NanoTEST

SEVENTH FRAMEWORK PROGRAMME

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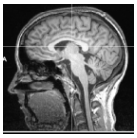
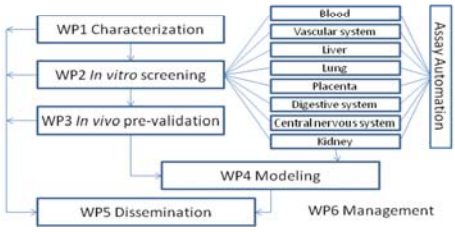
Overall Aim

Develop alternative testing strategies and high-throughput toxicity testing protocols using *in vitro* and *in silico* methods essential for the risk assessment of nanoparticles (NP) used in medical diagnostics



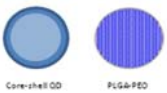
Project structure



Nanoparticles

NanoTEST aims to investigate NPs used in medical diagnostics, and will focus on:

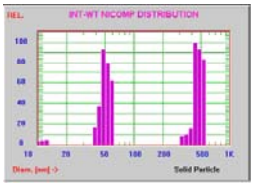
- **Iron oxide** and **rare earth oxide** (REO): Paramagnetic metal oxides used as contrast medium
- **PGLA-PEO**: Polymeric material as therapeutic device
- **Quantum Dot** (QD): Semiconductor used for medical imaging
- **Metal fullerene**: Fullerenes with enhanced contrast activity
- **Titanium dioxide:** Metal oxide as benchmark



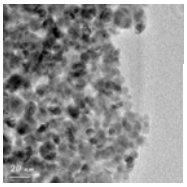
To be able to compare results, all participants will use same batch of each NP

Objectives and Preliminary Results

Characterization



Size distribution of 3% nano magnetite in DMEM + 10% FBS, measured by dynamic light scattering (DLS).
(Unive: G. Pojana, A. Marcomini)

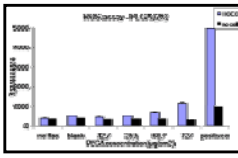


TEM image of nano magnetite.
(Unive: G. Pojana, A. Marcomini)

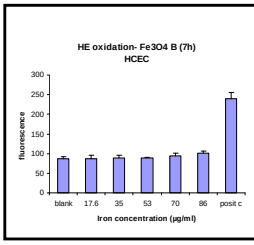
- Synthesize and to procure selected NPs according to the project beneficiary requirements
- Determine physio-chemical properties
- Determine interaction with culture media components, size distributions in stock solution/dispersion and after their addition to culture media
- Develop dispersion protocols
- Develop specific analytical protocols for determination of the NP's uptake and distribution in tissues

In vitro screening

- Investigate primary cells and cell lines from eight representative organs, which might be affected when exposed to intravenous-, inhalation and oral exposure of NPs.
- Four cross cutting topics: Oxidative stress, Inflammation/Immunotoxicity, Genotoxicity and Barrier transport
- Several assays will be performed to get general overview, and 3 NPs will be selected to investigate in more detail their cellular effect.



Increasing concentration of PLGA-PEO, slightly increases production of ROS in HCEC cells (but not significantly). There seem to be no influence of autofluorescence.
(CHUV: L. Juillerat, B Halamoda)



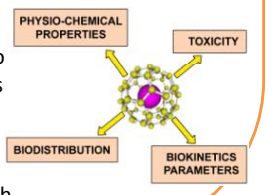
Measurement of dihydroethidium (HE) oxidation when exposing HCEC cells to Fe_3O_4 NP. No significant increase in oxidation with increasing concentration when measuring fluorescence with a multi well plate reader.
(CHUV: B Halamoda, L. Juillerat)

In vivo validation

- Validate the findings of the alternative *in vitro* assessment of the toxicological profile of the selected NPs
- Assessment of acute toxicity according to OECD guidelines
- 8-10 animals (male rats) per group
- Target organs are heart/aorta, lung, brain, blood, spleen, bone-marrow, liver and kidney
- Single exposure with sacrifice after 1, 2, 3 and 4 weeks

In silico models

- **Physiologically based pharmacokinetics** (PBPK): Describe the biodistribution of NPs, and calculations of deposition in the respiratory and cardiovascular system
- **Structure Activity models**: Relate structure to activity using tools developed at JRC (Dart, Toxtree) and Multivariate statistical approach



Outcome

- *In vitro* and *in vivo* toxicity assessment
- Common database, NapiraHUB
- Standardization and validation of assays
- High throughput assays and Assay Automation
- Set of assays for hazard evaluation of NP with standard operating procedures
- PBPK and structure activity models for toxicity prediction

Contact

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NanoTEST website:
www.nanotest-fp7.eu