PATROLS

Advanced Tools for NanoSafety Testing

Introduction

Exposure to engineered nanomaterials (ENM) poses a potential risk to human and environmental health and current ENM hazard assessment studies conducted have focused on short term, high-dose exposures on simple 2D *in vitro* test systems and a small selection of organisms. Both of which are deemed to lack environmental realism in terms of dose delivery, exposure duration and biological complexity.

PATROLS Project Aim:

Establish and standardise a battery of innovative, next generation **hazard assessment** tools that **more accurately predict** adverse effects caused by **long-term (chronic), low dose** ENM exposure in human and environmental systems to **support regulatory risk decision making** and help **reduce** the need for **animal testing**.

Work Package 1

ENM acquisition, identification & exposure assessment

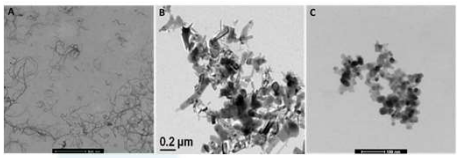


Figure 1. TEM images of (A) Multi-Walled Carbon Nanotubes (MWCNT), (B) Zinc Oxide (ZnO) and (C) Titanium Oxide (TiO_2) ENMs from the European Commission's Joint Research Centre (JRC). https://ec.europa.eu/jrc/en

- Collect and generate information required to characterise the ENMs.
- Model dispersion, transport and realistic dose exposure characteristics in advanced mammalian and ecological models.
- Establish ENM fate, uptake and translocation.

Work Package 2

Biodistribution, biokinetics and *in vivo* anchoring

- Collect existing animal data from inhalation and oral exposures.
- Both acute exposures and long term repeat exposures.
- Define the biokinetics and key tissues for distribution and target organs.
- Identify key events associated with these exposures.

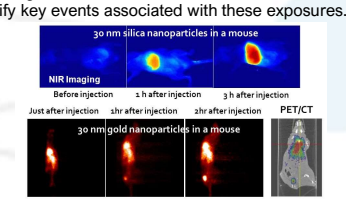


Figure 2. Biodistribution of Nanoparticles *in vivo*. Department of Nuclear Medicine, Seoul National University (Kang, 2016)

Work Package 7

Dissemination, exploitation and knowledge transfer

- Develop and implement the plans for communication, exploitation and dissemination.
- Deliver guidance for new tools relevant to hazard identification and/or risk assessment.
- Ensure data is accessible to the various PATROLS stakeholders.

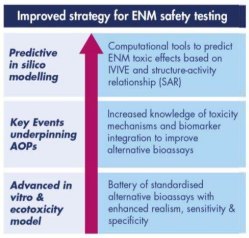
Physiologically Anchored Tools for Realistic nanOmaterial hazard aSsessment

24 Partnering Institutions
3 Continents
1 Project (€12.7m)

Work Package 6

In silico modelling strategies for hazard assessment

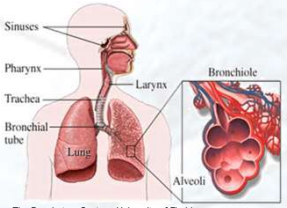
- Establish a PATROLS database to support *in silico* modelling.
- *In vitro* dosimetry, modelling and experimental design to support IVIVE and QSAR model development.
- Environmental dosimetry, modelling and experimental design.



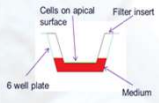
Work Package 3

Advanced *in vitro* lung models for ENM hazard assessment

- Optimise lung models for long-term repeated exposures
- Adapt lung models to enhance the physiological relevance
- Establish bioassays for long-term events.



The Respiratory System, University of Florida
https://pulmonary.pediatrics.med.ufl.edu/centers-programs/asthma-program/normal-lung-function/



Diagrammatic representation of the *In Vitro* Lung model

Kirsty Meldrum, SU, 2018

Work Package 5

Advanced ecotoxicity testing strategies and cross-species models

- Combining insights on ENM fate, uptake, bio-distribution and toxicological effects at increasing levels of bio- and ecological organisation (e.g. trophic transfer) in algae, daphnia and zebrafish to predict the risks of ENMs in environmentally relevant context.

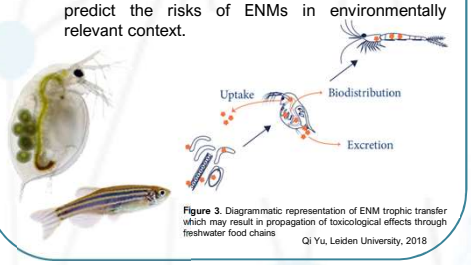


Figure 3. Diagrammatic representation of ENM trophic transfer which may result in propagation of toxicological effects through freshwater food chains

Qi Yu, Leiden University, 2018

Work Package 4

Advanced *in vitro* GastroIntestinal Tract (GIT) and liver models for engineered nanomaterial hazard assessment

Angela Kämpfer, IUF, 2018

3D *In Vitro* GIT Model

Samantha Llewellyn, SU, 2018

3D *In Vitro* Liver Model

- Optimise 3D GIT and liver models for long-term, repeated ENM exposures.
- Adapt GIT and liver models to enhance the physiological relevance through the addition of other cell types, fluid-flow and mechanical flexing.
- Establish bioassays that can identify key mechanistic indicators for chronic disease endpoints (AOPs).

Future Impact

1. Produce realistic and predictive *in vitro* 3D tissue models of the lung, gastrointestinal tract and liver for ENM safety assessment, reducing the need for animal testing.
2. Provide innovative methods for safety assessment in to a range of species or organisms and ecologically relevant test systems.
3. Create robust computational methods for predictive ENM exposure, dose and risk modelling.
4. Develop test method guidance to support hazard assessment frameworks and provide input into ongoing regulatory nanosafety policy development.
5. Characterise ENM under relevant experimental conditions dictated by the advanced human and environmental model development.

For more information, visit the PATROLS Website

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760813

@PATROLS_H2020 https://www.patrols-h2020.eu