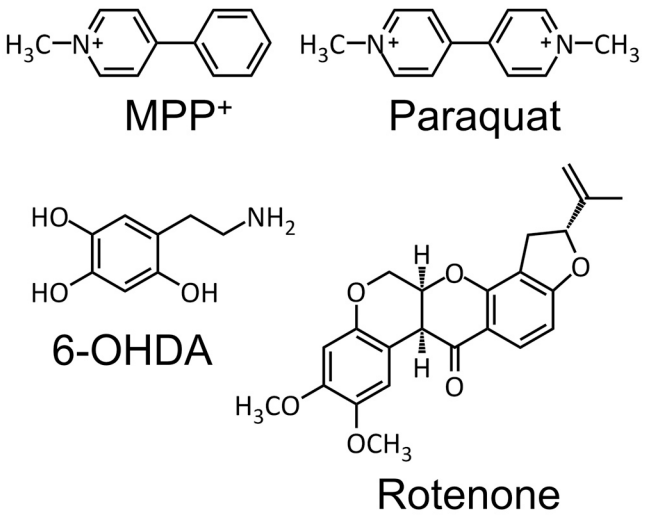
**Supplemental Information**

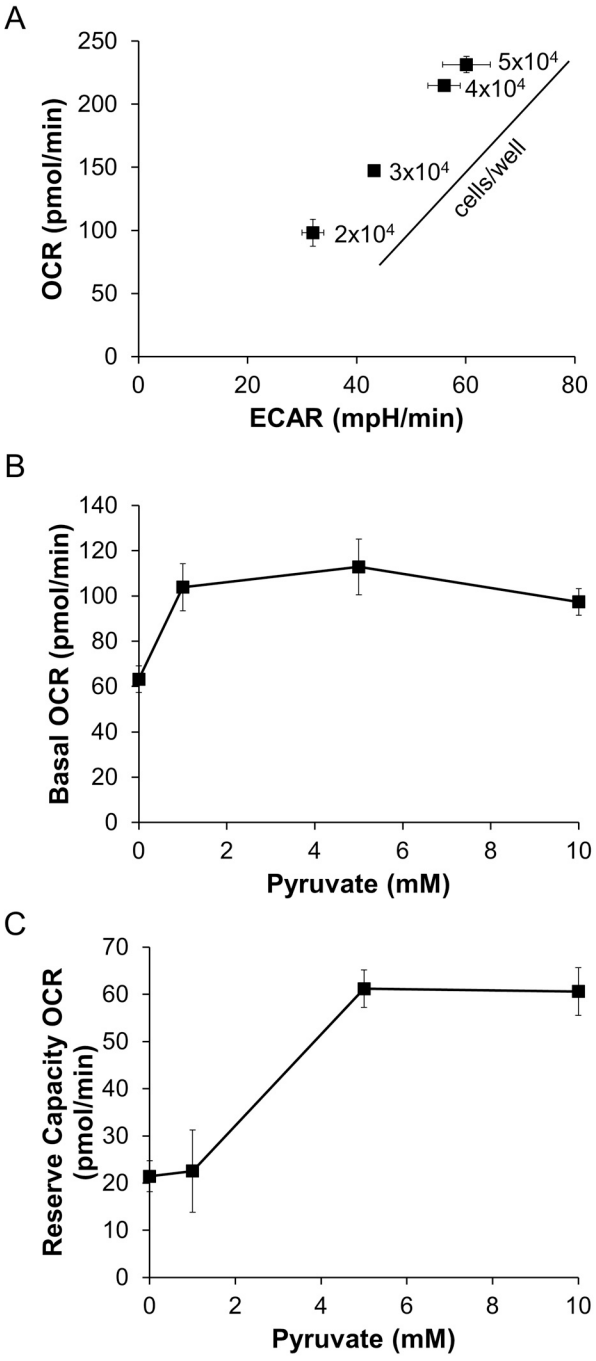
**Supplemental Figure 1: Structures of compounds used in this study.** The chemical structure of $MPP^+$, rotenone, 6-OHDA, and paraquat are shown.

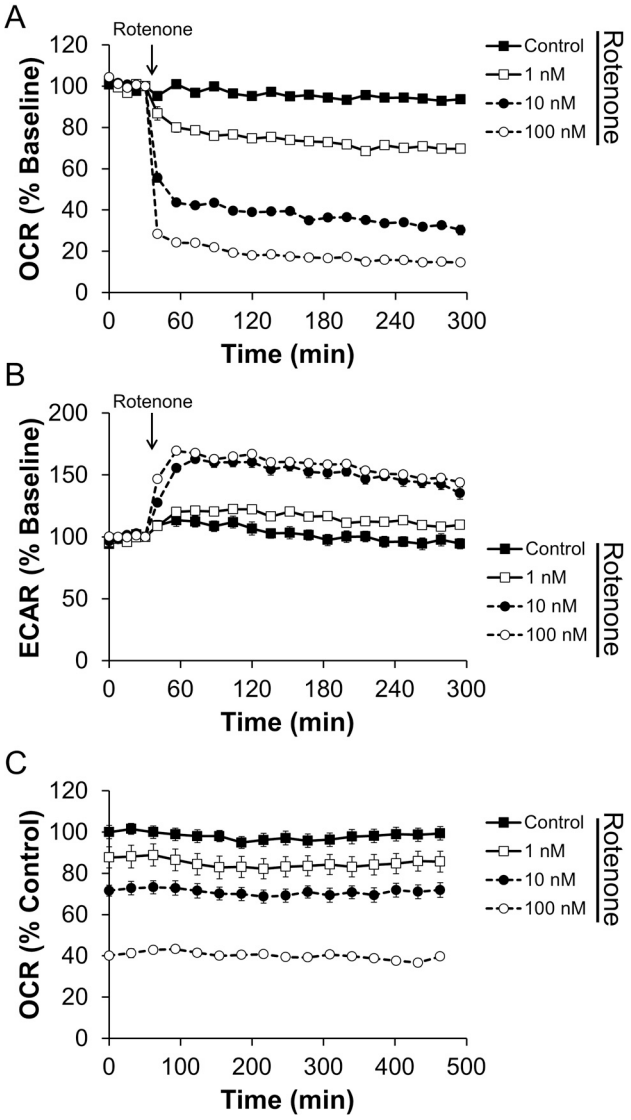
**Supplemental Figure 2: N27 cell seeding optimization.** N27 cells were seeded to $2x10^4$, $3x10^4$, $4x10^4$, or $5x10^4$ cells/well as indicated in Seahorse Bioscience V7 tissue culture plates. The cells were allowed to incubate for 24 h and then basal OCR and ECAR measurements were recorded (Panel A). N27 cells were seeded to $4x10^4$ cells/well and allowed to incubate for 24 h. The cells were then washed and changed to assay media containing 0, 1, 5, or 10 mM sodium pyruvate. After 1 h incubation in a non-$CO_2$ incubator mitochondrial function was assessed. Basal OCR (Panel B) and reserve capacity (Panel C) were calculated. Data shown are the mean ± sem. n=5 per treatment group.

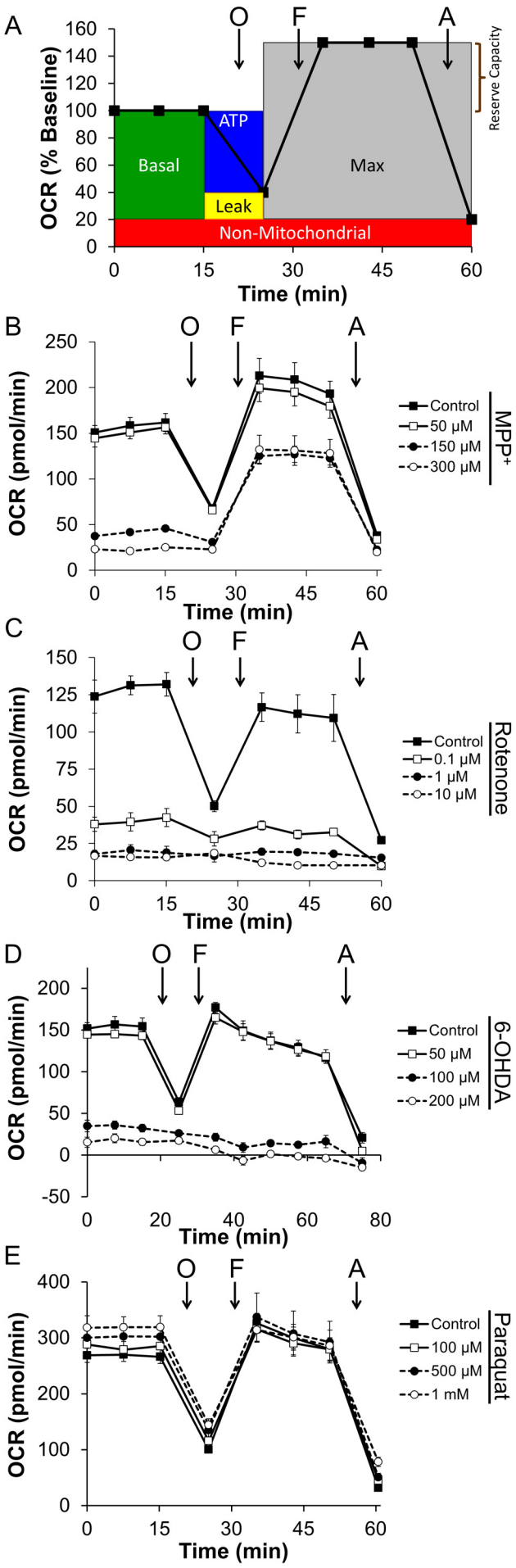
**Supplemental Figure 3: Effects of low dose rotenone on mitochondrial function.** N27 cells were seeded to $4x10^4$ cells/well in Seahorse Bioscience V7 culture plates. The indicated concentration of rotenone was injected after 5 baseline OCR and ECAR measurements, and OCR (Panel A) and ECAR (Panel B) were monitored for an additional 4 h. In a separate experiment, cells were treated with the indicated concentration of rotenone for 4 h. The cells were then washed 2x with serum free media, and OCR was monitored for 8 h. Data shown are the mean ± sem. n=5 per treatment group.

**Supplemental Figure 4: Effects of $MPP^+$, rotenone, 6-OHDA, and paraquat on mitochondrial function.** The experimental scheme is shown in Panel A. After at least three baseline measurements of OCR, oligomycin, FCCP, and antimycin A are injected in sequence. The indicated parameters of mitochondrial function are indicated on this graph. The effects of $MPP^+$, rotenone, 6-OHDA, and paraquat on mitochondrial function are shown in Panels B, C, D, and E respectively. Data shown are the means ± sem. n=5 per treatment group.


MPP+
Paraquat
6-OHDA
Rotenone


A
OCR (pmol/min)
ECAR (mpH/min)
5x10^4
4x10^4
3x10^4
2x10^4
cells/well
B
Basal OCR (pmol/min)
Pyruvate (mM)
C
Reserve Capacity OCR (pmol/min)
Pyruvate (mM)


A
Rotenone
OCR (% Baseline)
Time (min)
Control
1 nM
10 nM
100 nM
Rotenone
B
Rotenone
ECAR (% Baseline)
Time (min)
Control
1 nM
10 nM
100 nM
Rotenone
C
OCR (% Control)
Time (min)
Control
1 nM
10 nM
100 nM
Rotenone


A
O
F
A
OCR (% Baseline)
Reserve Capacity
ATP
Basal
Max
Leak
Non-Mitochondrial
Time (min)
B
OCR (pmol/min)
Control
50 μM
150 μM
300 μM
MPP+
C
Control
0.1 μM
1 μM
10 μM
Rotenone
D
Control
50 μM
100 μM
200 μM
6-OHDA
E
Control
100 μM
500 μM
1 mM
Paraquat