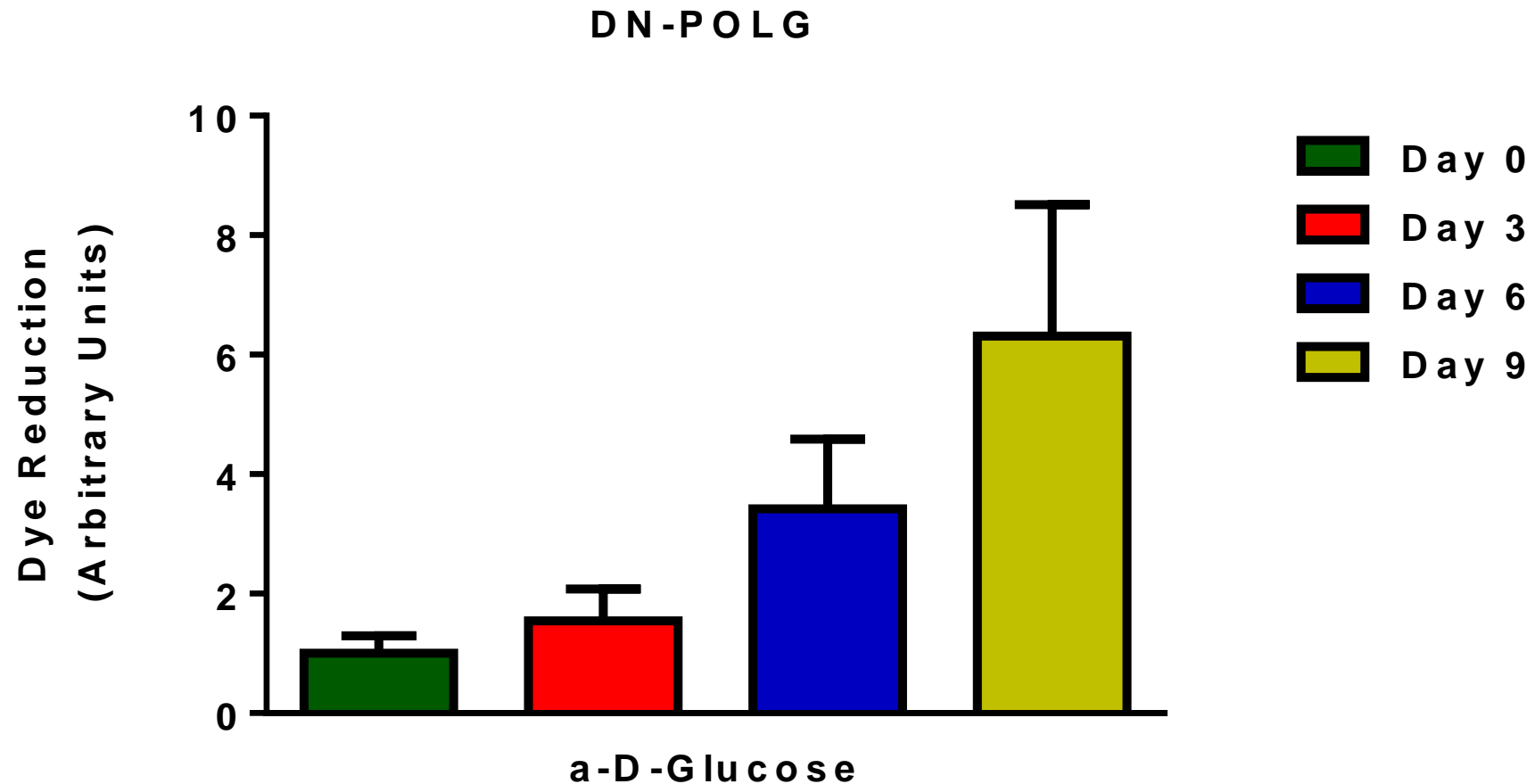
# Loss of mitochondrial DNA decreases oxygen consumption rate (OCR).



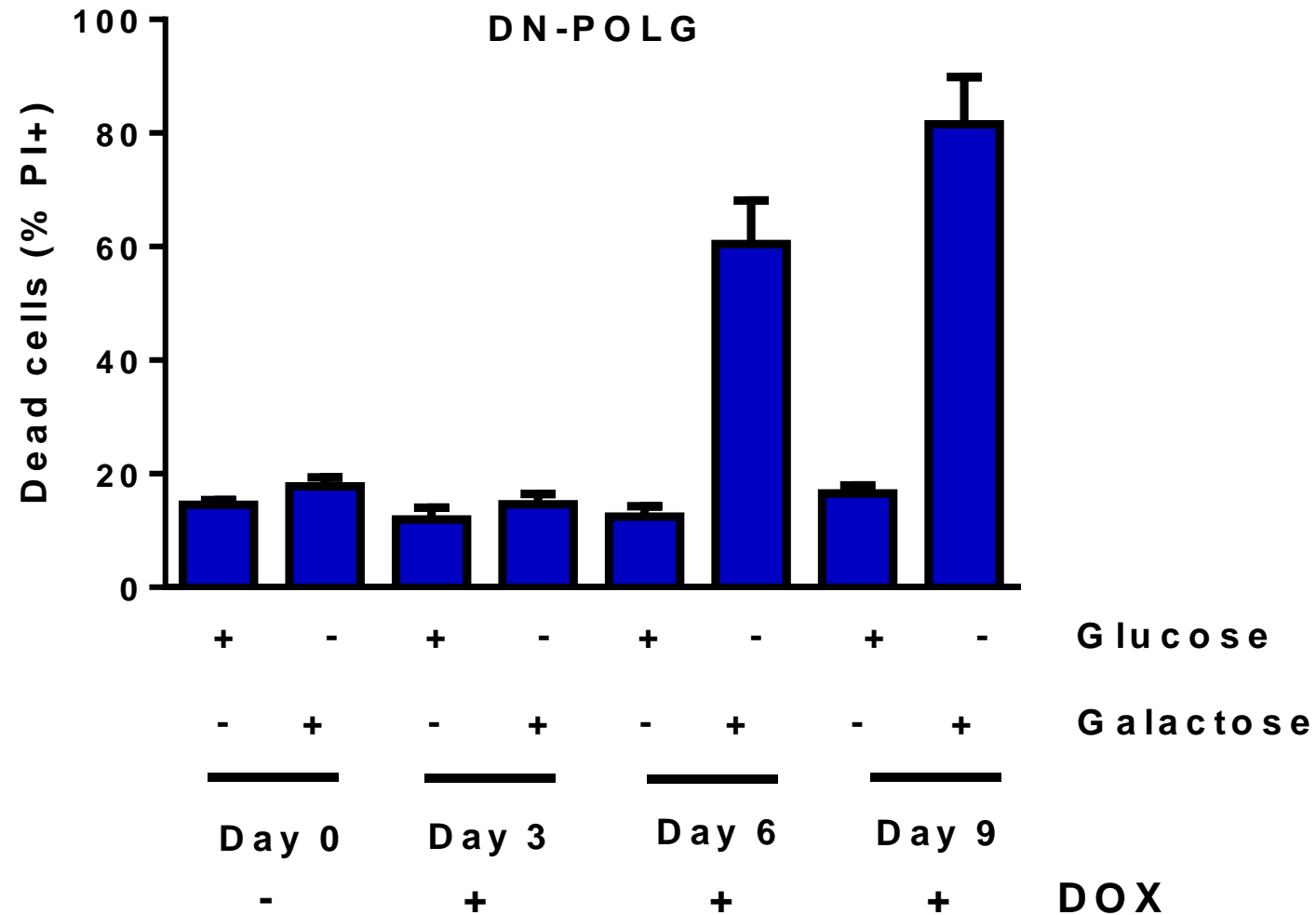
# Loss of mitochondrial DNA decreases mitochondrial membrane potential.



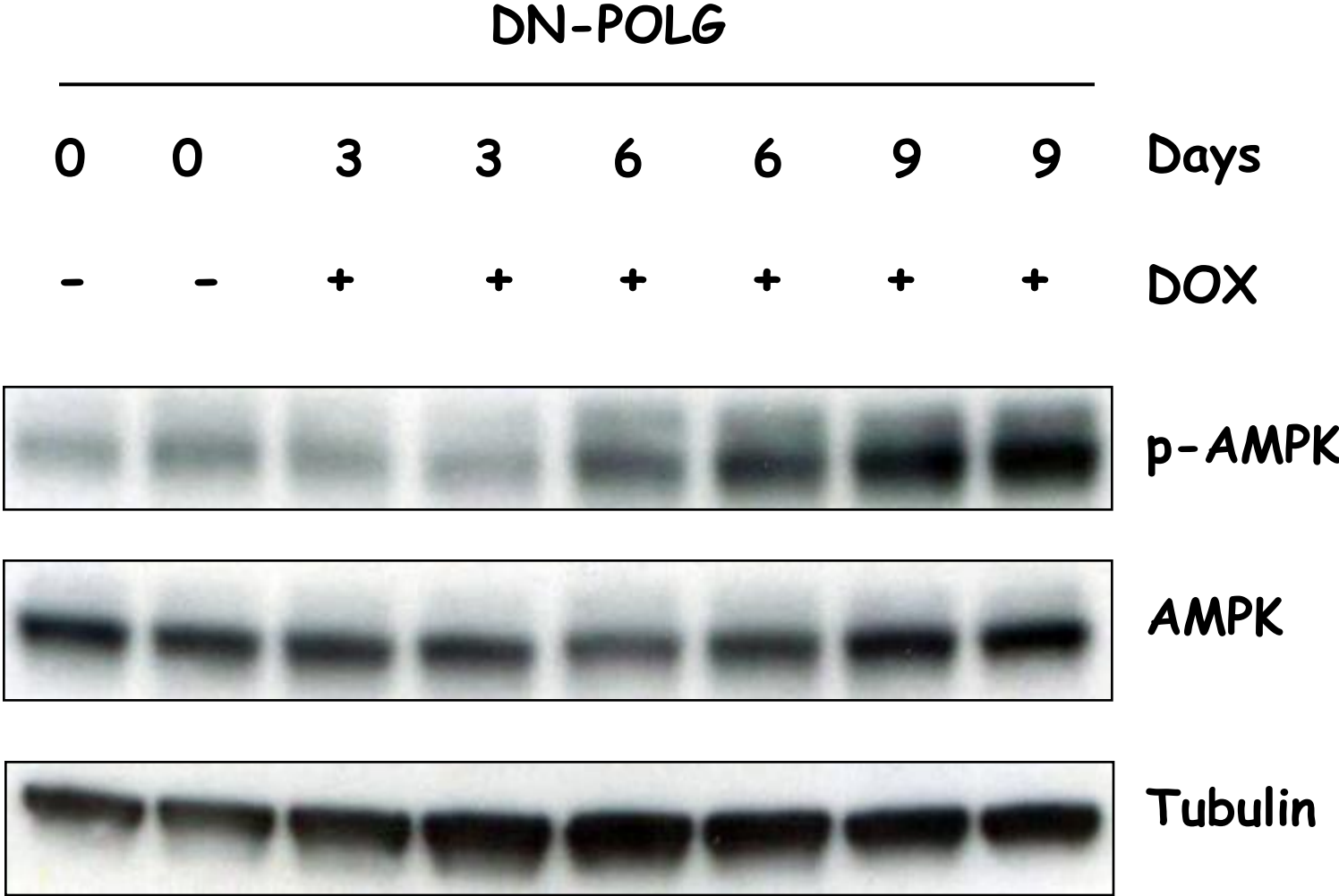
# Loss of mitochondrial DNA increases glucose catabolism.



# Loss of mitochondrial DNA induces dependence on glycolysis for survival.

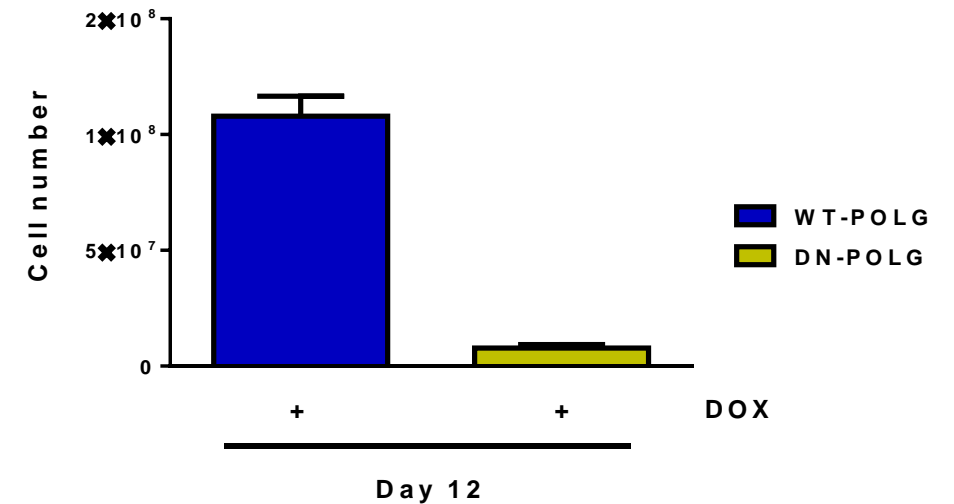
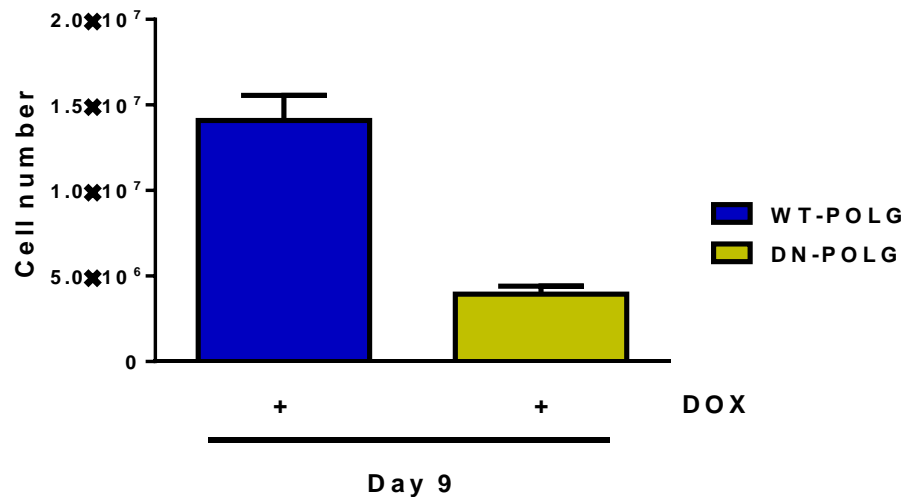
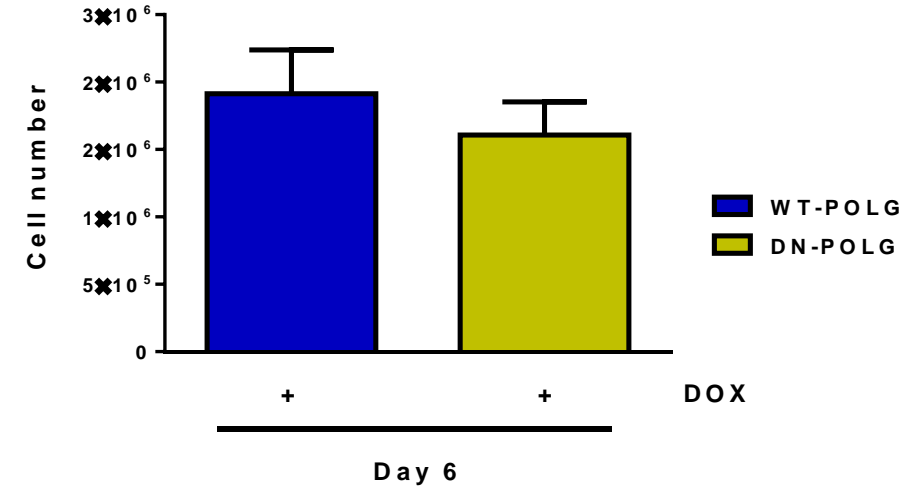
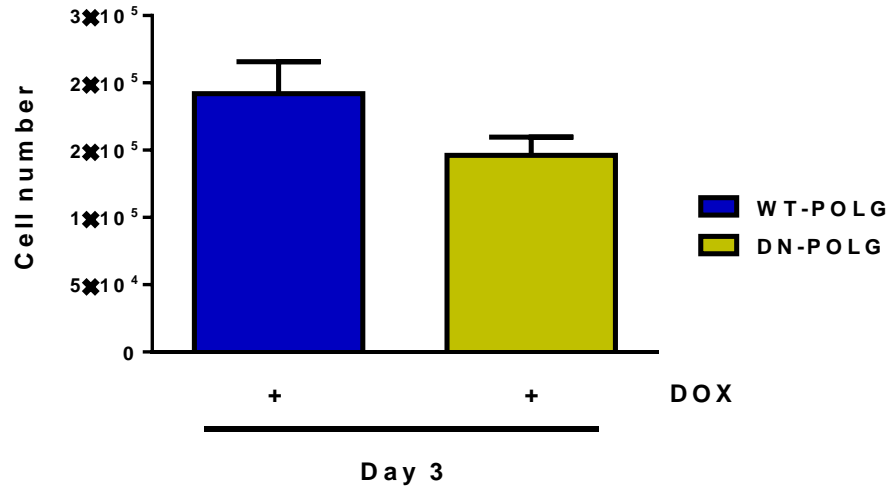


# Loss of mitochondrial DNA induces AMPK activation.

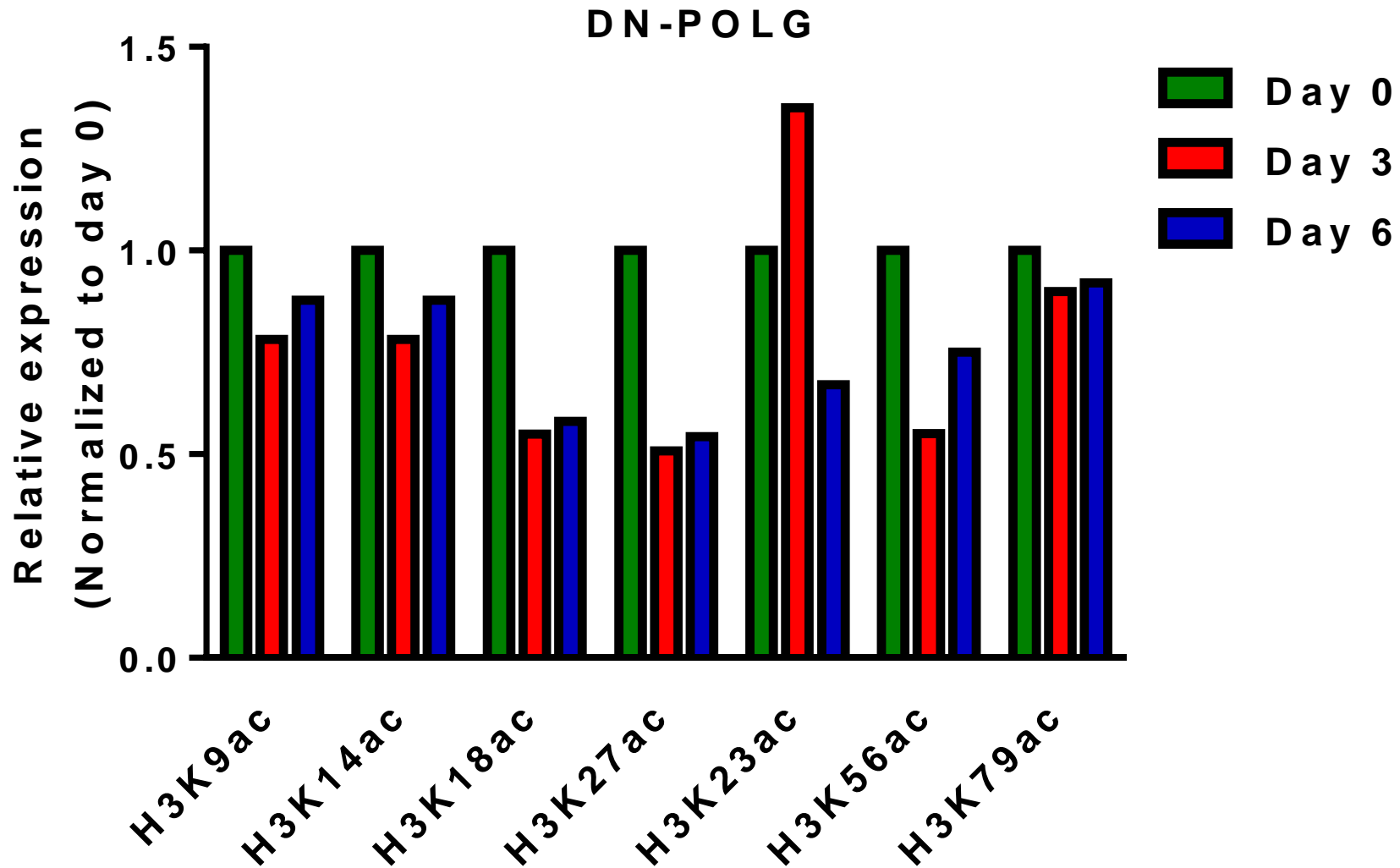




# Loss of mitochondrial DNA diminishes cell proliferation rate.



# Quantification of Histone modifications using Silac.

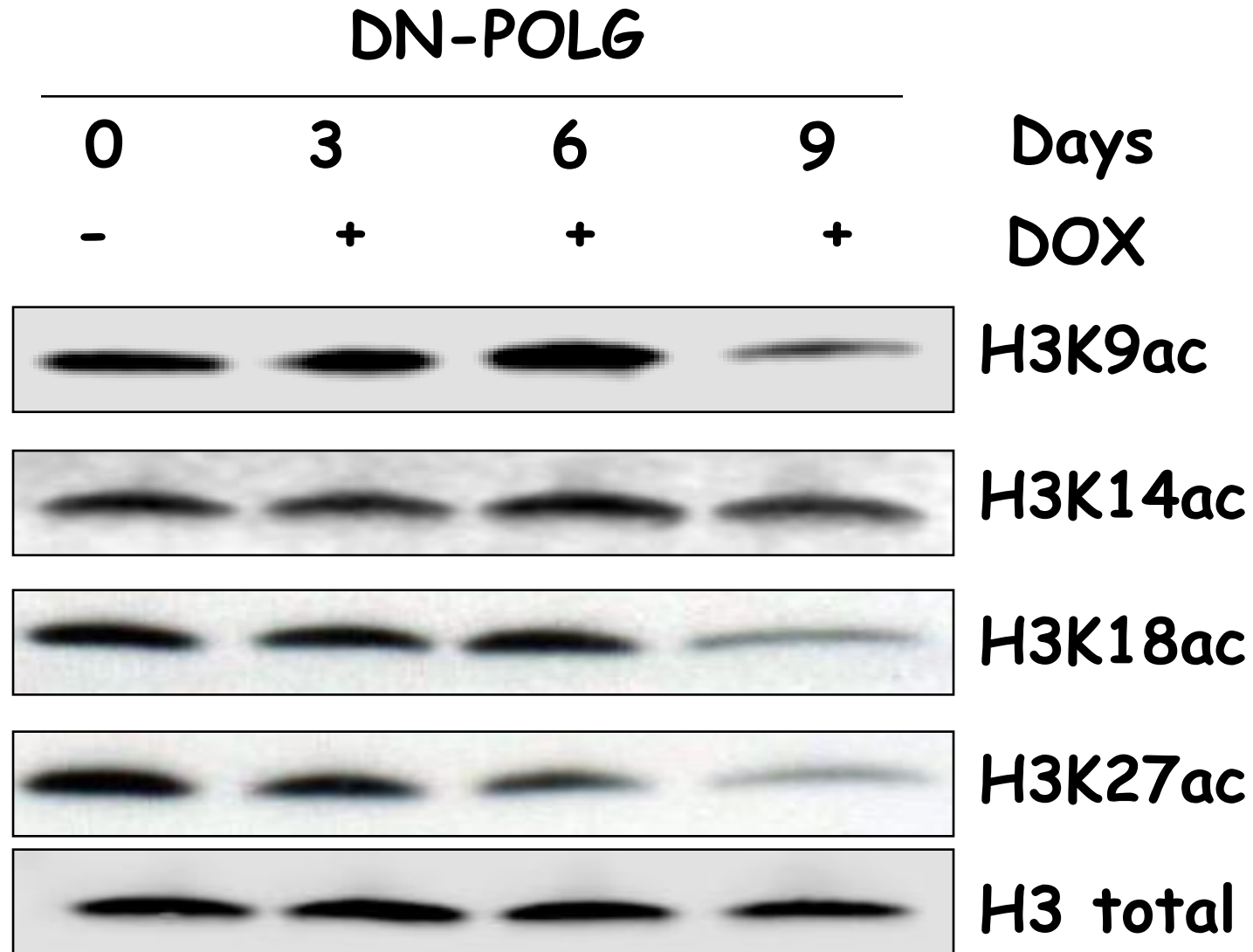


Minimal changes in methylation and acetylation of H2B and H4.

He Huang

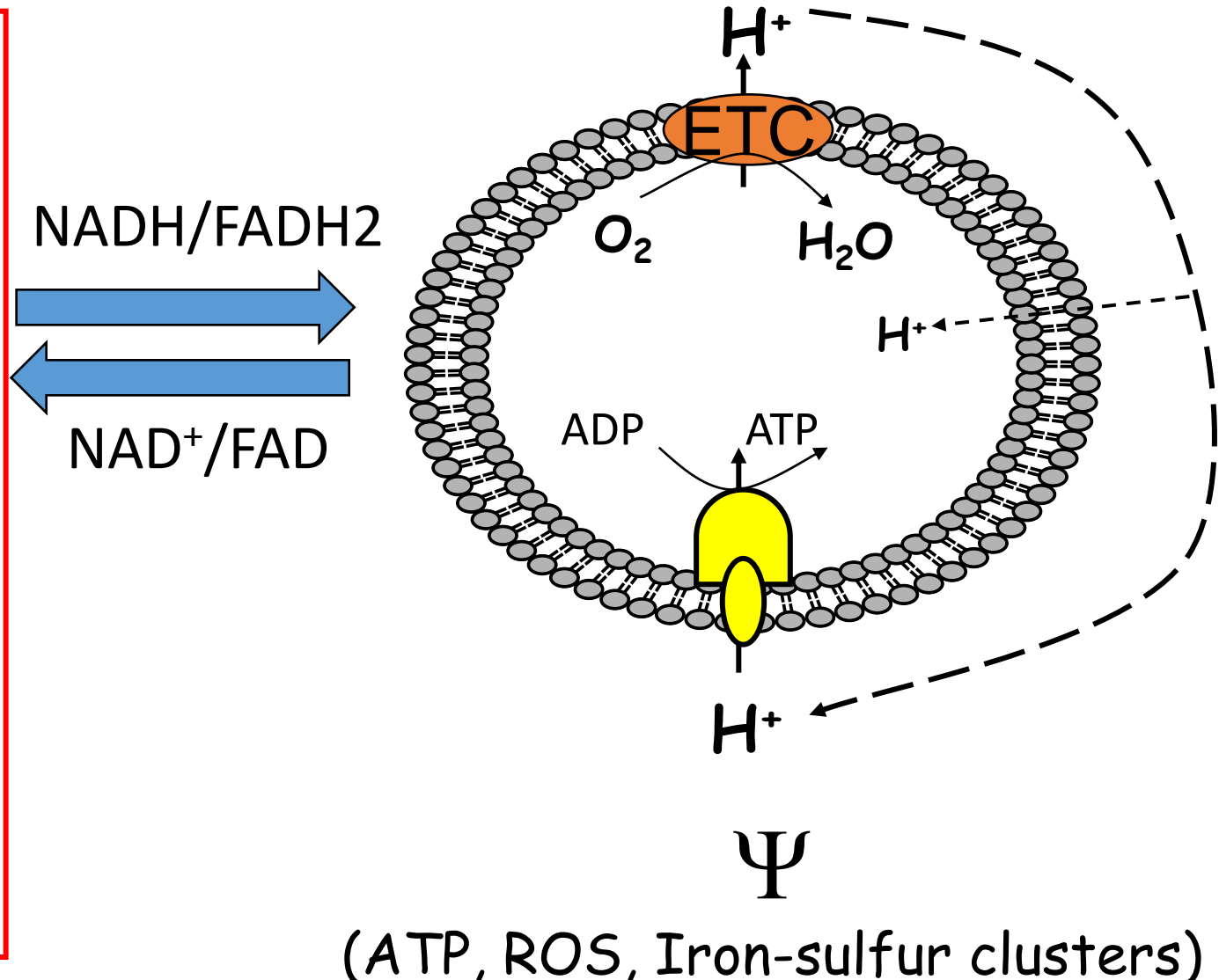
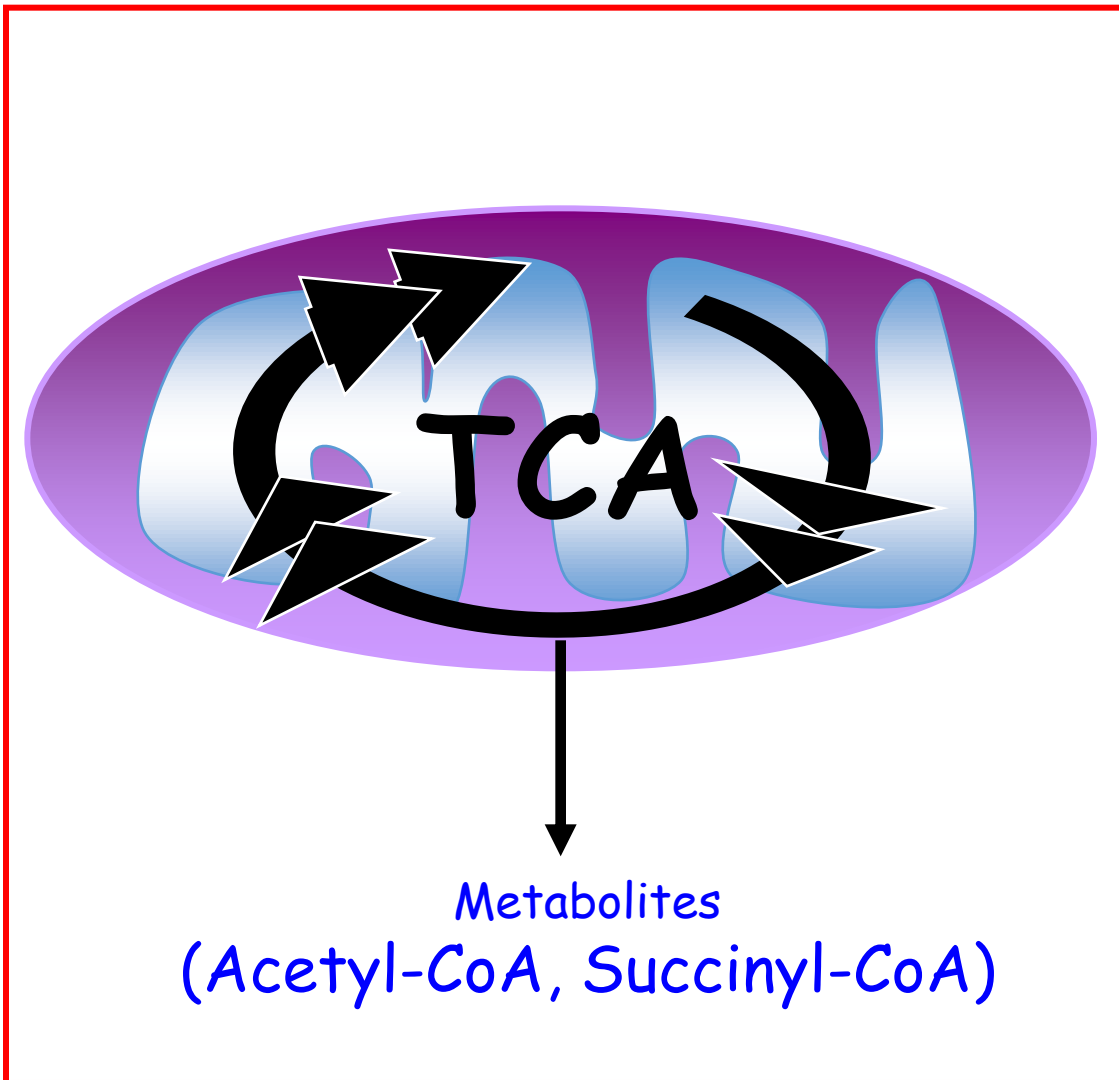
Yingming Zhao

# Loss of mitochondrial DNA decreases specific histone H3 acetylation.

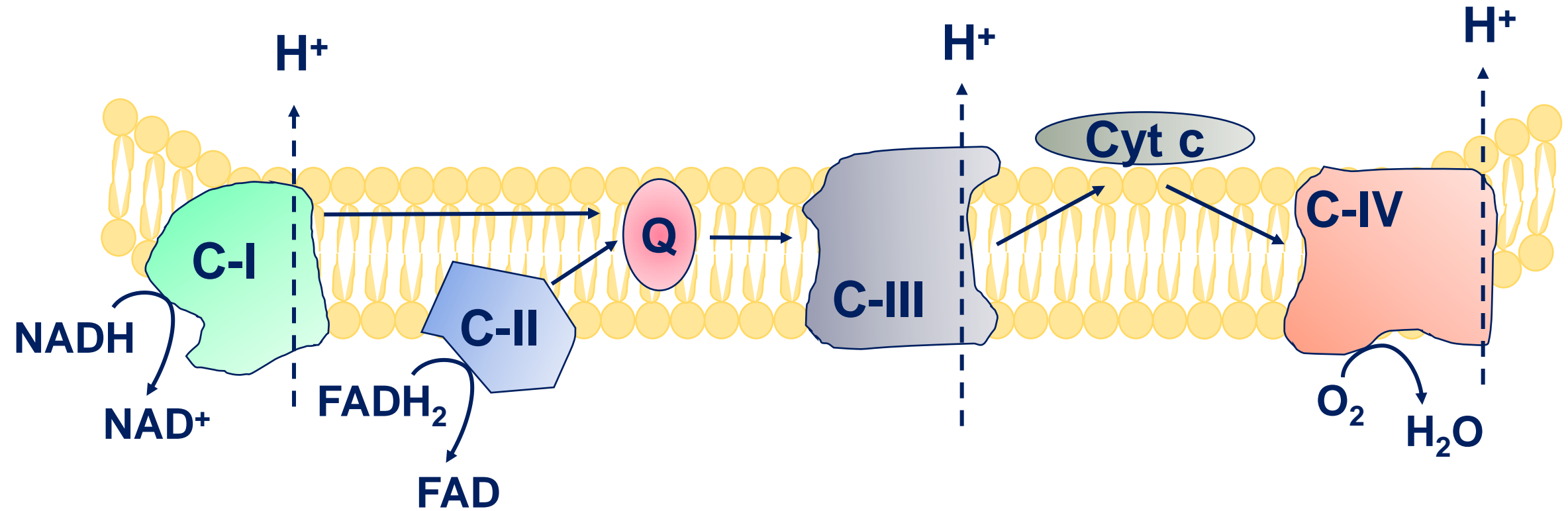


**Mitochondria metabolism is necessary for cell proliferation and specific histone acetylation.**

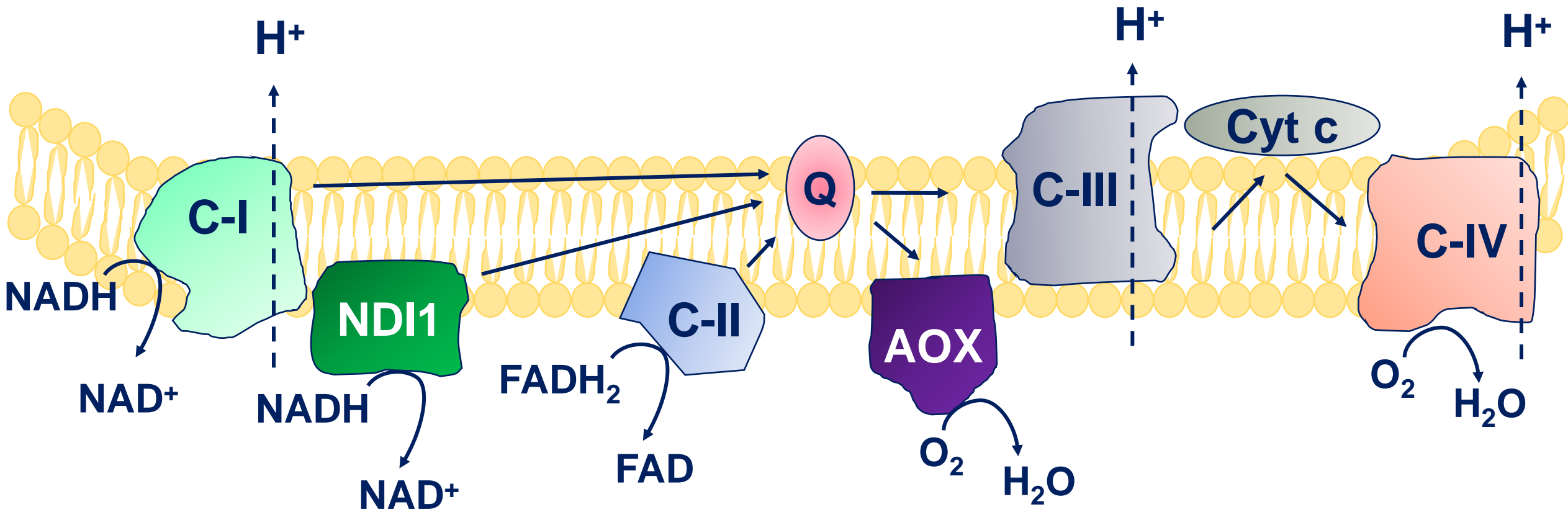
# Two functions of mitochondria: TCA cycle metabolites and membrane potential.



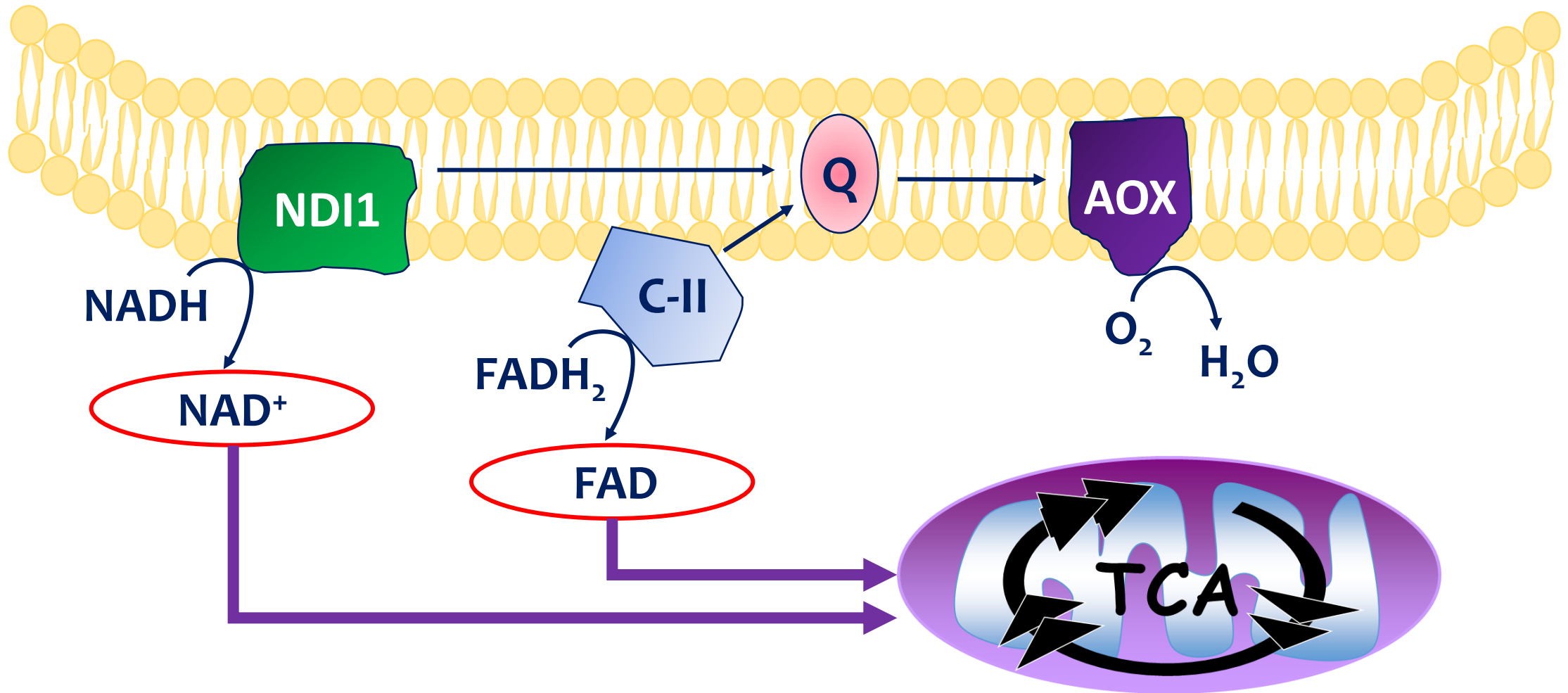
# Electron transport chain couples electron flux to proton pumping.



# NDI1 mimics complex I and AOX bypasses complex III and complex IV.

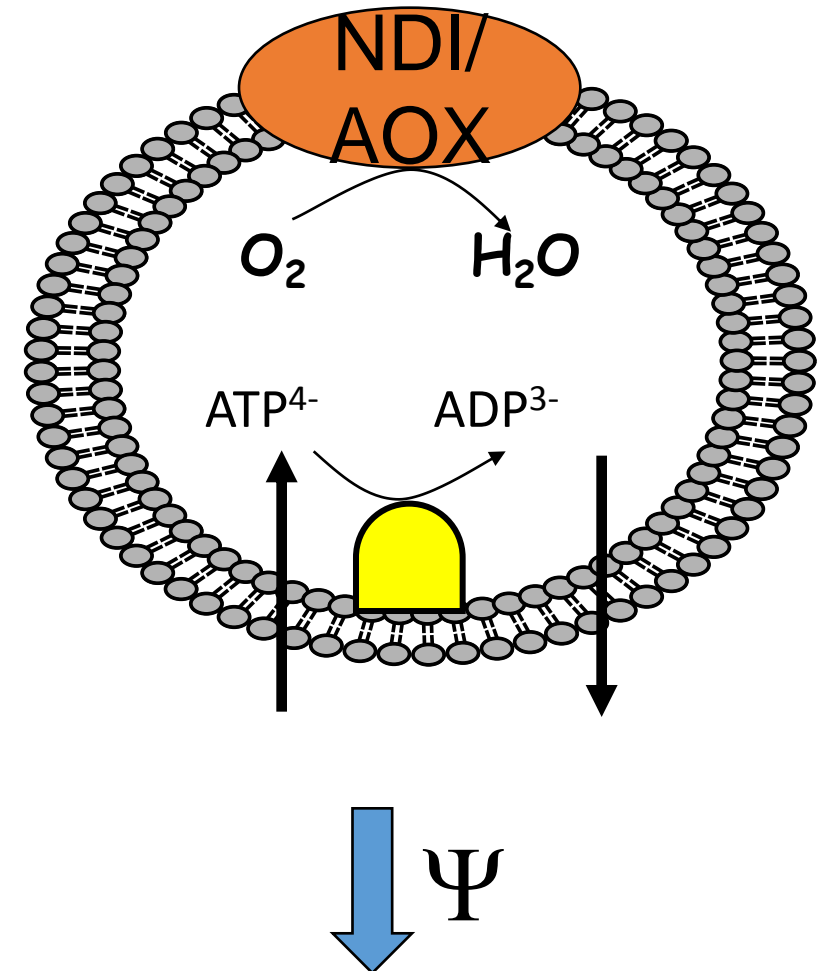
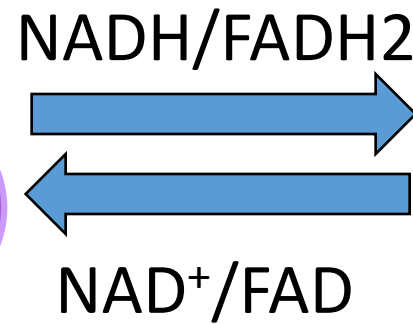
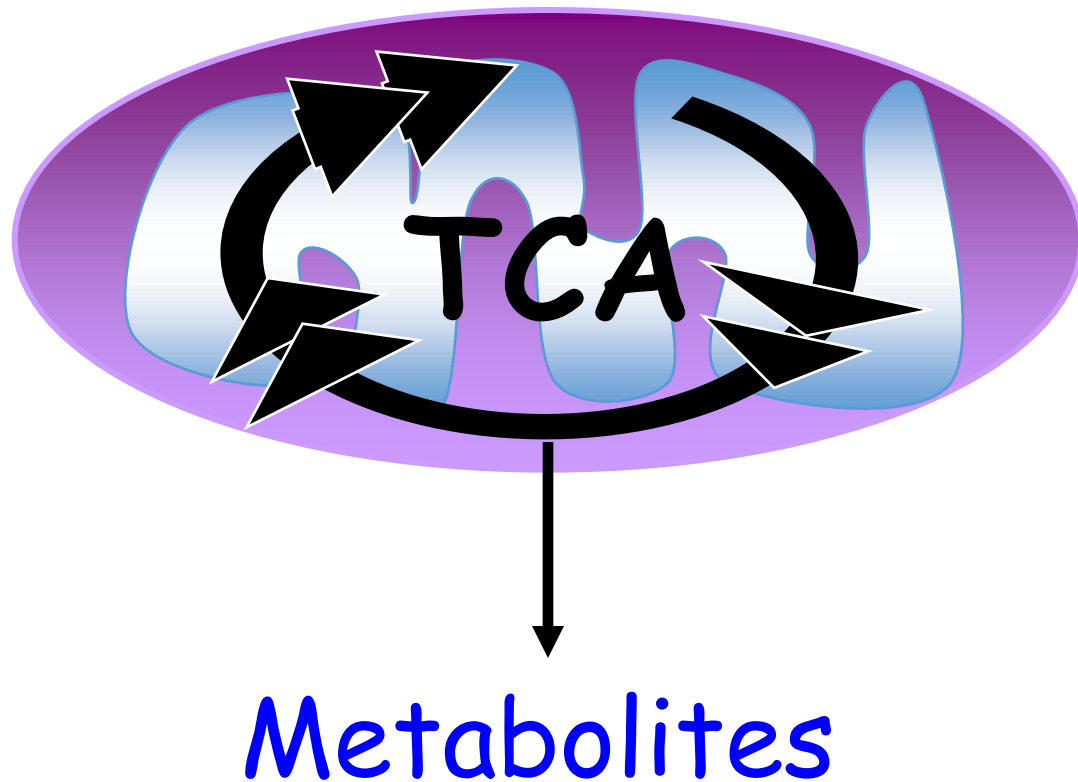


# NDI1 and AOX expression uncouples electron flux from proton pumping in cells with depleted mitochondrial DNA.

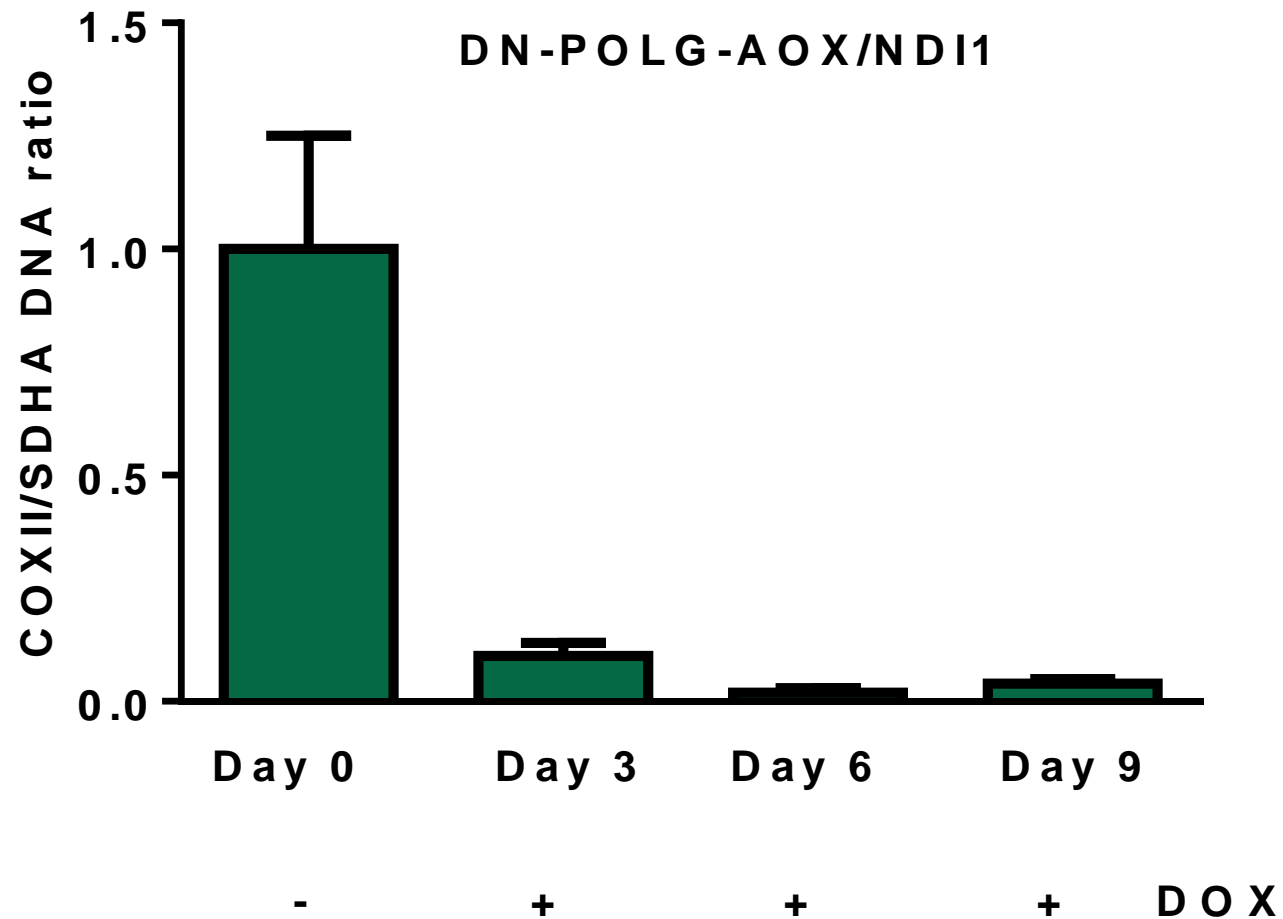




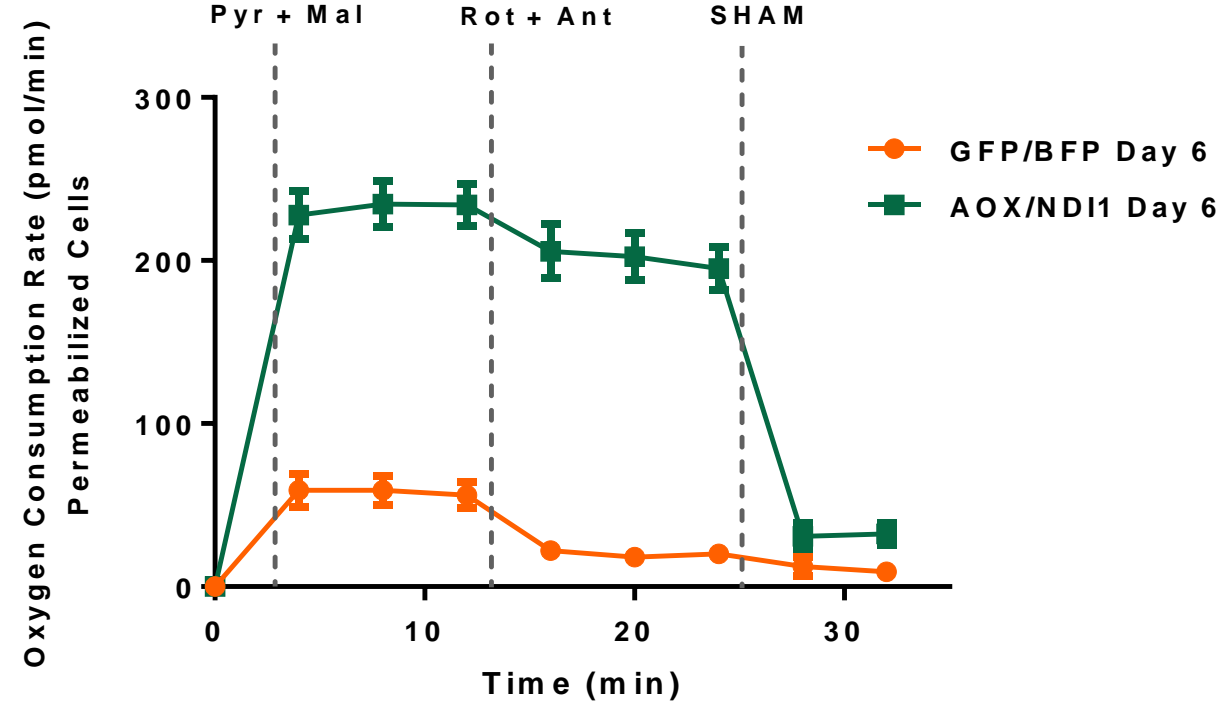
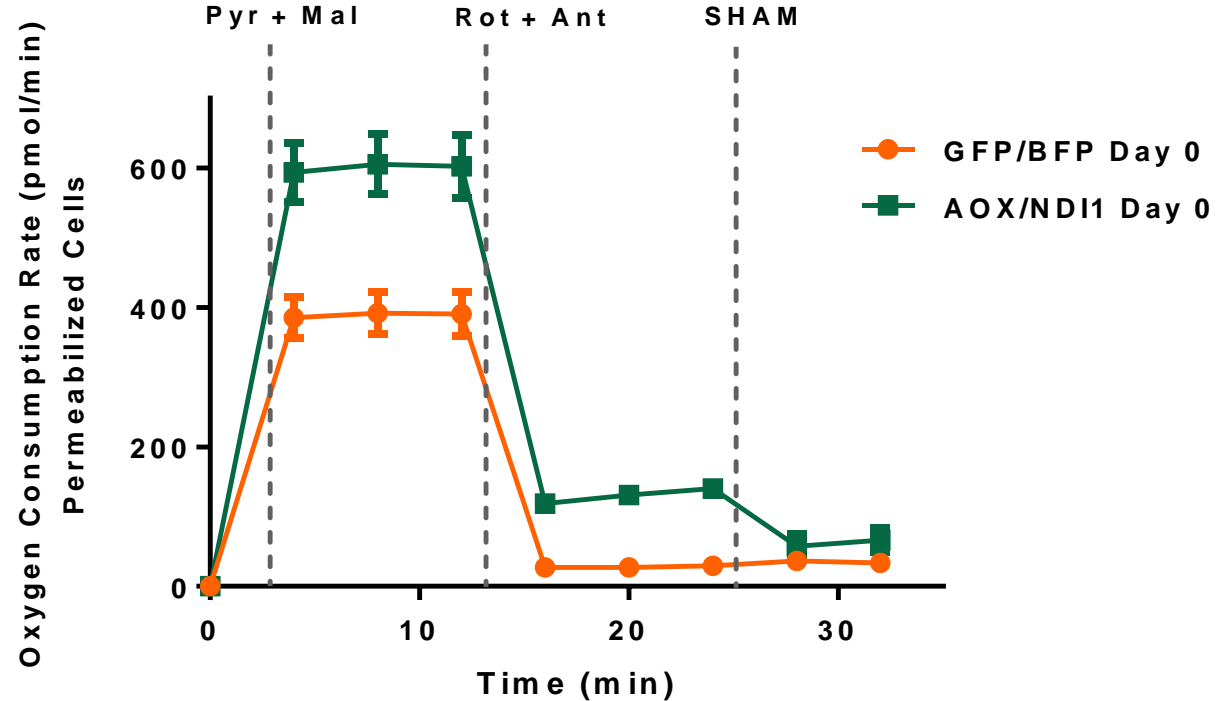
# AOX-NDI1 expression restores electron flux but not membrane potential.



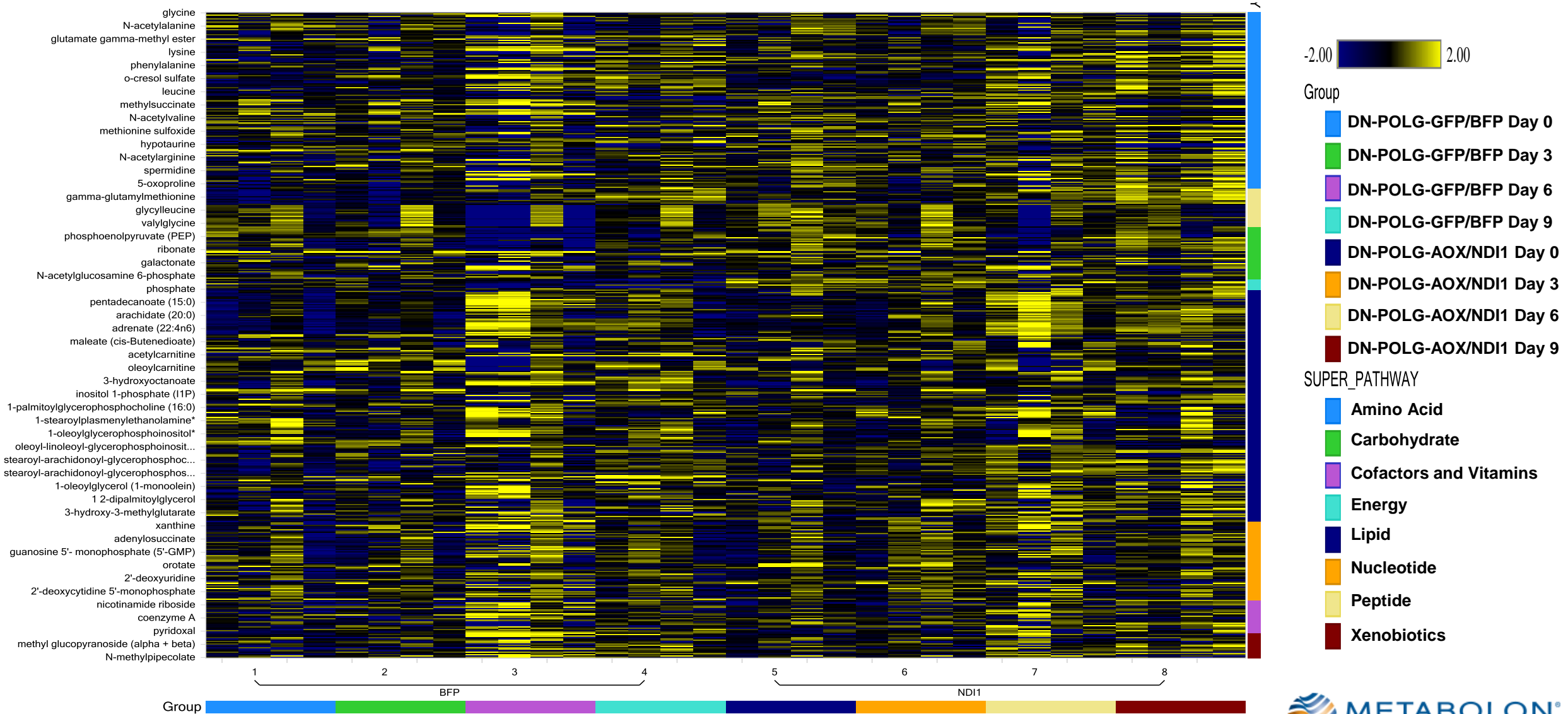
# AOX-NDI expression does not restore mitochondrial DNA.



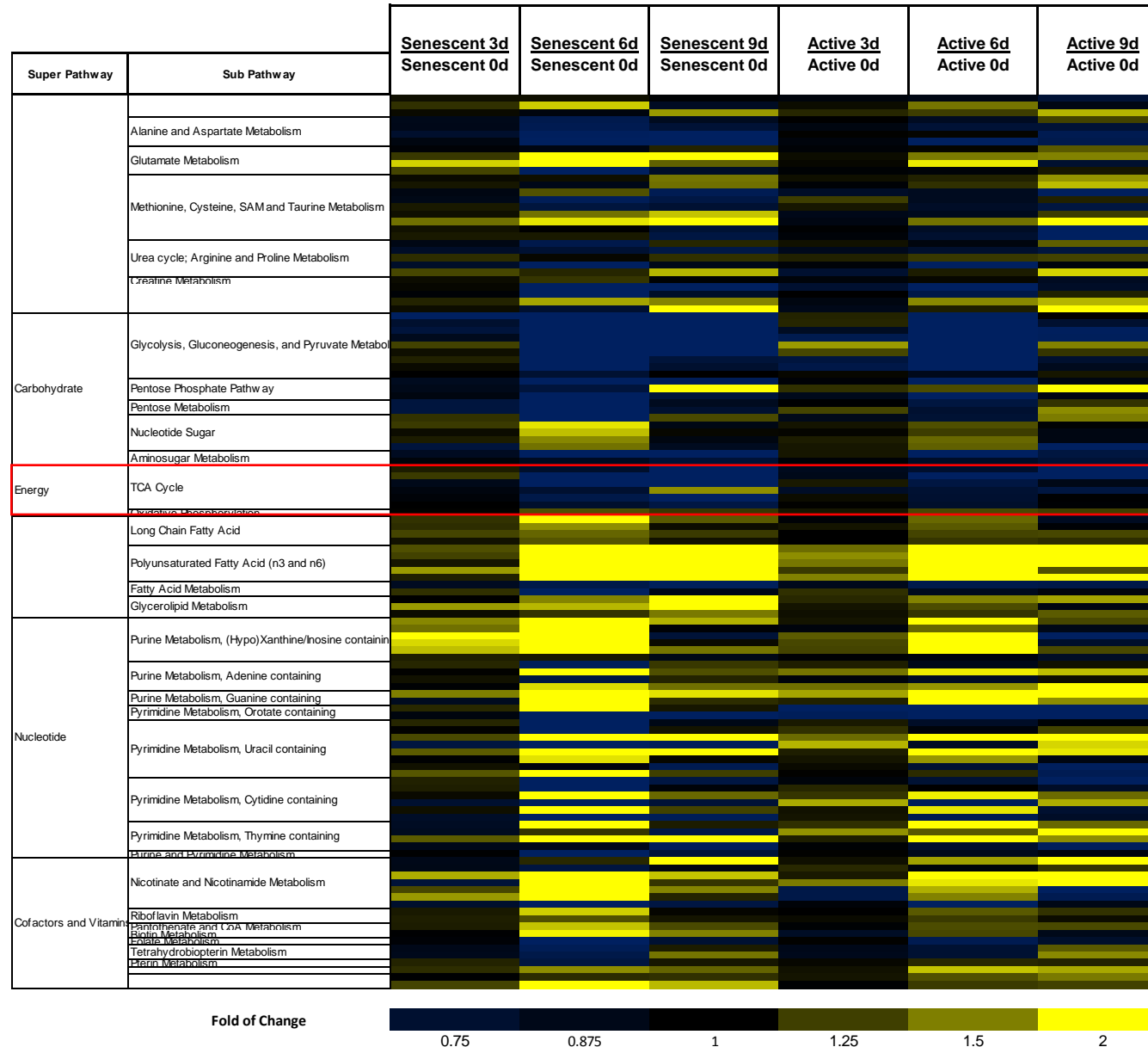
# AOX-NDI expression restores oxygen consumption rate in isolated mitochondria.



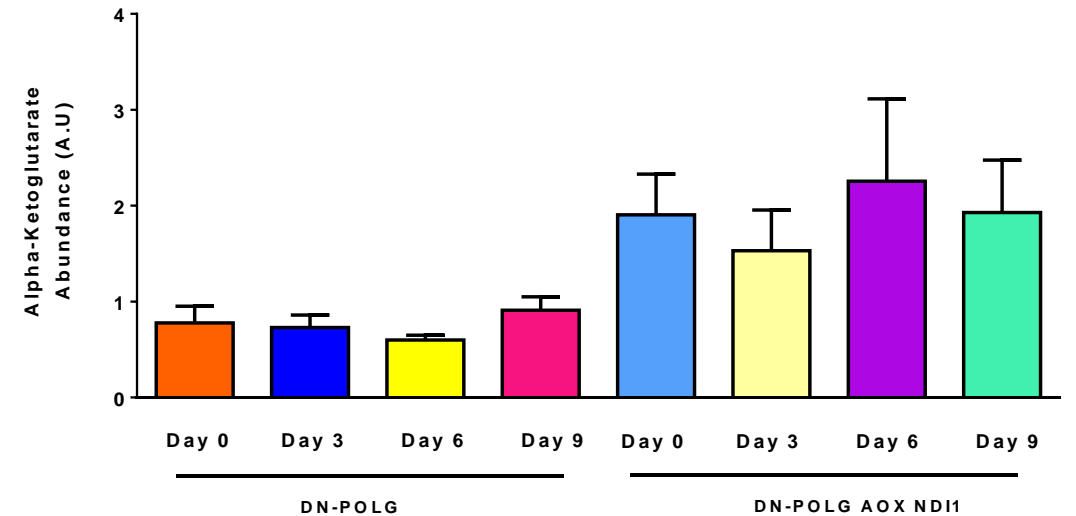
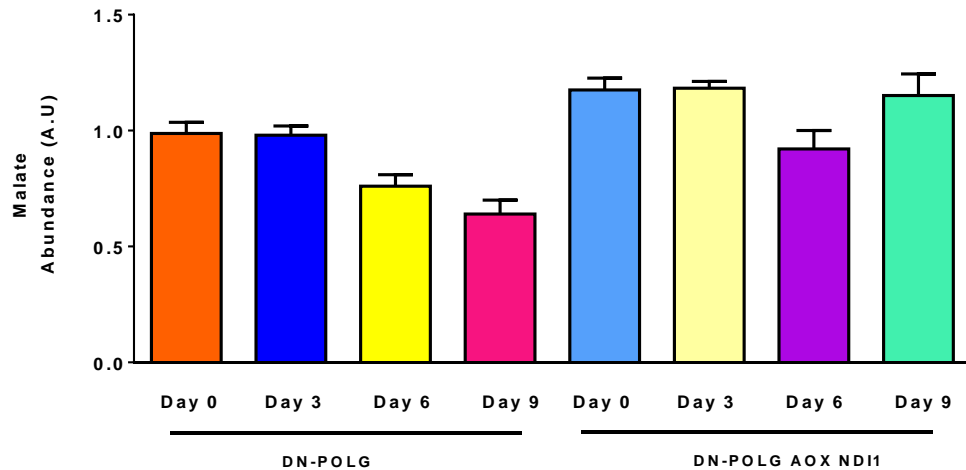
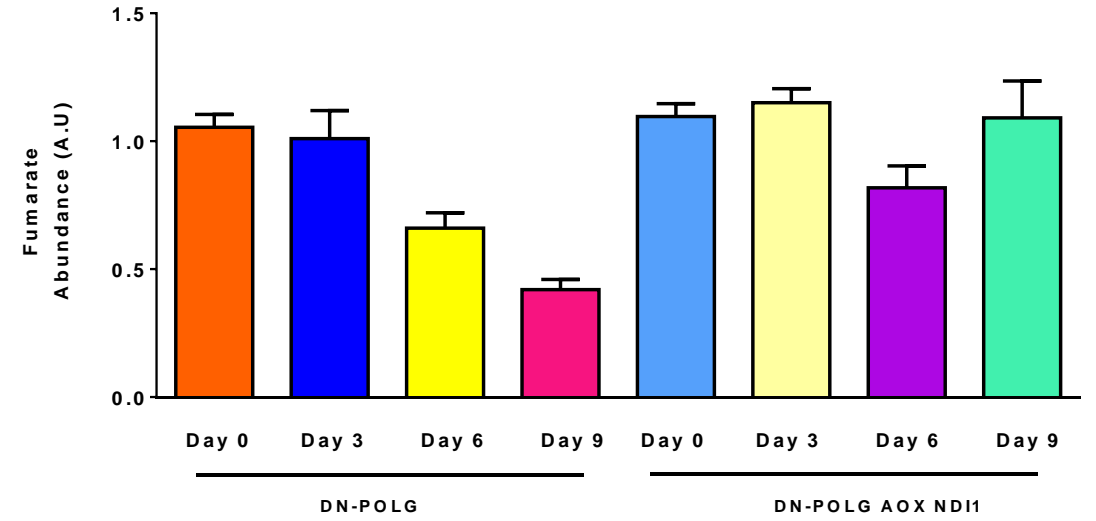
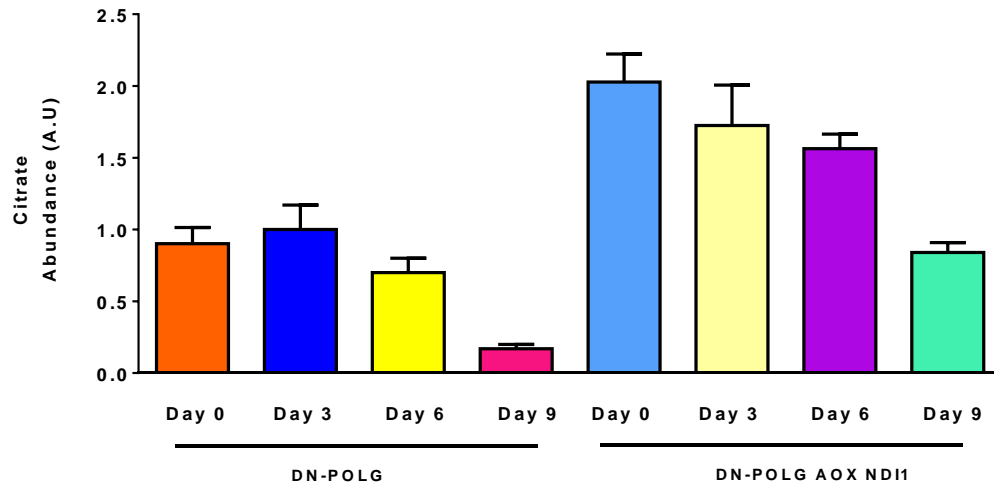
# Study of the metabolic profile of the cells



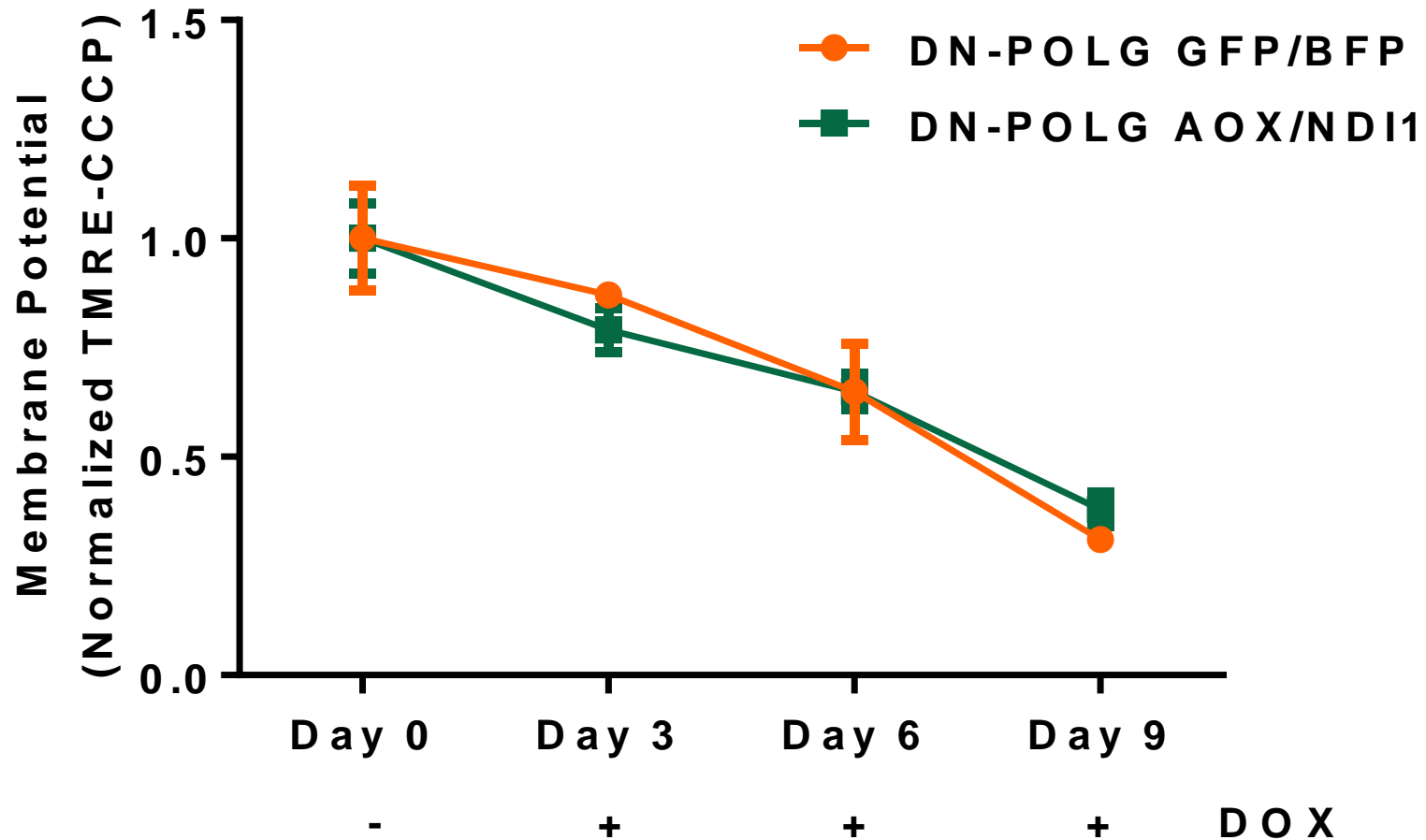
# Study of the metabolic profile of the cells



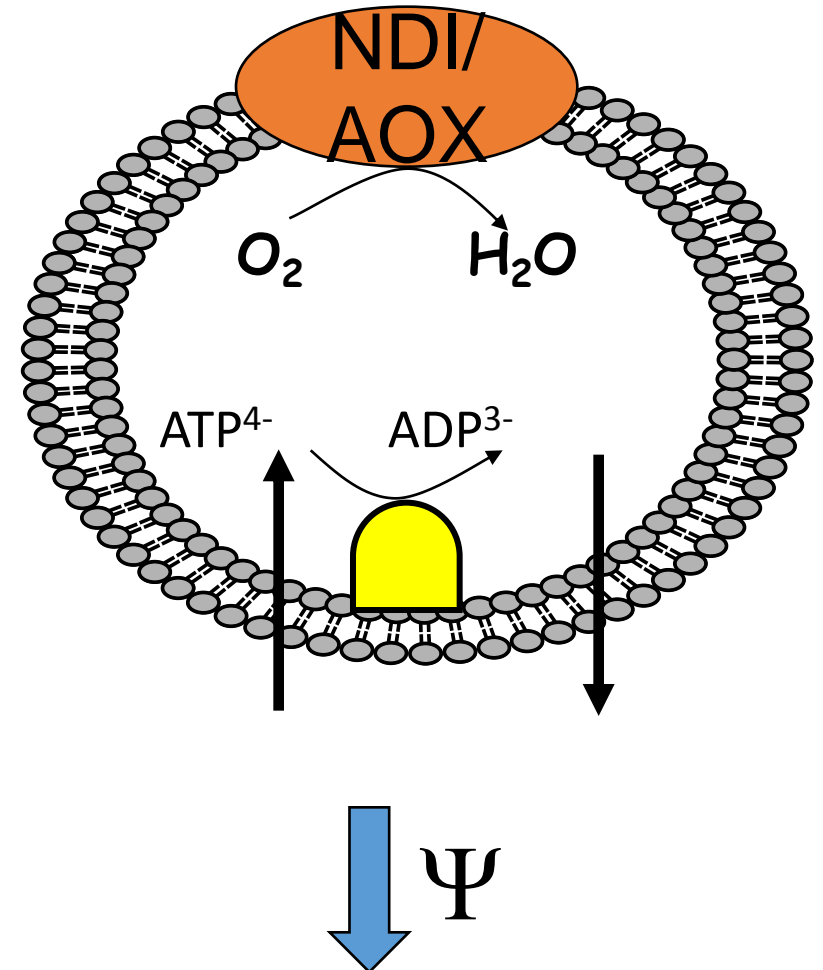
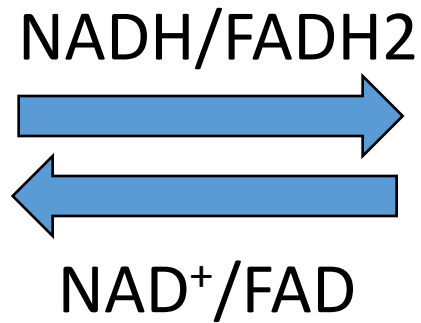
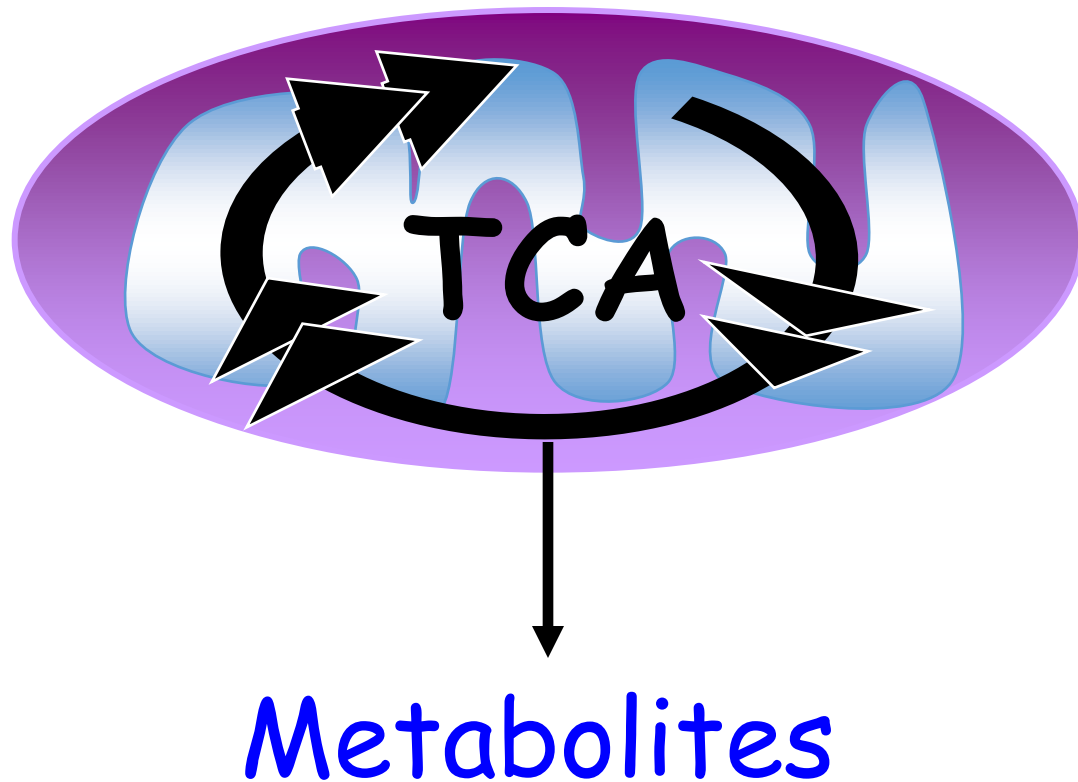
# AOX-NDI expression maintains levels of TCA cycle metabolites.



# AOX-NDI does NOT restore mitochondrial membrane potential.



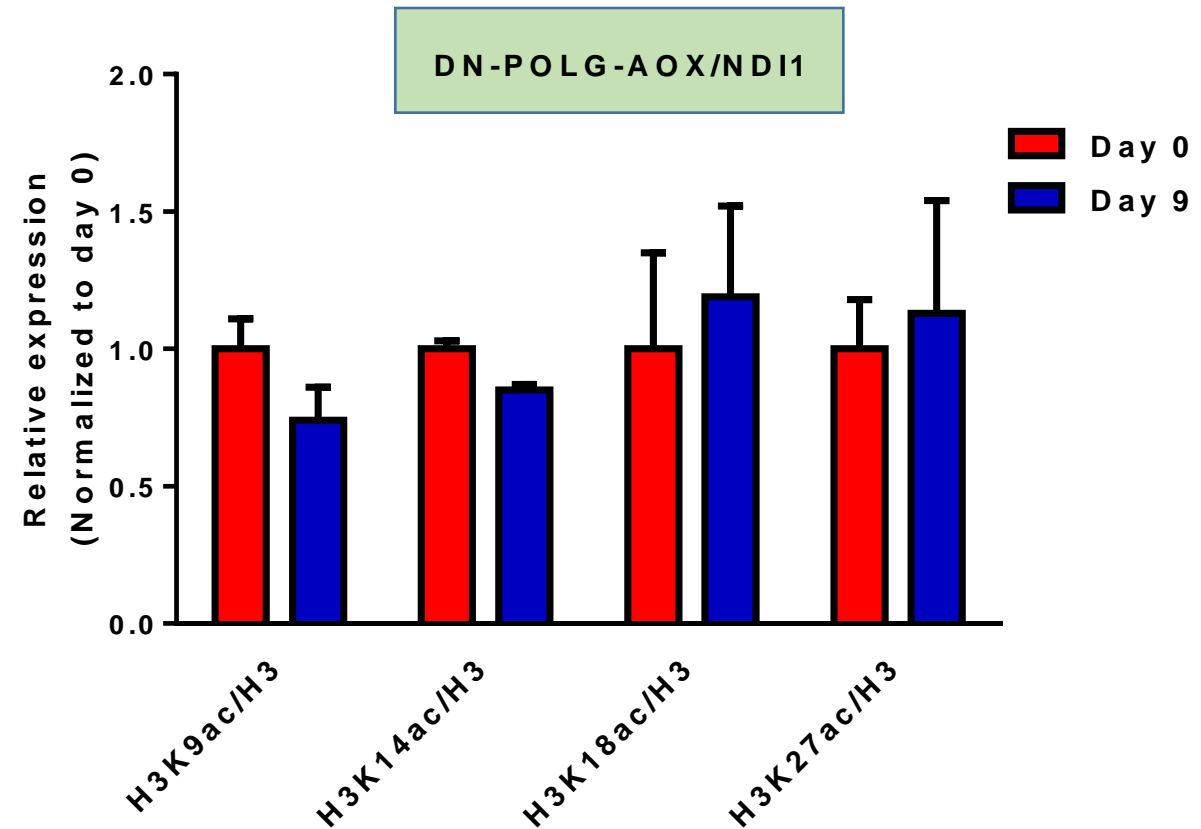
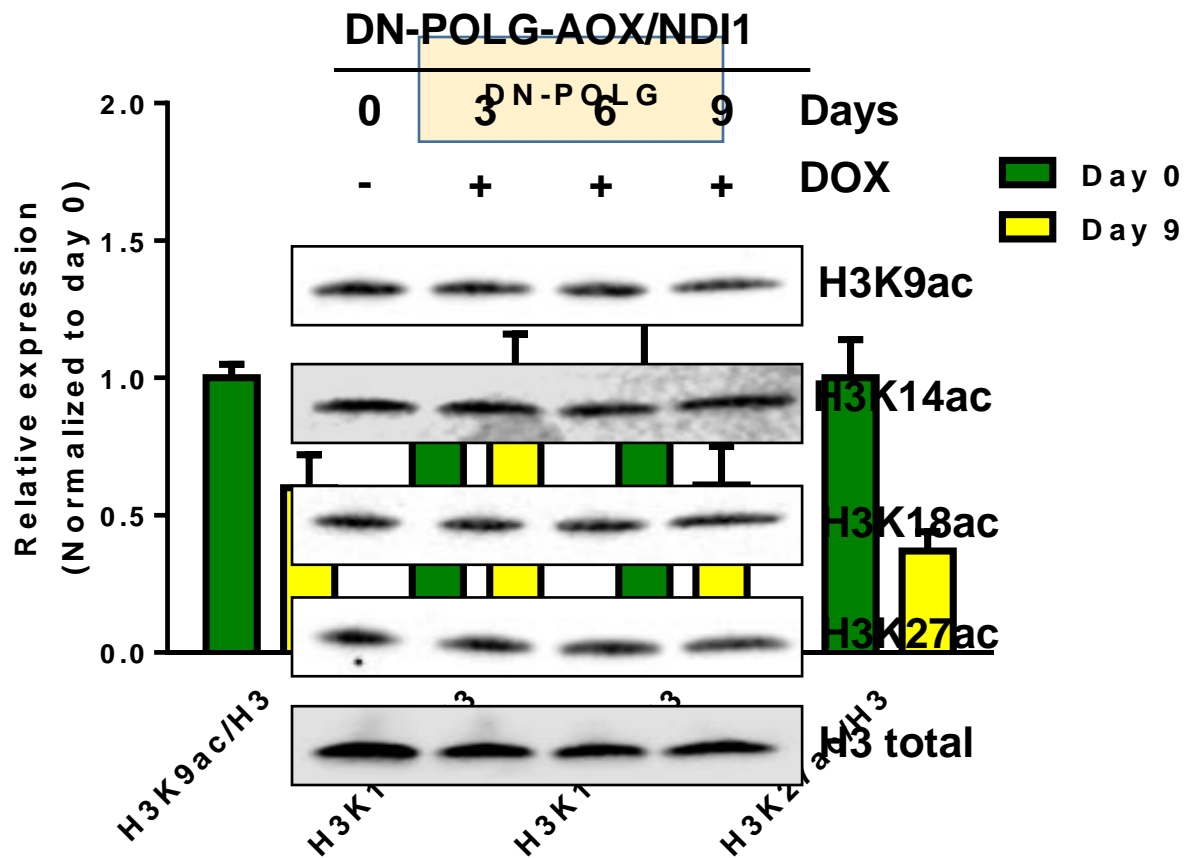
# AOX-NDI1 expression restores electron flux (TCA cycle) but not membrane potential.



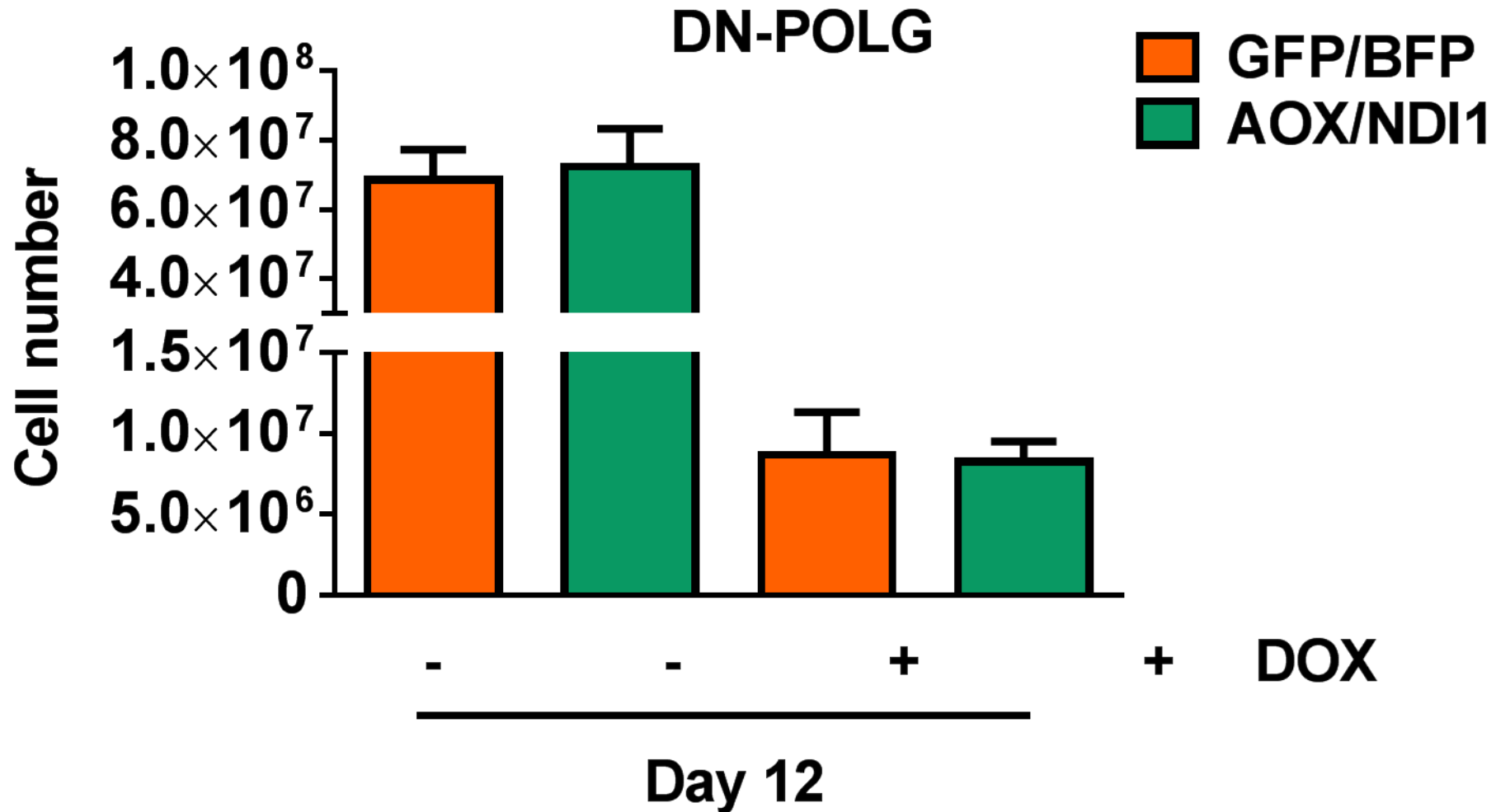


Is electron flux (TCA cycle) sufficient to restore cell proliferation and histone acetylation?

# Electron flux (TCA cycle) is sufficient to restore histone acetylation.

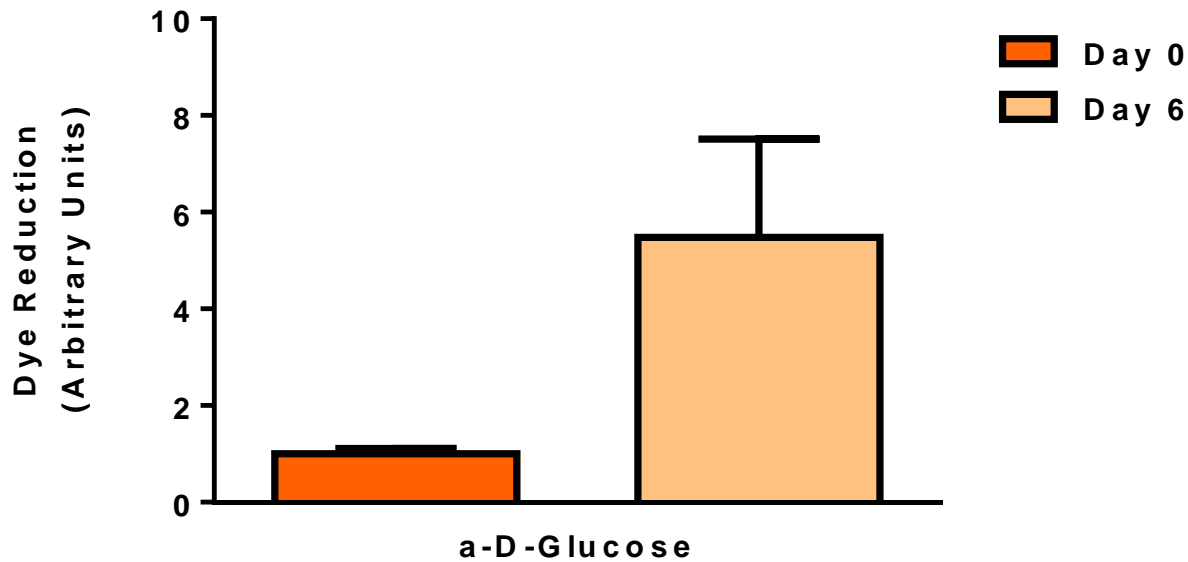


**Electron flux (TCA cycle) is NOT sufficient to restore cell proliferation.**

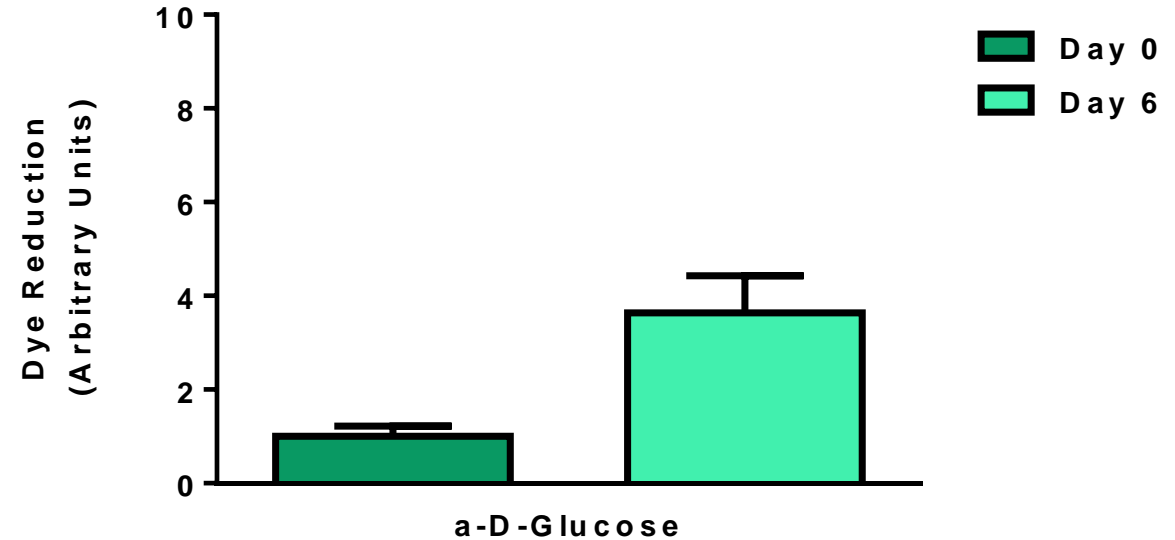


# Electron flux (TCA cycle) is NOT sufficient to restore increased glucose catabolism.

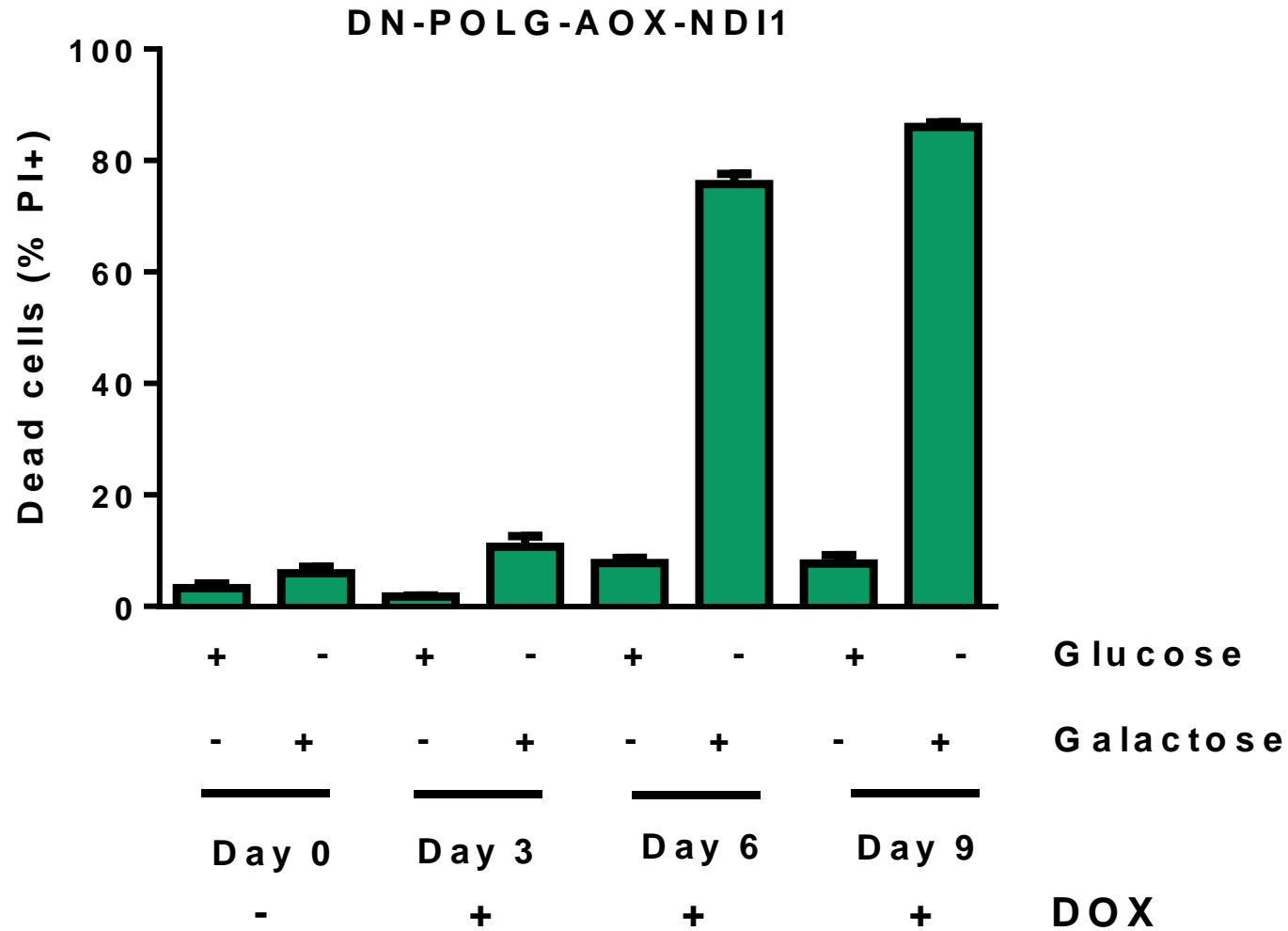
DN-POLG -GFP/BFP



DN-POLG -AOX NDI1

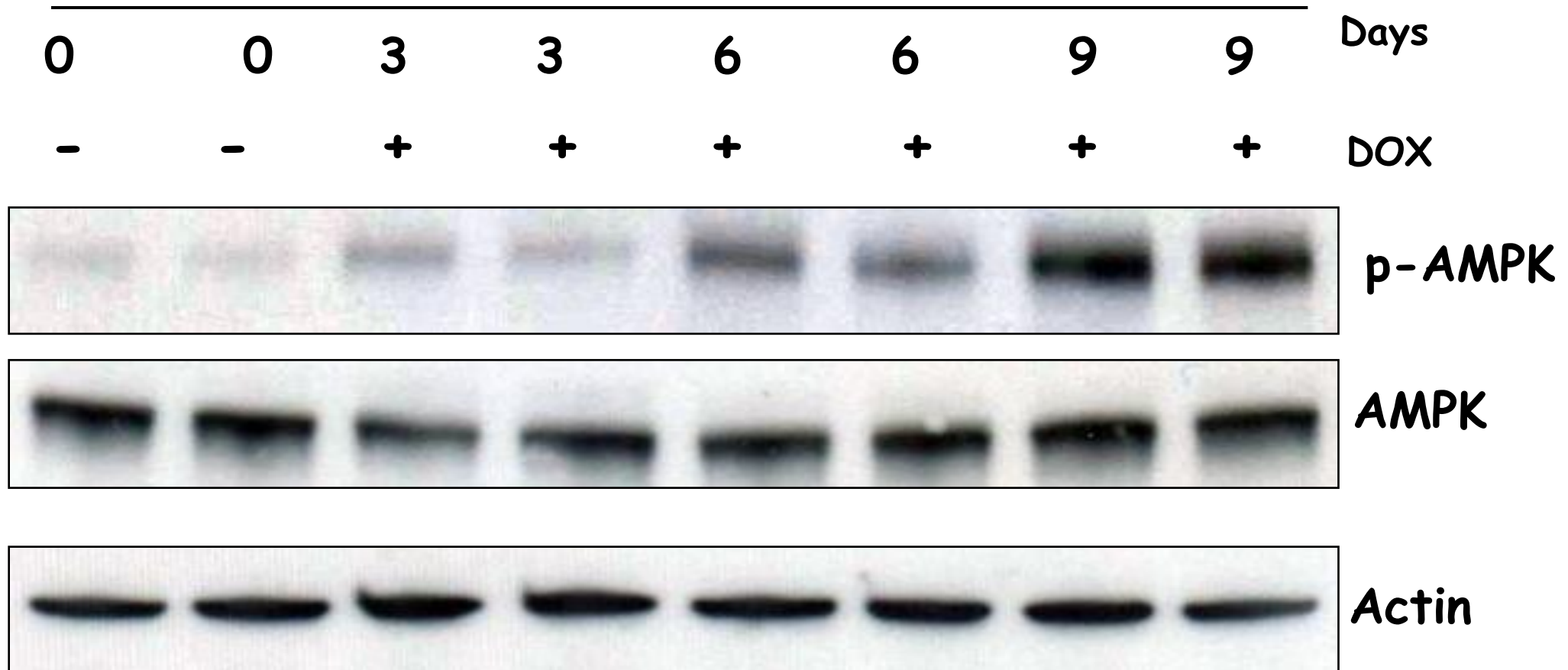


# Electron flux (TCA cycle) is NOT sufficient to restore glucose dependency for survival.

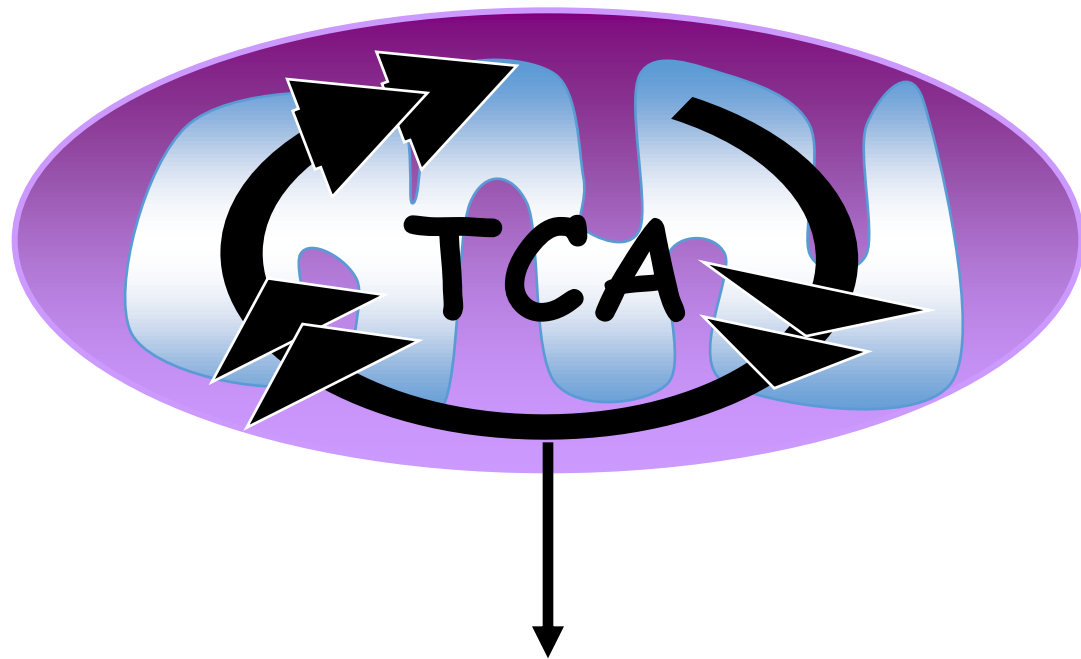


# Electron flux without proton pumping is NOT sufficient to alleviate energetic stress.

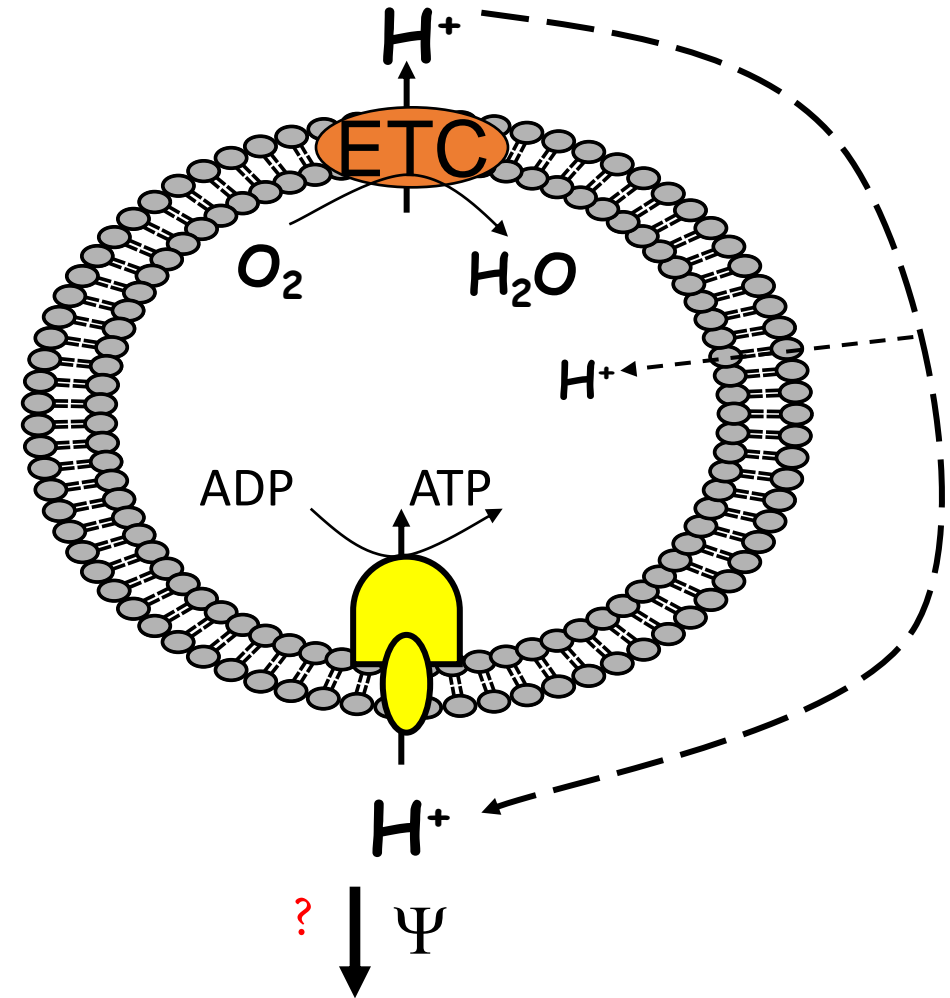
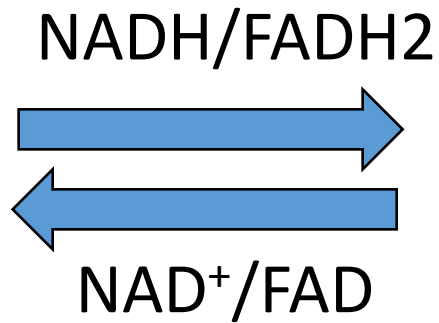
DN-POLG-AOX/NDI1



# Two functions of mitochondria: TCA cycle metabolites and membrane potential.



Histone Acetylation



Cell Proliferation

# Acknowledgements

## Chandel Lab

Nav Chandel

Sam Weinberg

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Manan Metha

Colleen Reczek

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## Collaborators

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Yingming Zhao

Ty Wang

Janine Santos

Eric Dufor

Hans Spelbrink

Ralph Deberardinis

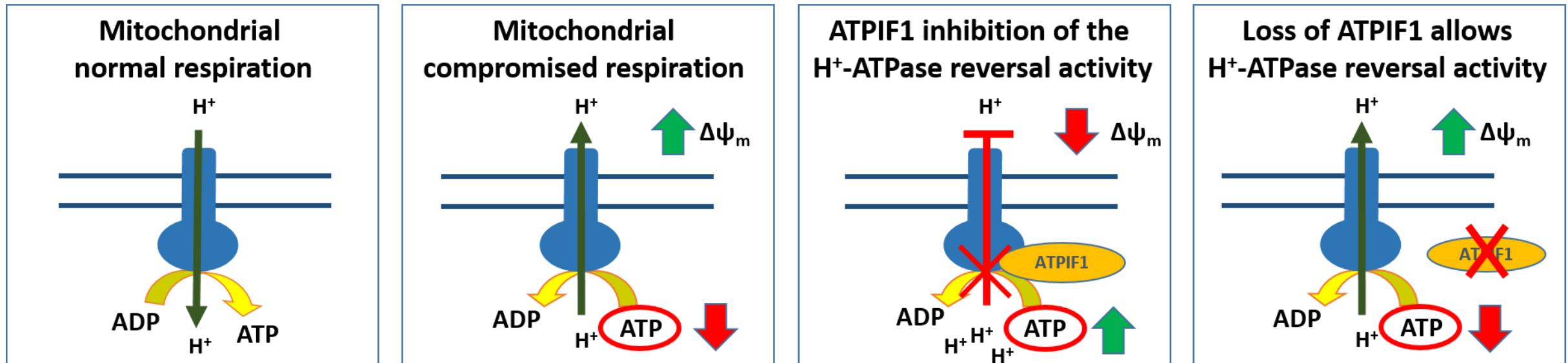


# Loss of ATPIF1 allows the maintenance of mitochondrial membrane potential

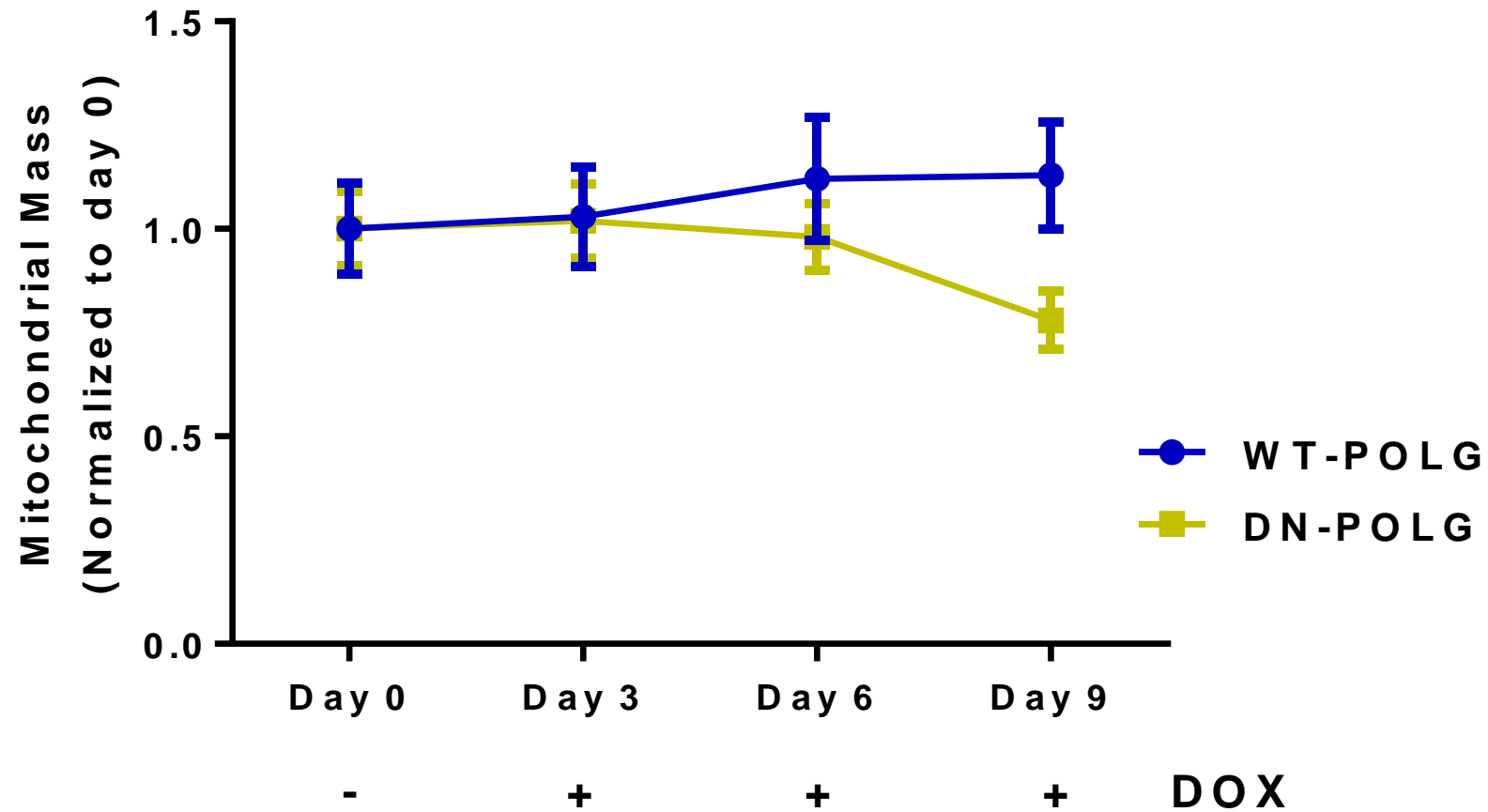
Cell Reports  
Report

## Inhibition of ATPIF1 Ameliorates Severe Mitochondrial Respiratory Chain Dysfunction in Mammalian Cells

Walter W. Chen,<sup>1,2,3,4,9</sup> Kıvanç Birsoy,<sup>1,2,3,4,9</sup> Maria M. Mihaylova,<sup>1,2,3,4</sup> Harriet Snitkin,<sup>6</sup> Iwona Stasinski,<sup>6</sup> Burcu Yucel,<sup>1,2,3,4</sup> Erol C. Bayraktar,<sup>1,2,3,4</sup> Jan E. Carette,<sup>7</sup> Clary B. Clish,<sup>3</sup> Thijn R. Brummelkamp,<sup>8</sup> David D. Sabatini,<sup>6</sup> and David M. Sabatini<sup>1,2,3,4,5,\*</sup>

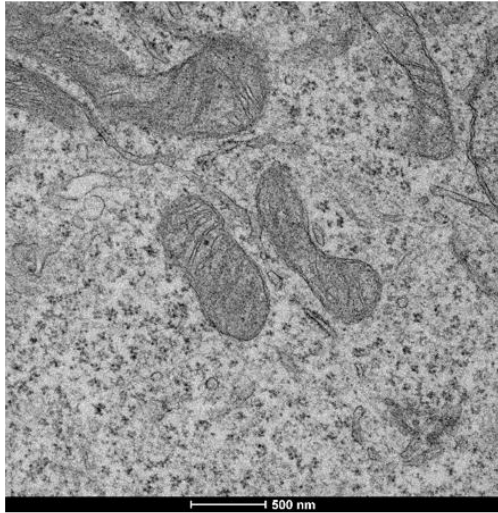


# Loss of mitochondrial DNA decreased mitochondrial mass.



# Loss of mitochondrial DNA alters mitochondrial morphology

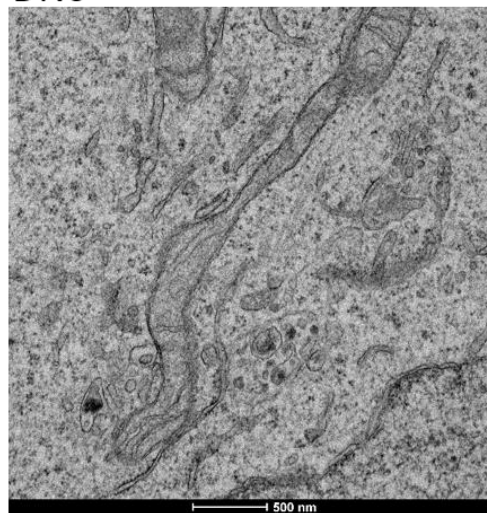
DN0



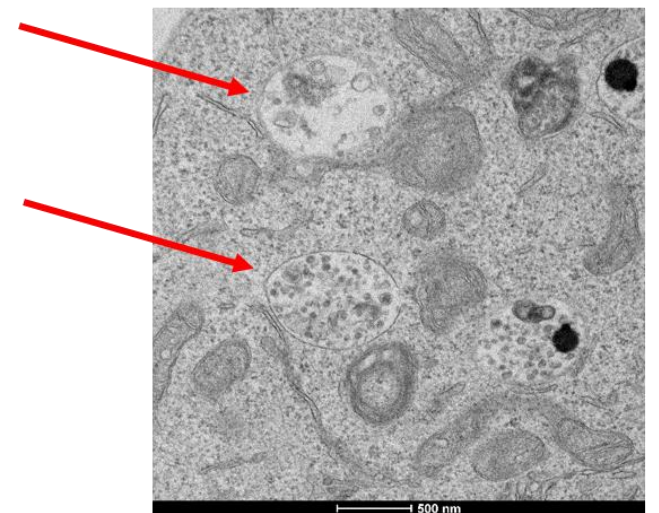
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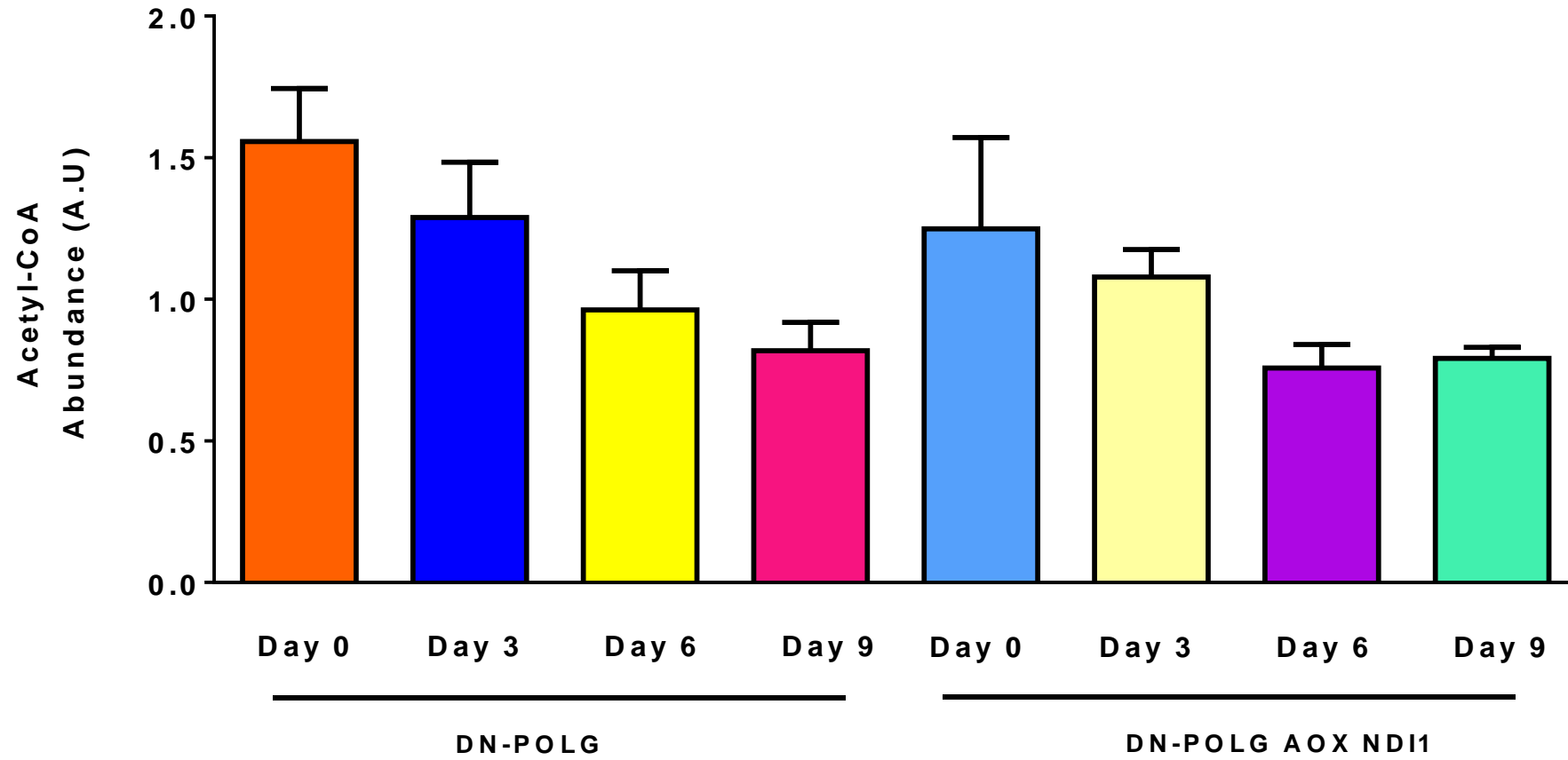


DN6



DN9







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