

CellSine

Case Study

Case: Hepatocyte toxicity

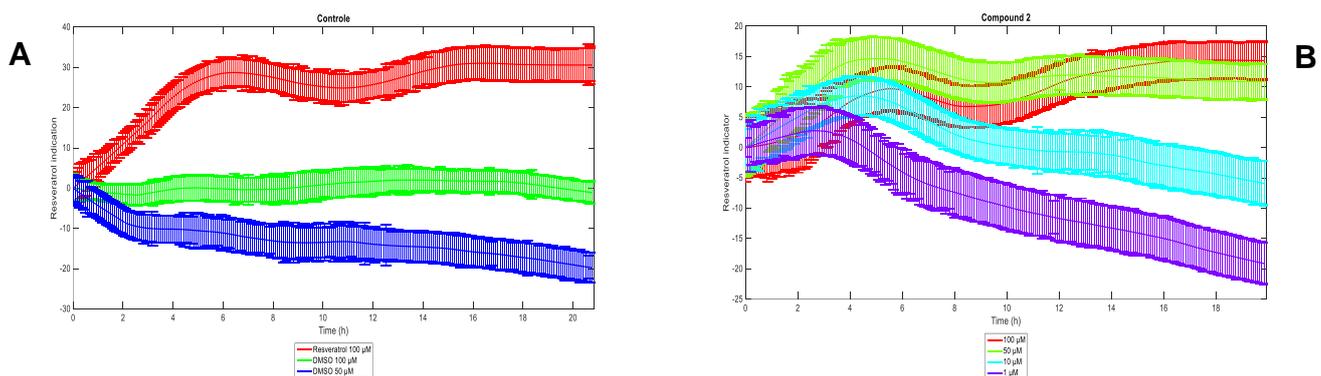
Metabolic syndrome is a condition that comprises insulin resistance, high triglycerides, high blood pressure and non-alcoholic steatohepatitis (NASH). The condition is often associated with diabetes and obesity. Numerous efforts have been undertaken to tackle the condition, but success rates are low.

Resveratrol, a stilbene compound produced by many plants is considered as a potent inhibitor of the metabolic syndrome. The compound can be found in high concentration in red wines and has been considered a key player in the “French paradox”. The latter theory states that the typical rich French diet needs to be counteracted in some way to explain the low incidence of cardiovascular diseases, diabetes and obesity in France.

Several *in vivo* studies have demonstrated the protective role of resveratrol against the different aspects of the metabolic syndrome and ever since, the search for compounds with similar activities has begun. However, since resveratrol activates (e.g. SIRT) and inhibits (e.g. NQO2) numerous molecular pathways at the same time, it is difficult to build a high throughput assay to screen for the phenotypic characteristics of resveratrol.

Results:

We have built an impedance based high throughput assay to monitor for the resveratrol phenotypic effect, based on a key hallmark of resveratrol: the ability to protect hepatocytes against toxic concentrations of ethanol, triglycerides and sugar. The assay was validated with a compound library from which known SIRT activators and NQO2 inhibitors could be identified in a blind way.



Figures: panel A shows the typical impedance profile of resveratrol on HepG2 cells treated with 10% ethanol. Panel B shows the effect of a compound that was tested in a blinded way and that was considered to have a resveratrol like mode of action. Gene expression studies confirmed this effect.

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