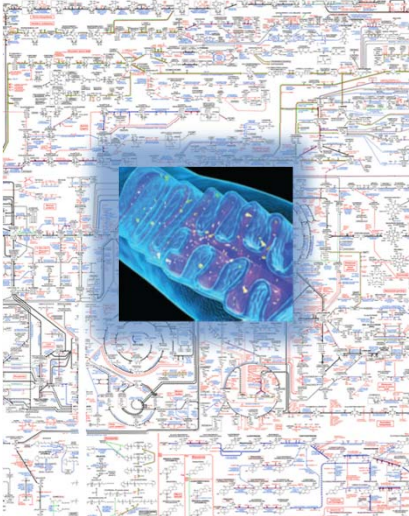



Metabolism and the extracellular flux bioanalyzer

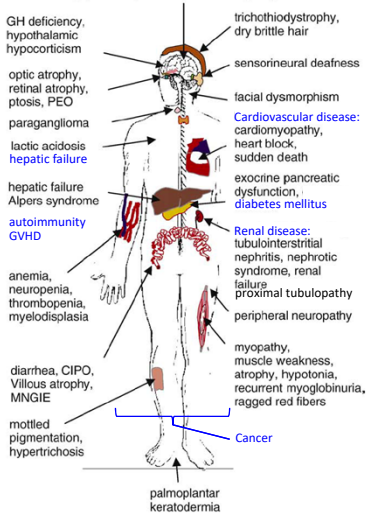
Jianhua Zhang
 Department of Pathology
 University of Alabama at Birmingham

2018

Bioenergetics and Metabolism



Neurodegeneration:
 Parkinson's, Huntington's, Alzheimers
 Hypotonia, cerebellar ataxia, leukodystrophy,
 Friedreich ataxia, hereditary spastic paraplegia,
 Leigh, MERRF, MELAS, Kearns-Sayre syndrome

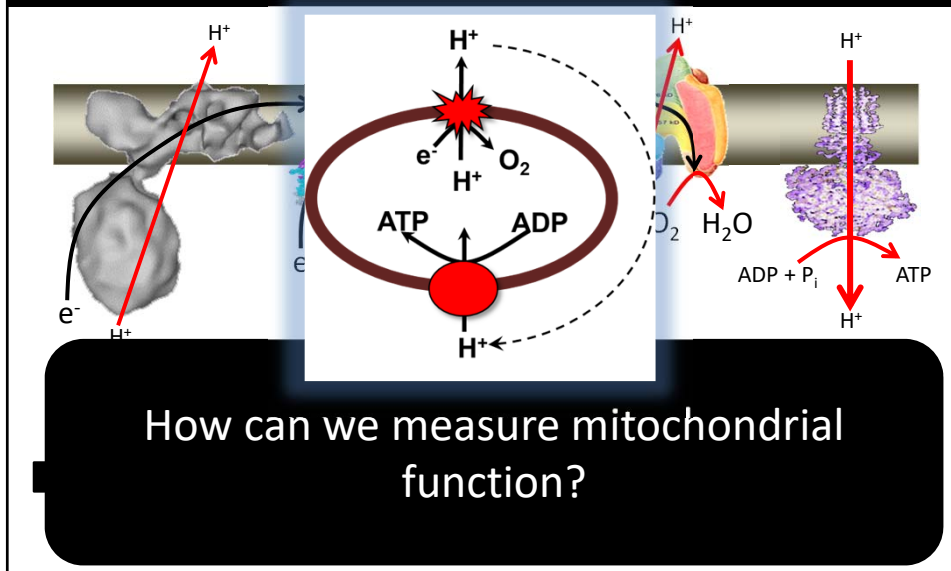


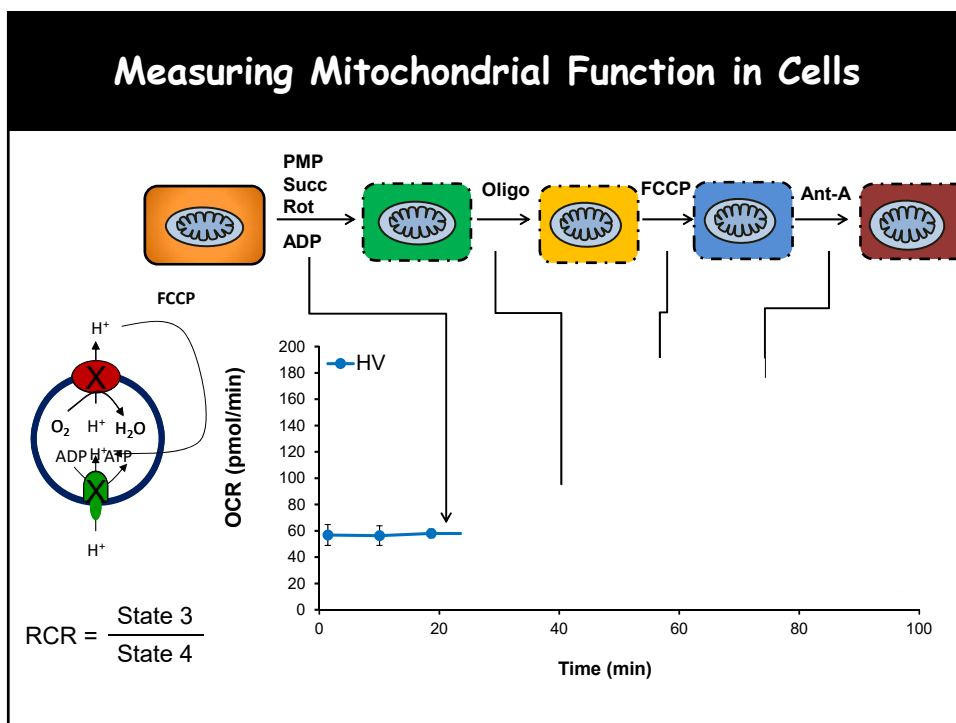
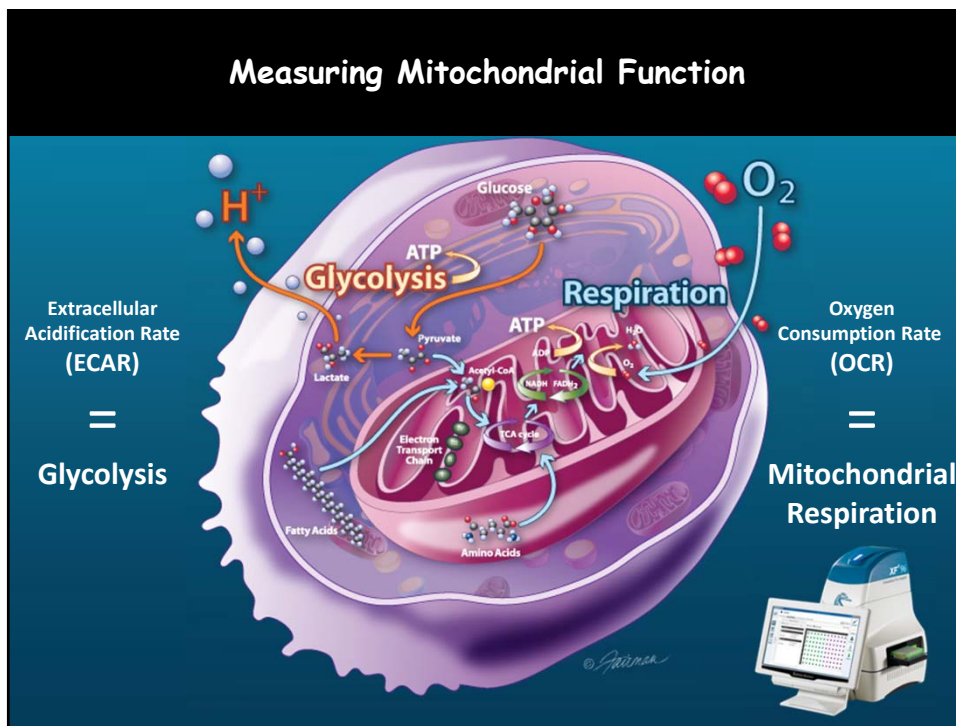
- GH deficiency, hypothalamic hypocorticism
- optic atrophy, retinal atrophy, ptosis, PEO
- paraganglioma
- lactic acidosis
- hepatic failure
- hepatic failure
- Alpers syndrome
- autoimmunity
- GVHD
- anemia, neuropenia, thrombopenia, myelodysplasia
- diarrhea, CIPO, Villous atrophy, MNGIE
- mottled pigmentation, hypertrichosis
- trichothiodystrophy, dry brittle hair
- sensorineural deafness
- facial dysmorphism
- Cardiovascular disease:**
cardiomyopathy, heart block, sudden death
- exocrine pancreatic dysfunction, **diabetes mellitus**
- Renal disease:**
tubulointerstitial nephritis, nephrotic syndrome, renal failure
- proximal tubulopathy
- peripheral neuropathy
- myopathy, muscle weakness, atrophy, hypotonia, recurrent myoglobinuria, ragged red fibers
- Cancer**
- palmoplantar keratoderma

Outline

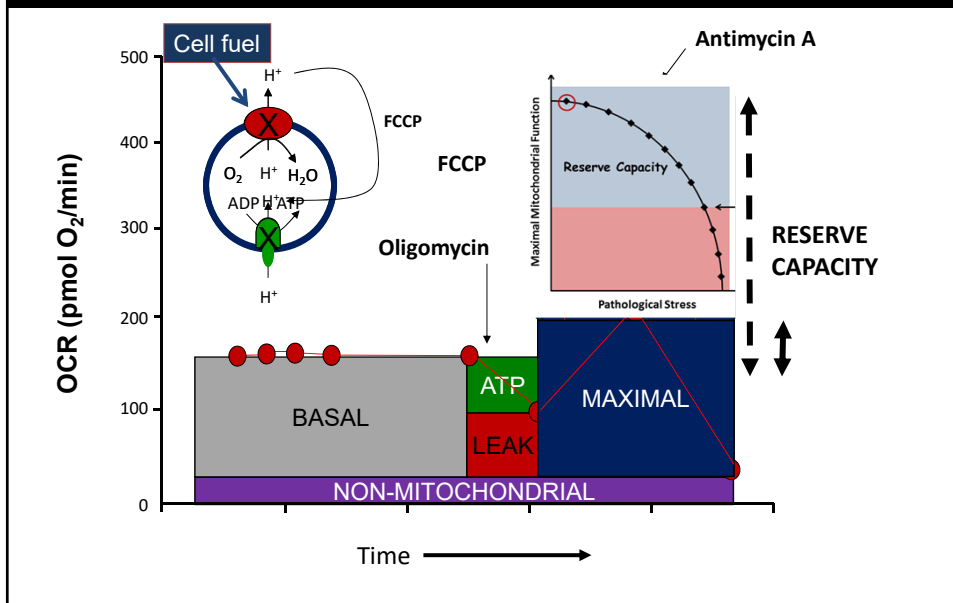
- how parameters of mitochondrial bioenergetics can be measured
- integrate with biology
- integrate with metabolomics

The Mitochondrial Electron Transport Chain

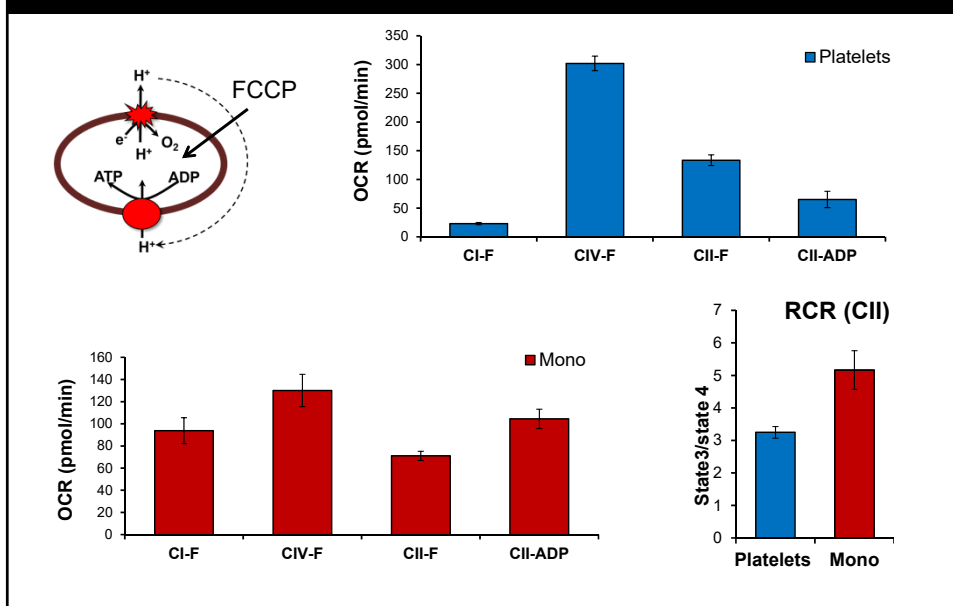


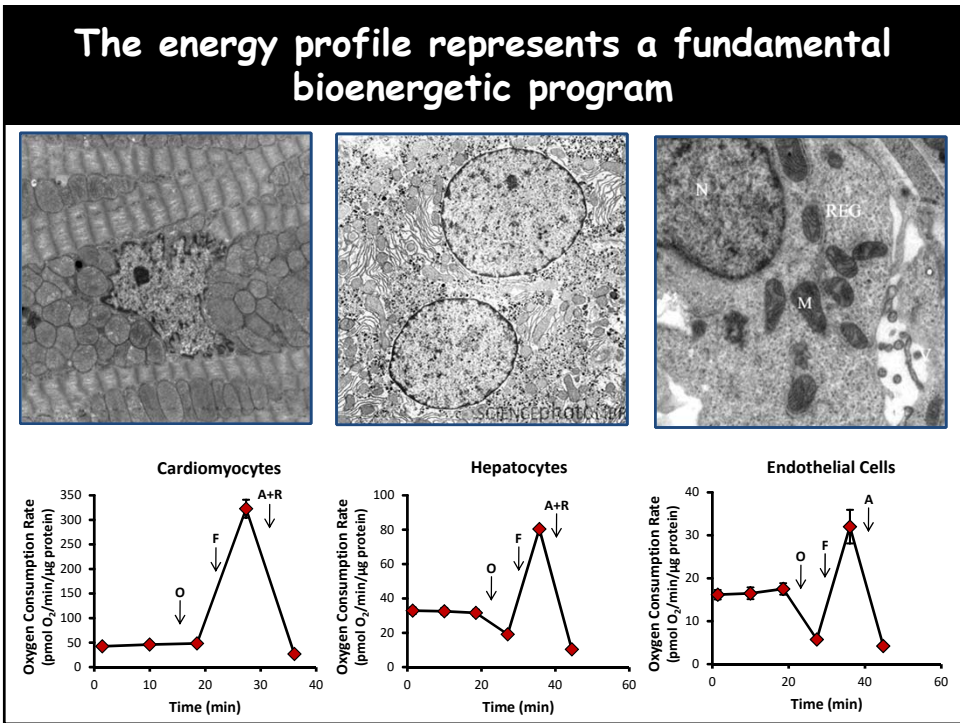
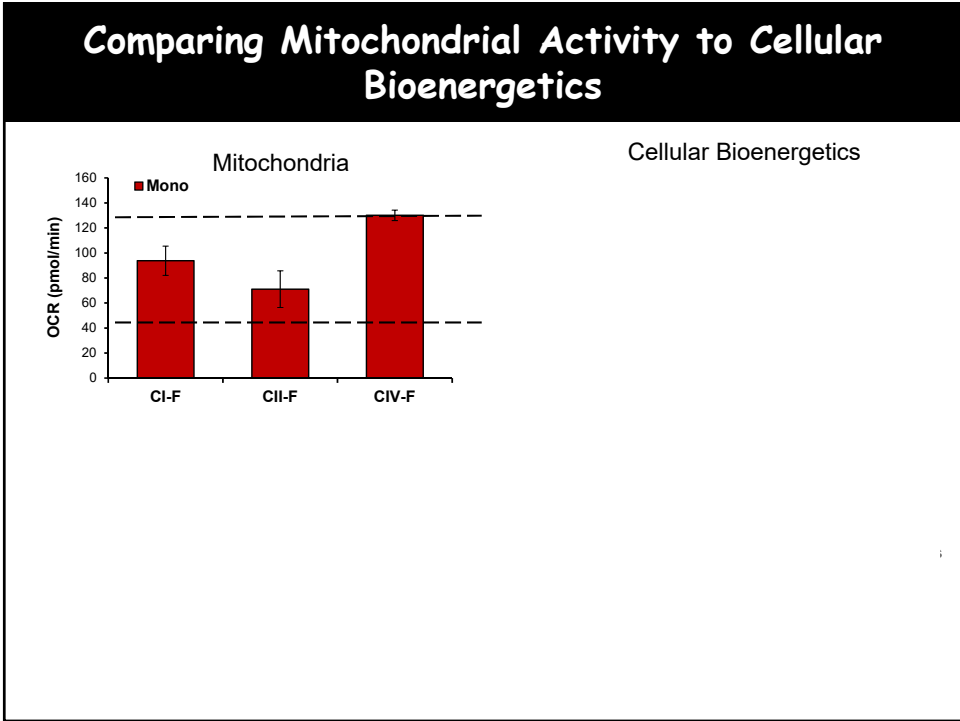


Letting the cell drive its own mitochondria

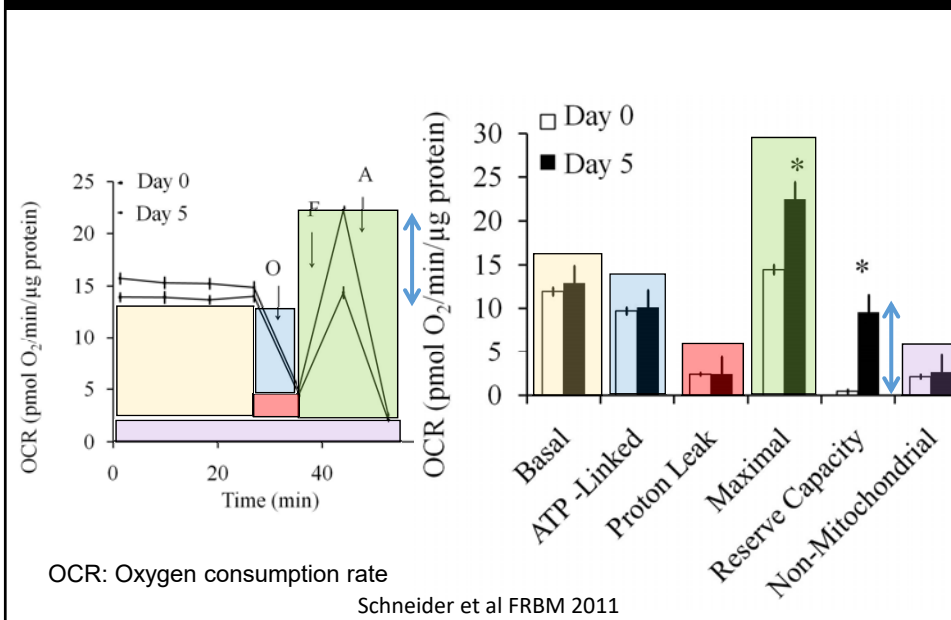


Measuring Mitochondrial Function in Cells

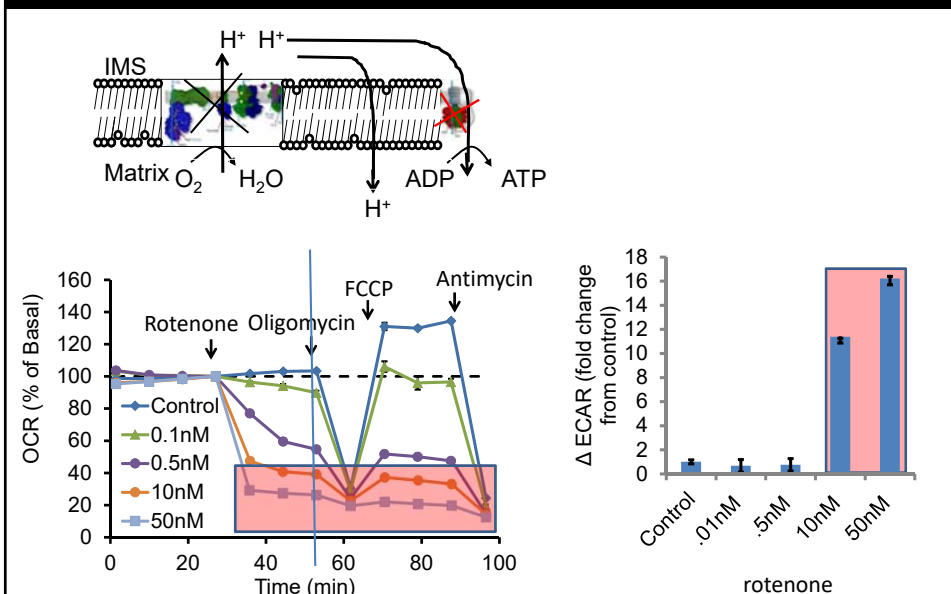




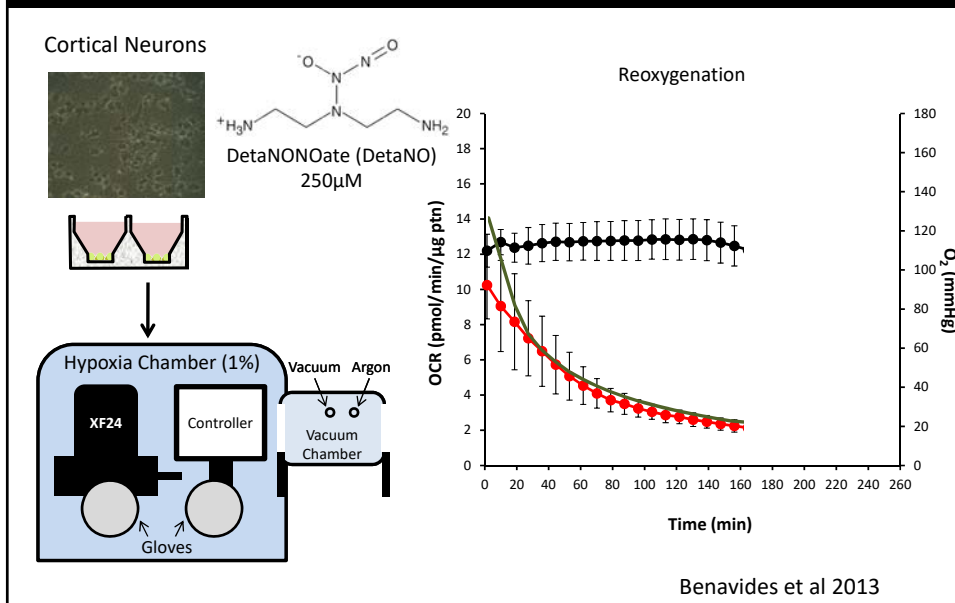
Differentiation changes cellular bioenergetics



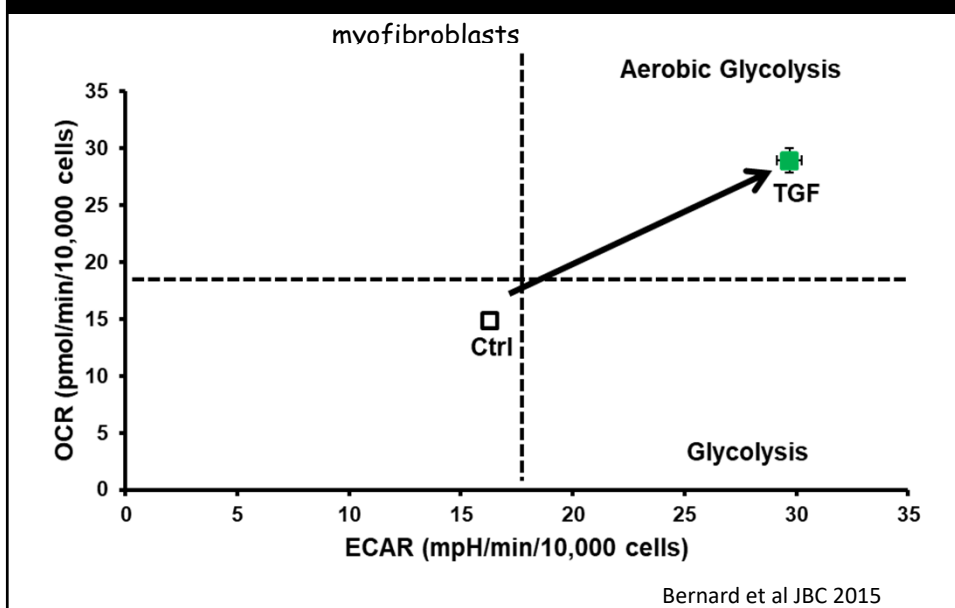
Inhibition of mitochondrial function induces compensatory upregulation of glycolysis

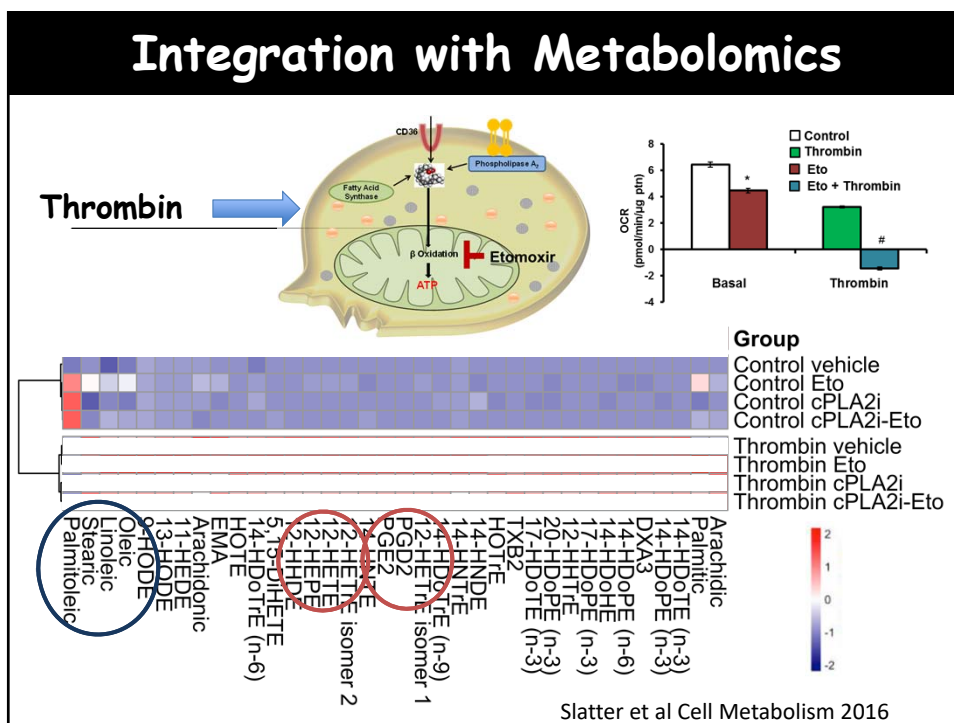
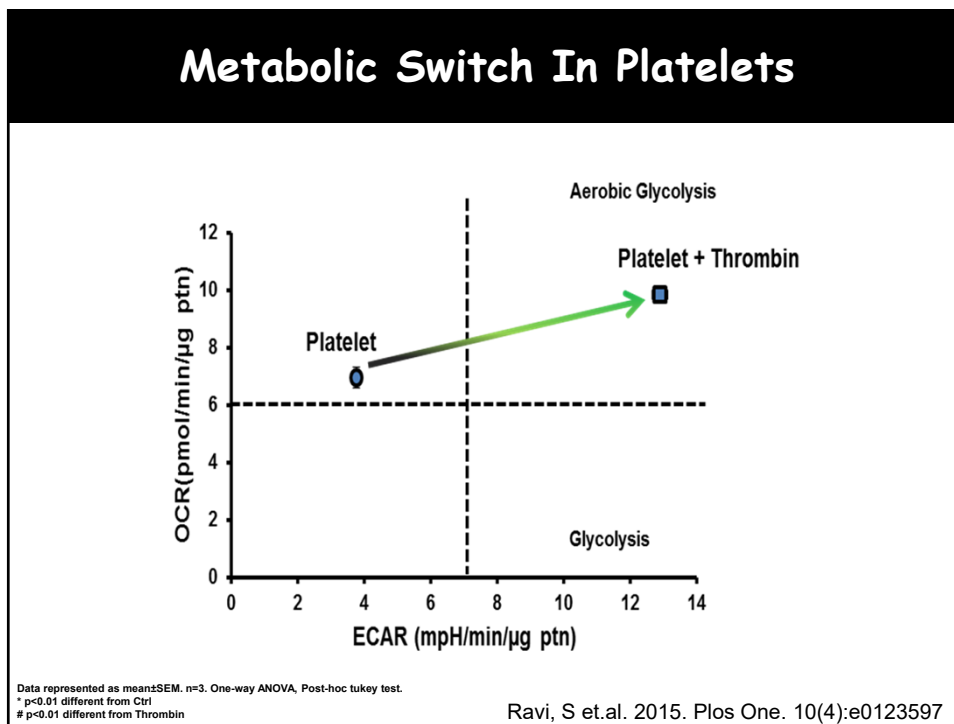


Effects of NO on OCR during hypoxia-reoxygenation

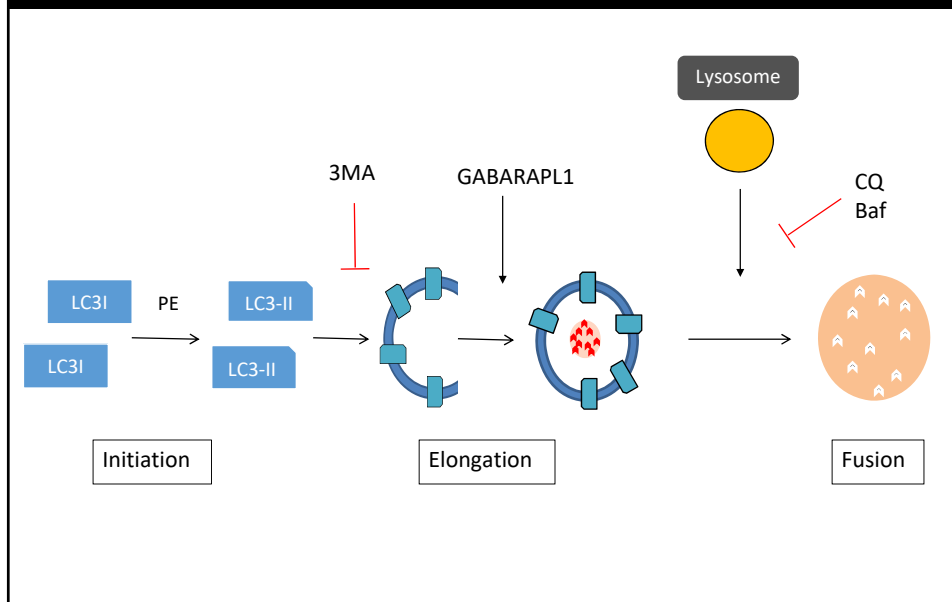


Metabolic Plasticity in Lung

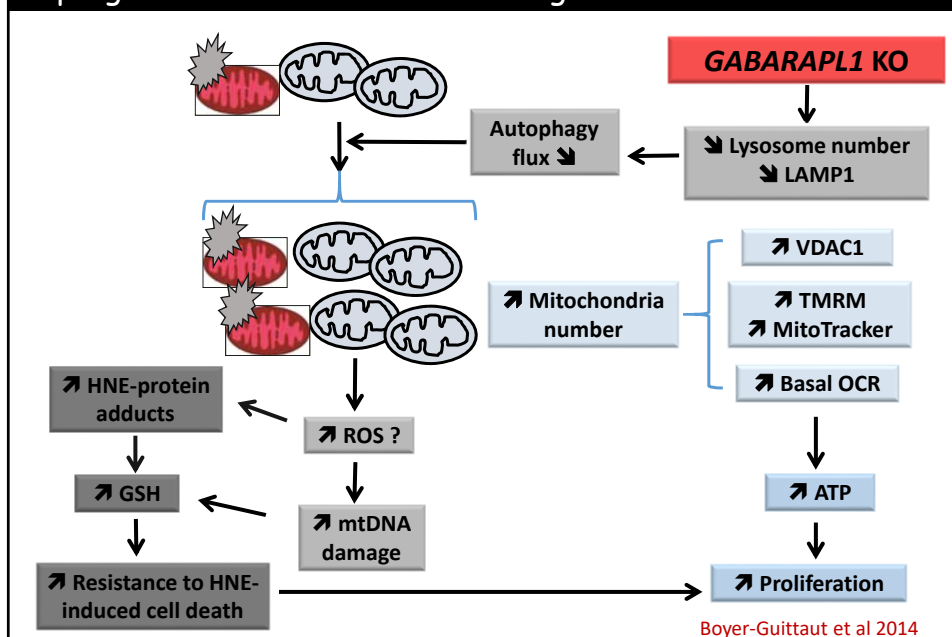




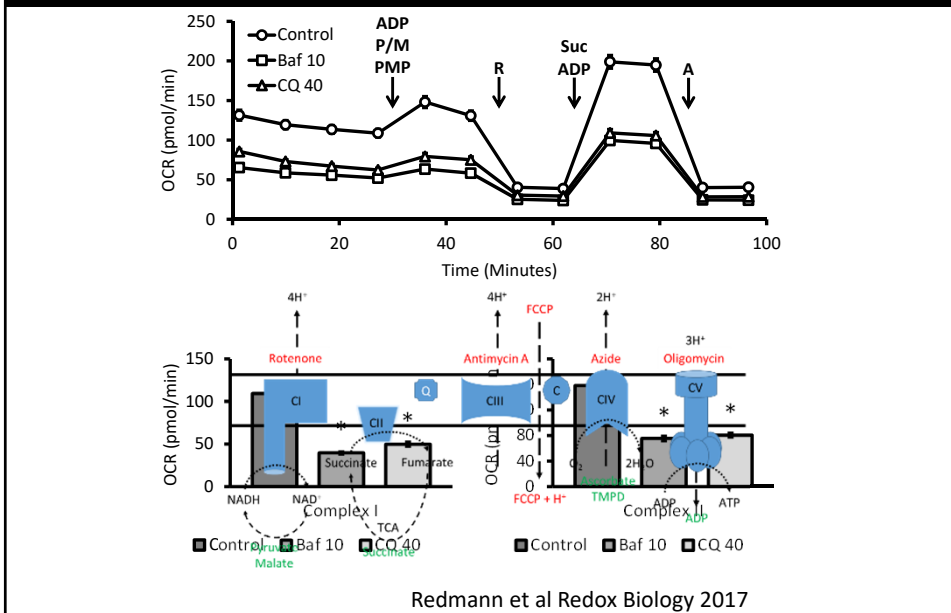
Mitochondrial Quality Control and Autophagy



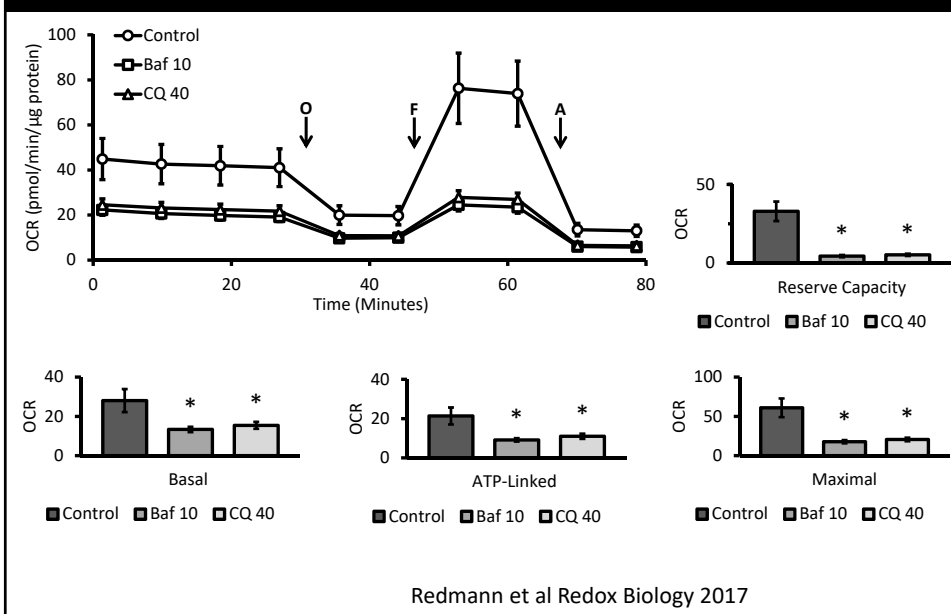
Downregulation of autophagy reprograms redox tone and bioenergetic health in cancer cells

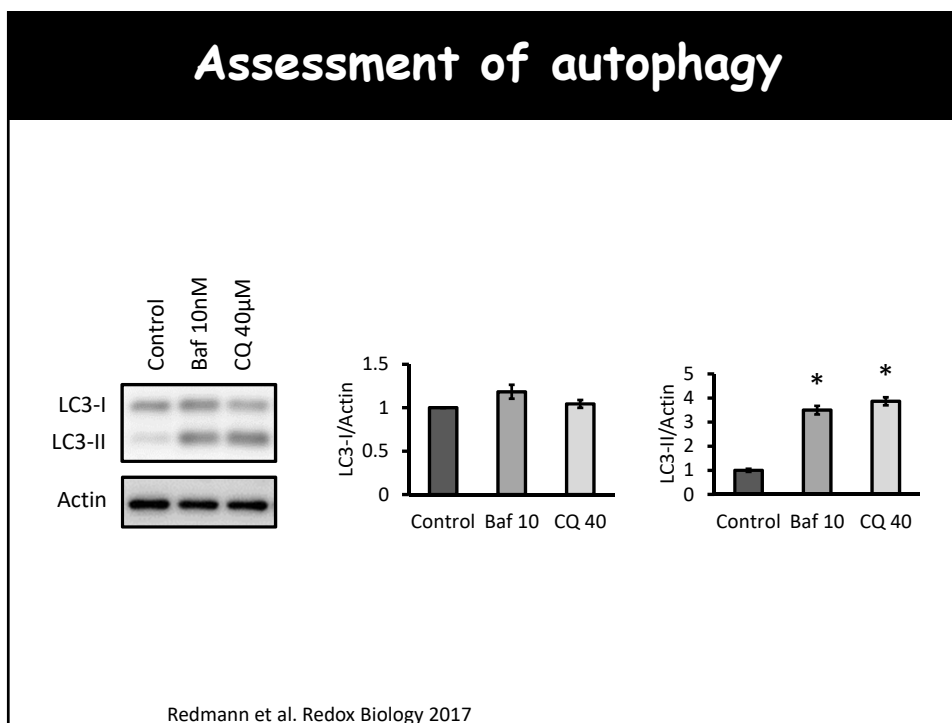
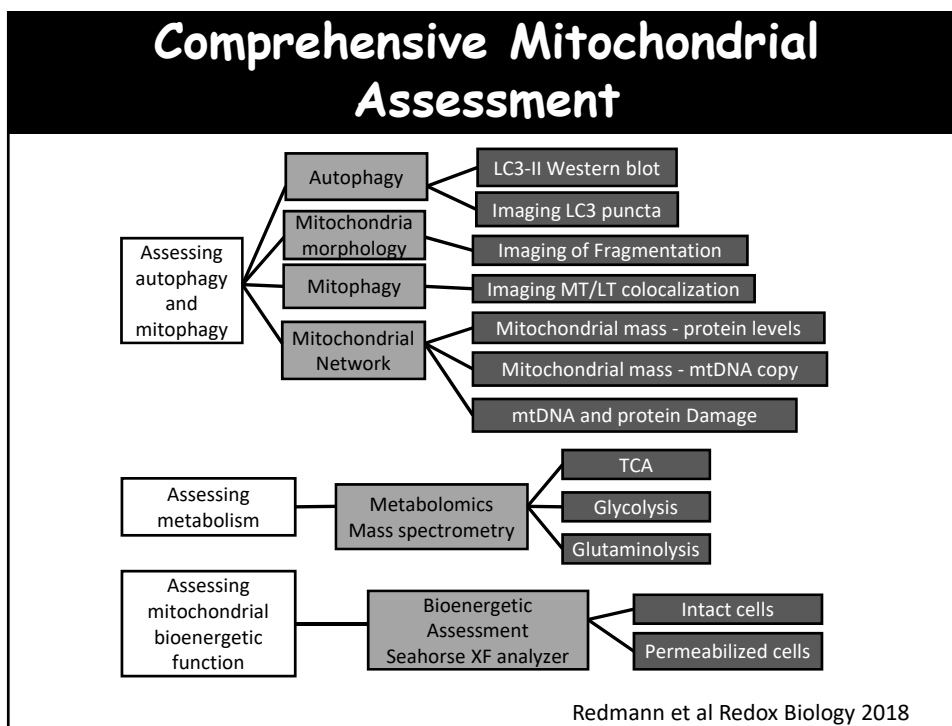


Autophagy inhibition suppresses complexes I and II activities in permeabilized primary neurons

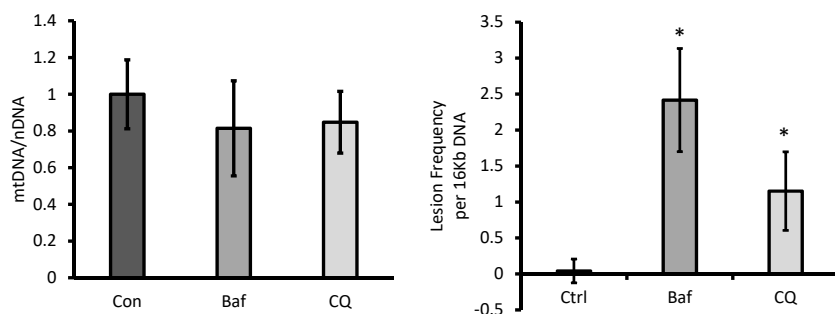


Autophagy inhibition suppresses mitochondrial function in primary neurons



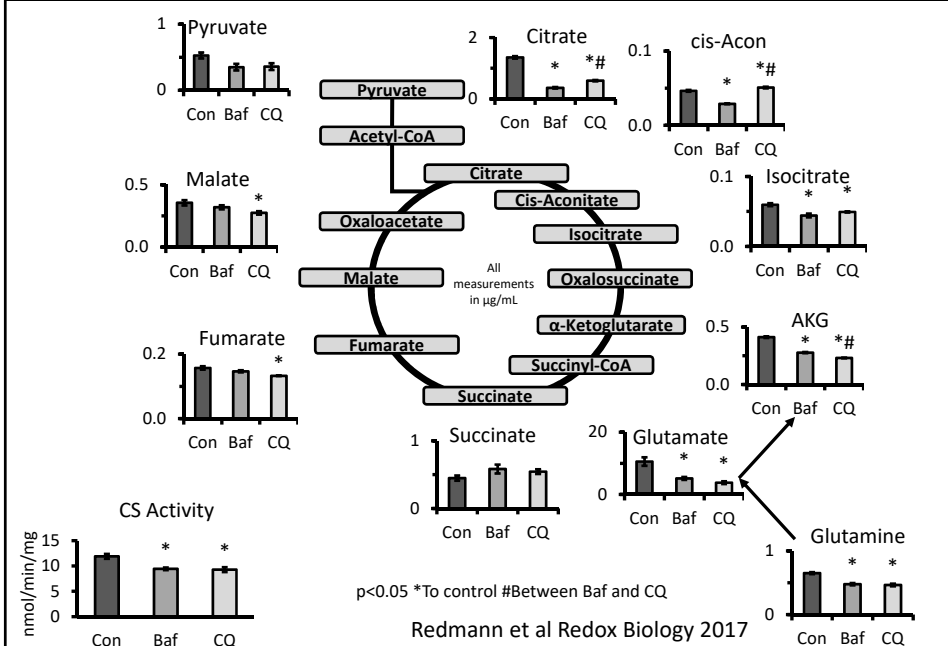


No change of mitochondrial mass but significant increase of mitochondrial DNA damage in response to autophagy inhibition



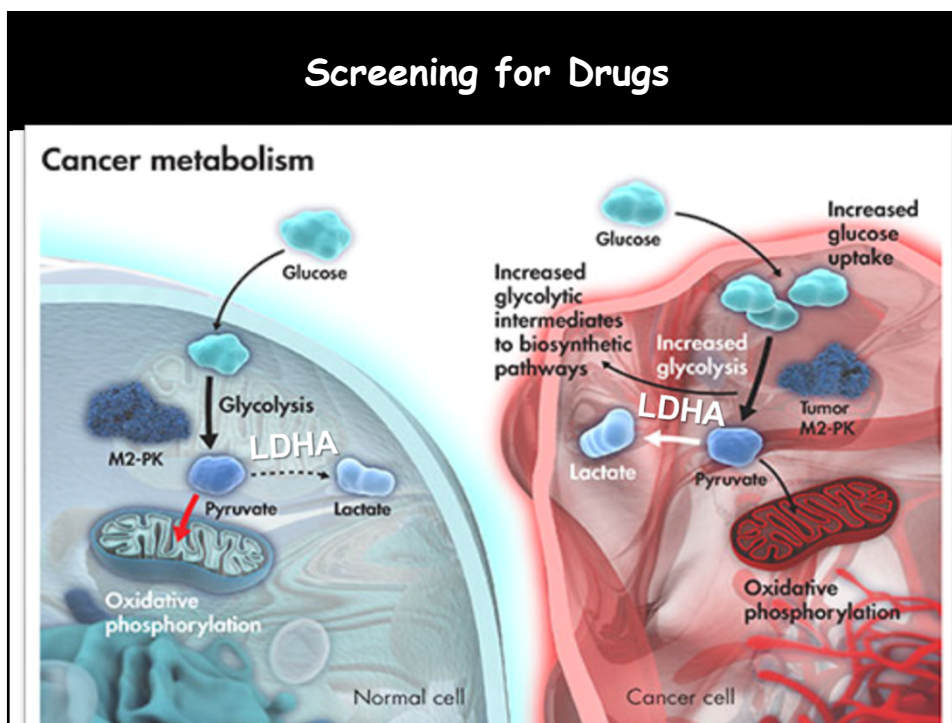
Redmann et al. Redox Biology 2017

Integration with Metabolomics

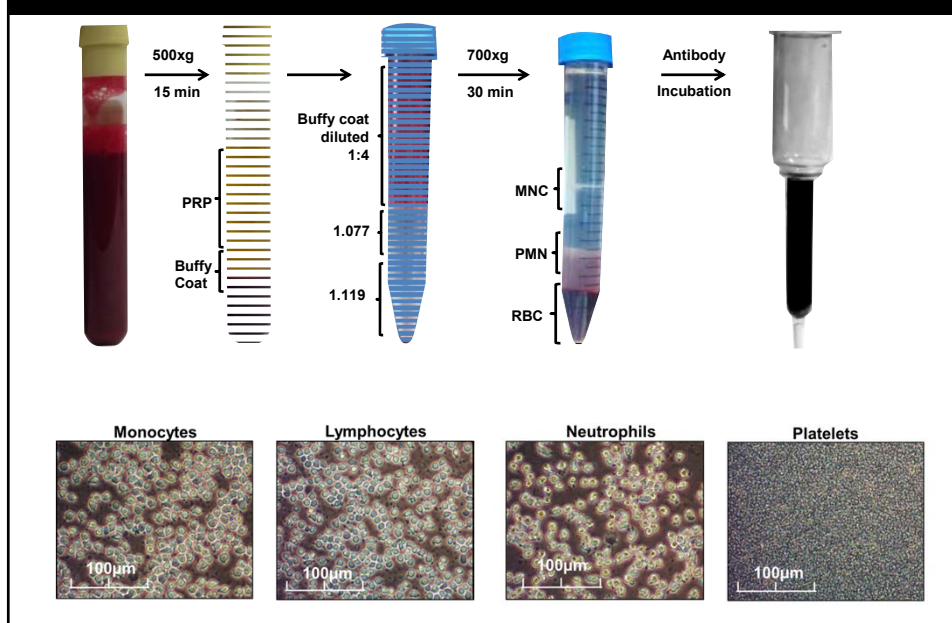


Redmann et al Redox Biology 2017

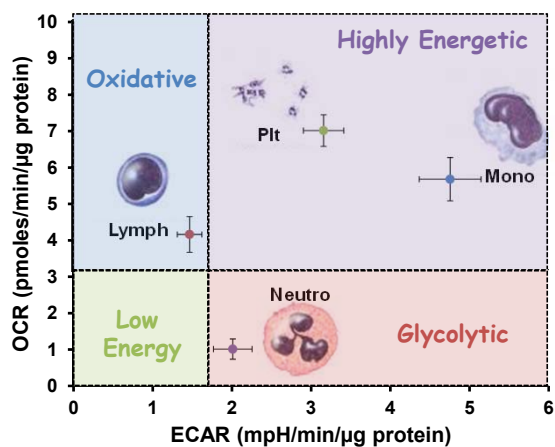
Screening for Drugs



From Human Blood; 4 Bioenergetic Programs



Energy mapping of leukocyte and platelets



- PBMCs are a mixed population with different metabolic programs

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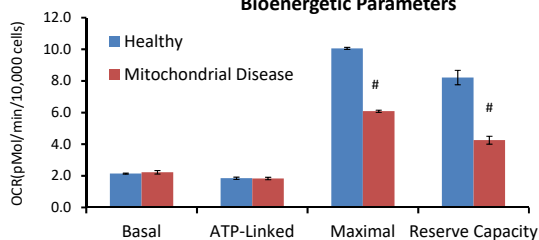
Mitochondrial defect in patients

38 year old Male
Episodes of
extreme fatigue

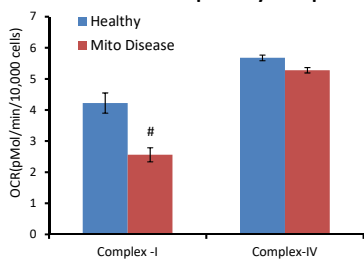


Monocytes

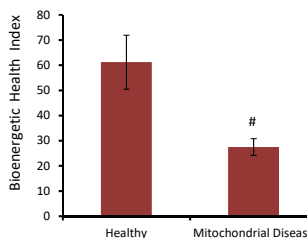
Bioenergetic Parameters



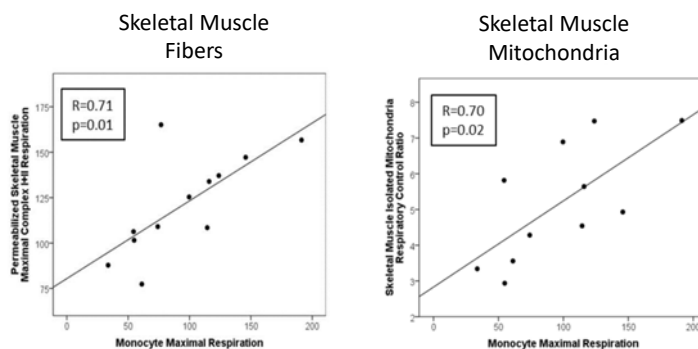
Mitochondrial Respiratory Complexes



Bioenergetic Health Index

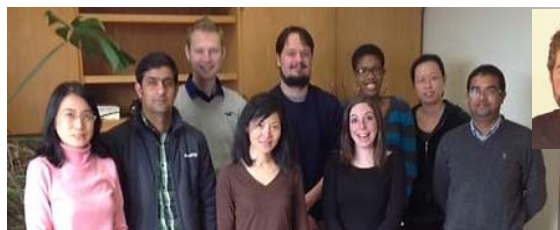


Monocyte energetics vs skeletal muscle (vastus lateralis)



Anthony Molina: Wake Forest School of Medicine
Redox Biology, 2016

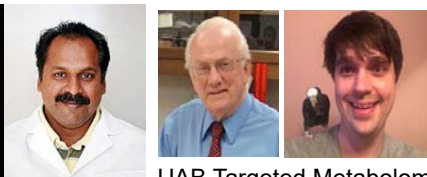
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& Proteomics Laboratory
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