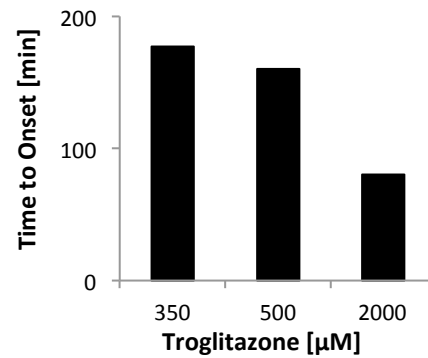
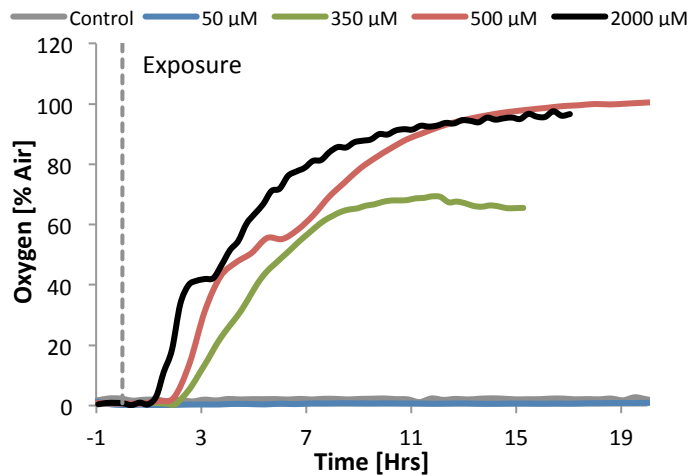
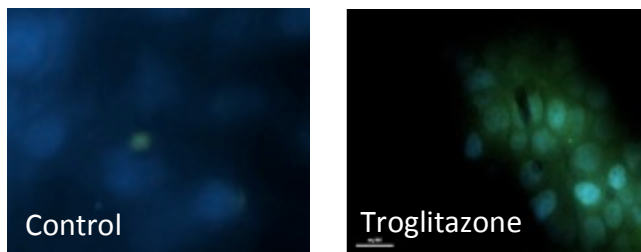


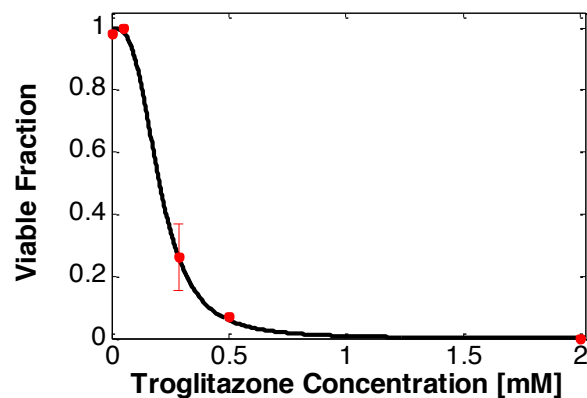
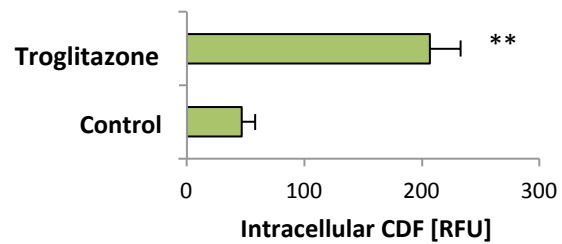
Real Time evaluation of metabolic function during constant drug exposure carried out on HepG2-C3A hepatocytes aggregates. Exposure carried out for 24 hours.



Cholestasis



CDFDA / Hoechst



Results:

$\text{TC}_{50} = 204 \pm 33 \mu\text{M}$

Time to Onset = 80 to 177 min

Staining for cholestasis conflict with the rapid change of function observed in *real time*, suggesting primary mechanism of damage may be more direct.

Goodness of fit:

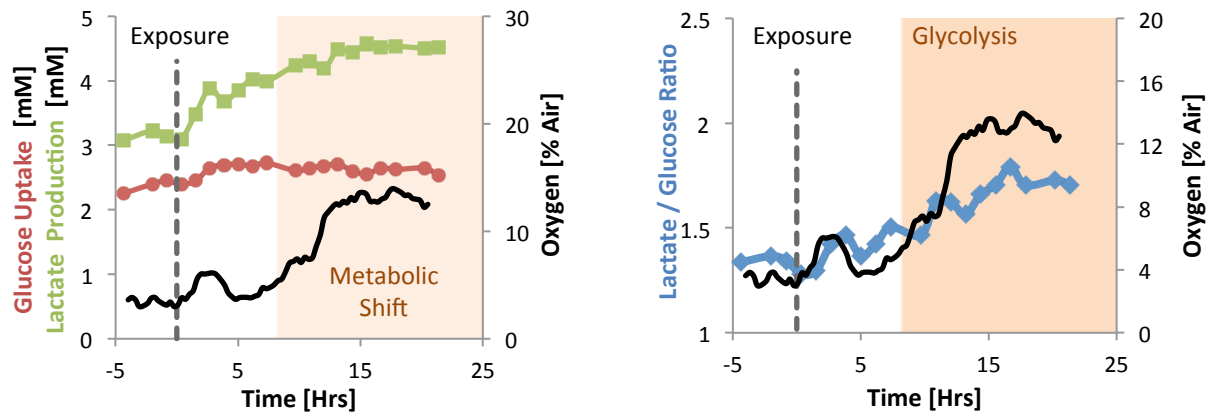
SSE: 0.0005957

R-square: 0.9994

Adjusted R-square: 0.9992

RMSE: 0.01409

Real time metabolic analysis carried out on HepG2/C3A hepatocyte aggregates exposed to 50 μM troglitazone. Cell viability throughout was greater than 90%



Calculated metabolic fluxes in $\text{nmol}/\text{min}/10^6$ cells untreated cells (control) and cells exposed to troglitazone for 15 hours. ATP production of troglitazone-exposed cells is within 97% of untreated cells.

Pathway	Control (0h)	Troglitazone (15h)	Comments
Glycolysis	1.49	2.25	51% increase
Respiration	0.31	0.25	20% decrease
Glutaminolysis	0	0.02	Minor contribution
Lipogenesis	0.62	0	Indication for long-term accumulative damage

