# **Microplastics Health Effects Symposium: A Webinar Series**

Influence of Particle chemistry on Uptake, Transport and Toxicity

Hans Bouwmeester, Monday November 2<sup>nd</sup>, 2020







Hosted By: Southern California Coastal Water Research Project Authority (SCCWRP); San Francisco Estuary Institute, University of Toronto, In coordination with the California Water Resources Control Board and the California Ocean Protection Council









### Topics to cover

- Lessons-learned form engineered nanoparticles
- Biomolecular corona?
- Novel approaches in human risk assessment
- Critical points



### Interactions of particles with their environment



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### Effect of stomach and intestinal conditions of particles



From pH 2 to pH 7

Enlarged in pH 2



ACSnano 2012;6;3;2441-2451 7

500 nm  $SiO_2$  NP



# **Digestion with proteins**



Walczak et al., Nanotoxicology 2012





TNO Microscopy and Analysis 60nm AgNP digestion



MIRA\\ TESCAN TNO Microscopy and Analysis Ag NPs gastric digestion

5 µm

### 50 nm Ag NP



TNO Microscopy and Analysis digestion AgNP 60nm

SEM HV: 15.00 kV View field: 2.011 µm



500 nm MIRAN TESCAN TNO Microscopy and Analysis Ag NPs gastric digestion

SEM HV: 15.00 kV View field: 2.011 µm



Walczak et al., Nanotoxicology 2012

### Agglomerates of particles



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# Intestinal uptake

- Transcellular through normal intestinal enterocytes
- Paracellular transport (between enterocytes)
- Peyer's patches intestinal lymphatic tissue containing M cells = specialized phagocytotic enterocytes





https://doi.org/10.1016/j.addr.2016.07.007 Meike van der Zande (WR)

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### Mechanism of uptake





www.rpi.edu

### Role of surface coating of particles







Abdelkhaliq et al. J Nanobiotechnol (2018) 16:70 https://doi.org/10.1186/s12951-018-0394-6

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### Biomolecular layer on particles

#### nature nanotechnology

#### REVIEW ARTICLE

Biomolecular coronas provide the biological identity of nanosized materials

Marco P. Monopoli<sup>1,2</sup>, Christoffer Åberg<sup>1</sup>, Anna Salvati<sup>1,2</sup> and Kenneth A. Dawson<sup>1\*</sup>







### Surface coating dependent protein coverage







Abdelkhaliq et al. J Nanobiotechnol (2018) 16:70 https://doi.org/10.1186/s12951-018-0394-6

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### Protein corona affects interactions with bacteria

### Biomolecules in corona

- Microbial fragments
- Environmental
  - Chemicals
  - Lipids
  - Proteins
  - • •







Small Meets Smaller: Effects of Nanomaterials on Microbial Biology, Pathology, and Ecology Roland H. Stauber,<sup>&†</sup><sup>©</sup> Svenja Siemer,<sup>†</sup> Sven Becker,<sup>†</sup> Guo-Bin Ding,<sup>†‡®</sup> Sebastian Strieth,<sup>†</sup> and Shirley K. Knauer,<sup>& §</sup>

### Interactions of particles and micro-organisms





### Particles in human tissues

- 15 post mortem human liver spleen
- Sample preparation techniques
- Validation of Single particle ICP-HRMS LODs (size) = 85 nm; LODn (number) = 0.8 × 109/kg; LODc (calculated Ti in particles) = 0.005 mg/kg
- Validation ICP-HRMS LODt (total-Ti) = 0.01 mg/kg

Heringa et al. Particle and Fibre Taxicobgy (2018) 15:15 https://doi.org/10.1186/s12989-018-0251-7

%

Particle number based percentage

Particle and Fibre Toxicology

#### RESEARCH **Open Access** CrossMark Detection of titanium particles in human liver and spleen and possible health implications M. B. Heringa<sup>1\*</sup>, R. J. B. Peters<sup>2</sup>, R. L. A. W. Bleys<sup>3</sup>, M. K. van der Lee<sup>2</sup>, P. C. Tromp<sup>4</sup>, P. C. E. van Kesteren<sup>1</sup>, J. C. H. van Eijkeren<sup>1</sup>, A. K. Undas<sup>2</sup>, A. G. Oomen<sup>1</sup> and H. Bouwmeester<sup>25</sup> 25.0 25.0 20.0 20.0 mass-based percentage (%) 15.0 10.0 10.0 🖁 arti 5.0 5.0 0.0 Particle size bins (nm







#### Article | Open Access | Published: 17 September 2019

# Ambient black carbon particles reach the fetal side of human placenta

Hannelore Bové, Eva Bongaerts, Eli Slenders, Esmée M. Bijnens, Nelly D. Saenen, Wilfried Gyselaers, Peter Van Eyken, Michelle Plusquin, Maarten B. J. Roeffaers, Marcel Ameloot & Tim S. Nawrot 🖂









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# When is a nanoplastic toxic?





Cellular uptake

### Novel approaches for testing <-> material diversity





Microplastics EP 24

# A mechanistic approach to understand toxicity



Adverse Outcome Pathway

Adverse Outcome Pathway Knowledge Base (AOP-KB)

- An Adverse Outcome pathway allows to structure the experimental work and to integrate *in vitro* assays
- An AOP is 'blind' to the chemical of interest: it focusses on the biological effect

rtal || AOP-KB || Background || How to contribute || HandBook |



Please click on any of the AOP-KB components or third party modules you want to use. Please note that the AOP-KB is work in progress and interface updates and more functionality will become available soon.





### Main AOPs for particles





### Systemic fate of nanoplastics (and associated chemicals)





# In vitro to in vivo extrapolations: integrate AOP and PBK models



# Critical points

- Great diversity in materials
- Need for analytical methods
- Development of particle kinetic models (toxicokinetics)
- Which in vitro approach/model to use?
  - Cell line; stem cell-based; organ-on-chip models (toxicodynamics)
- Extrapolation from in vitro to in vivo
- Point of departure (Benchmark Dose Modelling) for Risk Assessment



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