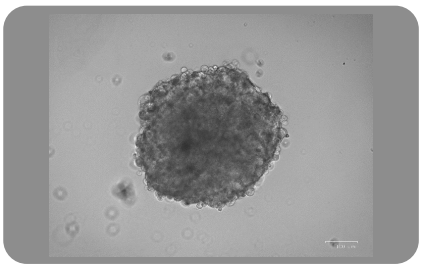
PATROLS

Advanced Tools for NanoSafety Testing

Enhancing the Physiological Relevance of a 3D *In Vitro* Liver Model for Engineered Nanomaterial Hazard Assessment

Due to the expanding use of nanotechnology in consumer applications, human and environmental exposure to engineered nanomaterials (ENM) is inevitable. Liver toxicology is important when considering ENM exposure as it is the a major site of ENM deposition and accumulation post exposure. The vast range of ENMs available makes it untenable to rely solely on animal based methods to fully comprehend the immediate and lasting effects of ENM exposure. The PATROLS project has therefore developed a 3D liver model that has the potential to be an alternative test system to to better understand health hazards associated with hepatic ENM exposure and help reduce the reliance on animal testing approaches.



Interlaboratory validated model displaying good concordance with no significant difference between the two data sets (Figure 1).

Relatively inexpensive 3D cell-line based model adapted to simulate human physiology.

Able to support acute (≤24 hours), prolonged (≥ 14 days) and/or repeated ENM exposure regimes

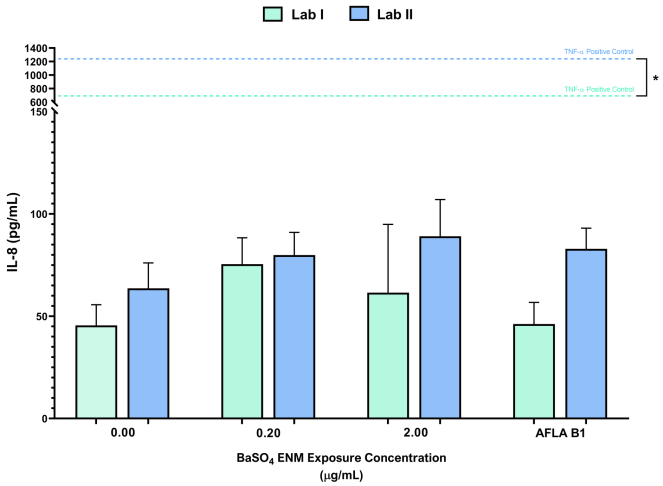


Figure 1: (Pro-)inflammatory IL-8 response in 3D HepG2 liver spheroids, following prolonged exposure to Barium Sulfate (BaSO) ENMs, across two independent academic laboratories; Lab I = Swansea University and Lab II = Heriot Watt University. Mean data + SD presented. Statistical significance indicated as follows: * = $p < 0.05$.

1. Advanced 3D *in vitro* liver model able to support a range of toxicity endpoints for ENM hazard assessment (*e.g.* pro-inflammatory response, cell death and DNA damage).

2. Successful interlaboratory trial highlights the transferability and reproducibility of this 3D model.

3. This innovative 3D liver model could provide a potential alternative test system to help reduce the reliance on animal based methods.

4. Standard operating protocols are available and openly accessible, including those for the application of this model.

This factsheet is based on the publication Llewellyn, S. V., Conway, G. E., Shah, U. K., Evans, S. J., Jenkins, G. J. S., Clift, M. J. D., Doak, S. H. Advanced 3D Liver Models for *In vitro* Genotoxicity Testing Following Long-Term Nanomaterial Exposure. J. Vis. Exp. (160), e61141, doi:10.3791/61141 (2020).

www.patrols-H2020.eu

This project has received €12.7M in funding from the European Union's Horizon 2020 research and innovation programme under grant agreement 760813