

Toxicité humaine des microplastiques

Vers une démarche d'évaluation des risques pour les micro- et nano- plastiques (MNP)

Raymond Pieters

Institute for Risk Assessment Sciences (IRAS), Utrecht University





POLYRISK

Comprendre l'exposition humaine et les risques sanitaires
des micro- et nanoplastiques contaminant notre
environnement

RISQUE = DANGER * EXPOSITION

RISQUE = EFFET TOXIQUE * CONCENTRATION (CIBLE)

Toxicité potentielle et voies d'exposition aux MNP

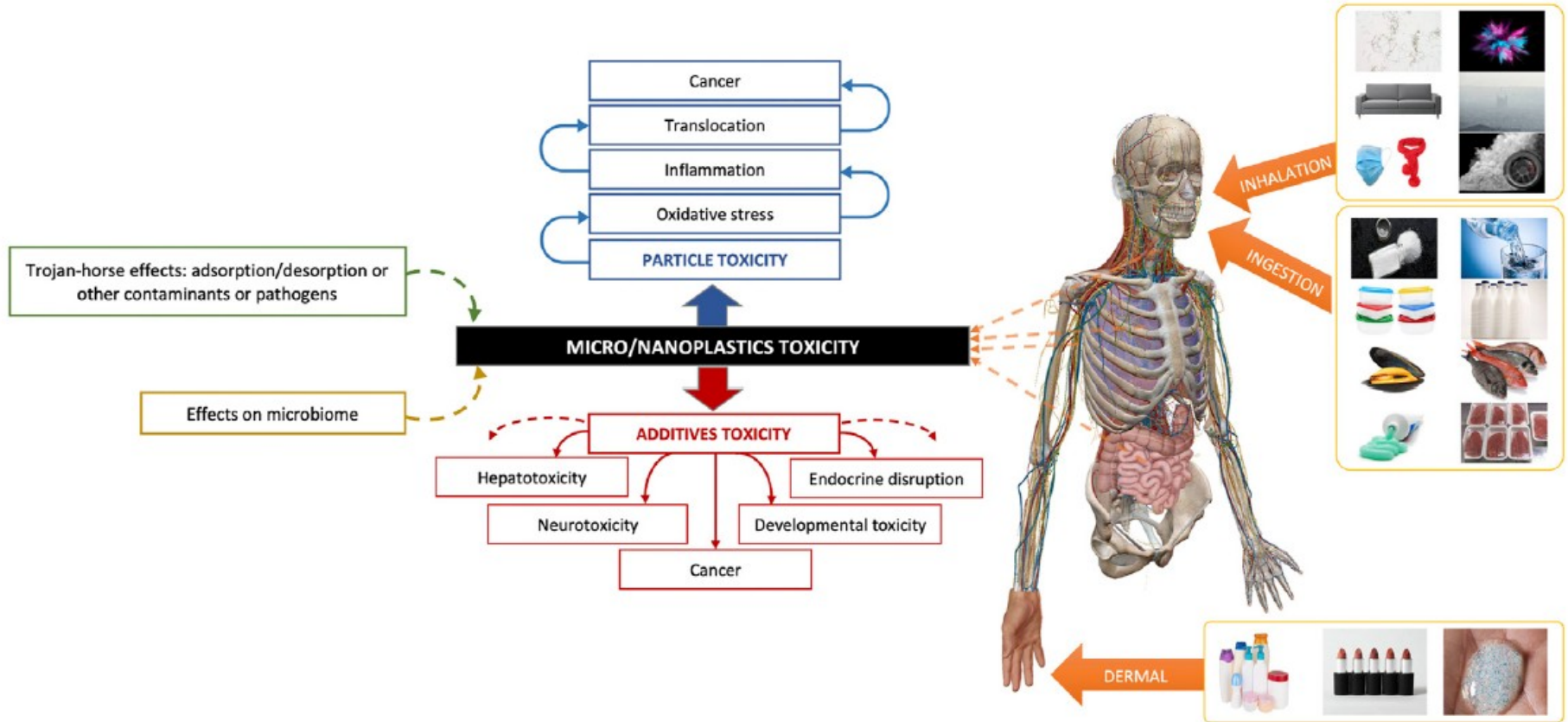


FIGURE 1 | Summary of the human routes of exposure to MNPLs and their potential effects on health.

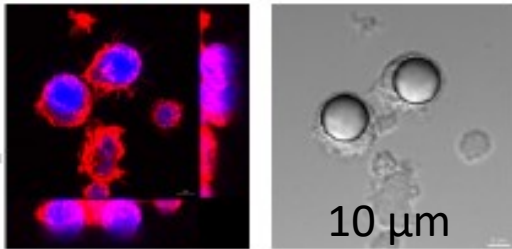
Challenges associés aux recherches sur les MNP

- Comment détecter et doser les MNP (dans des échantillons/matrices complexes) ?
 - Chimie et physique analytiques
 - Dosages de particules individuelles (en culture cellulaire) (dosage in silico)
- Quelles sont les caractéristiques importantes de l'exposition du le danger ?
 - Forme, taille, chimie de surface
 - Chimie---composition/surface (biofilm)---lixiviats
- Comment évaluer les dangers (propriétés toxiques intrinsèques ?)
- MNP natifs vs Agé/vieilli
- MNP primaires vs secondaires

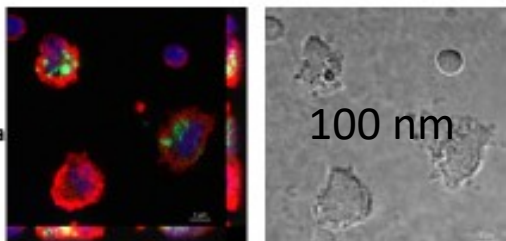
Taille des MNP

Nanoparticles plastique de 50-200 nm ~ ordre de grandeur des virus

Microplastiques < 1-5 mm
ou < 1 mm



Nanoplastiques < 100 nm



Tête d'épingle	1 mm
Diamètre d'un cheveu humain	80 μm (60-120)
Taille de la queue d'un spermatozoïde	50 μm
Diamètre d'un macrophage	21 μm
Diamètre d'un ovule	20 μm
Diamètre d'une cellule dendritique	10-15 μm
Epaisseur d'une feuille d'aluminium	10 μm
Diamètre d'une bactérie	2 μm
Epaisseur d'une bulle de savon	750 nm
Taille d'un virus	100 nm (20-500 nm); (SARS-CoV-2: 60-140nm)
Epaisseur d'un brin d'ADN	2 nm
Diamètre H-atome	0.1 nm

CHEMICALS IN PLASTICS

A TECHNICAL REPORT

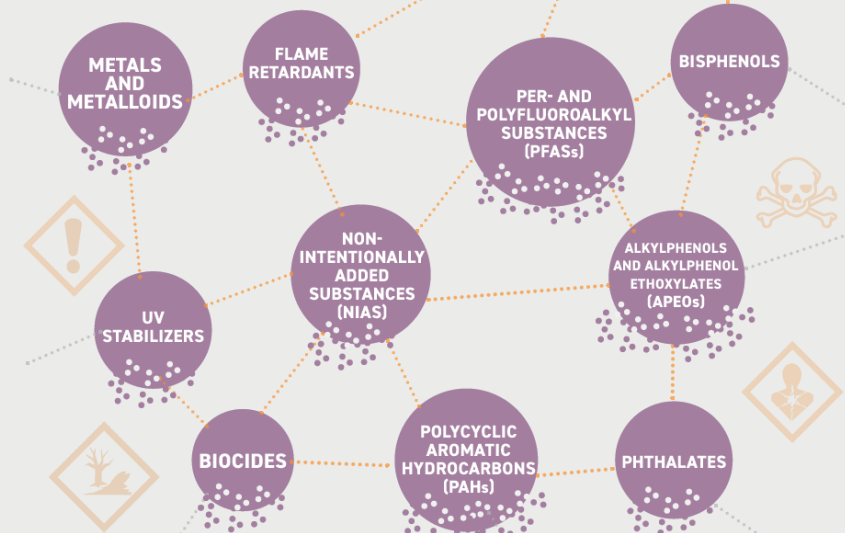
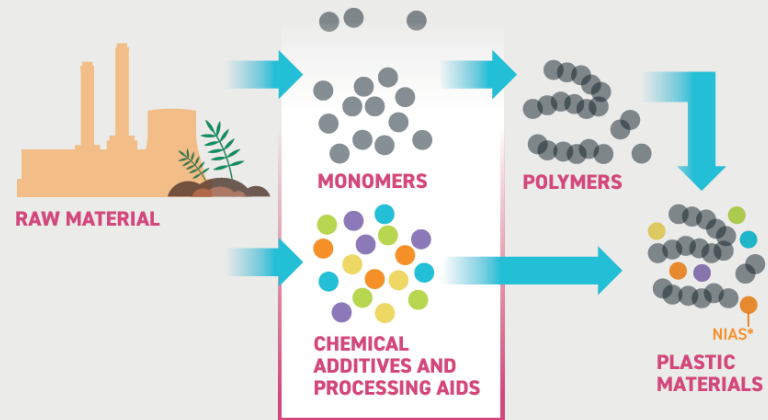


<https://www.unep.org/resources/report/chemicals-plastics-technical-report>



02.02.2024

CHEMICALS IN PLASTICS OVERVIEW



Micro-/nanoplastics

Exposure levels

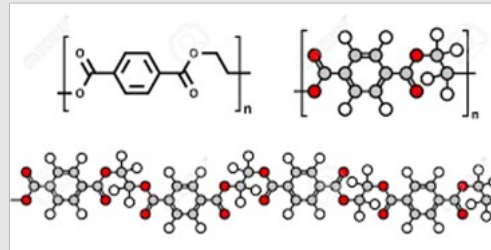
Bioaccumulation potential



Particle toxicity

Chemical effects

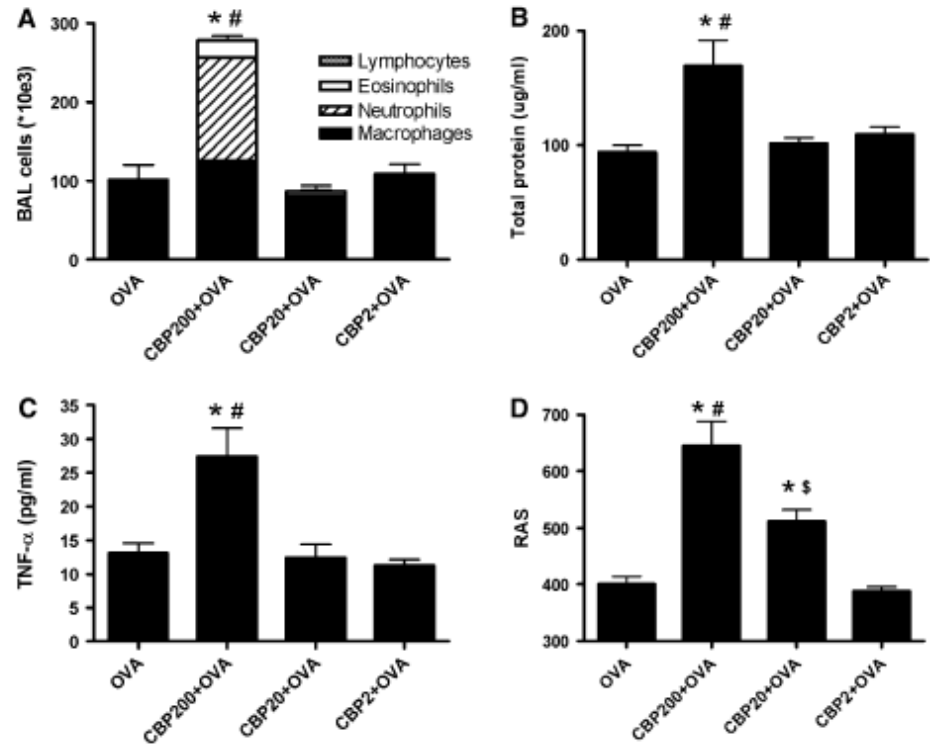
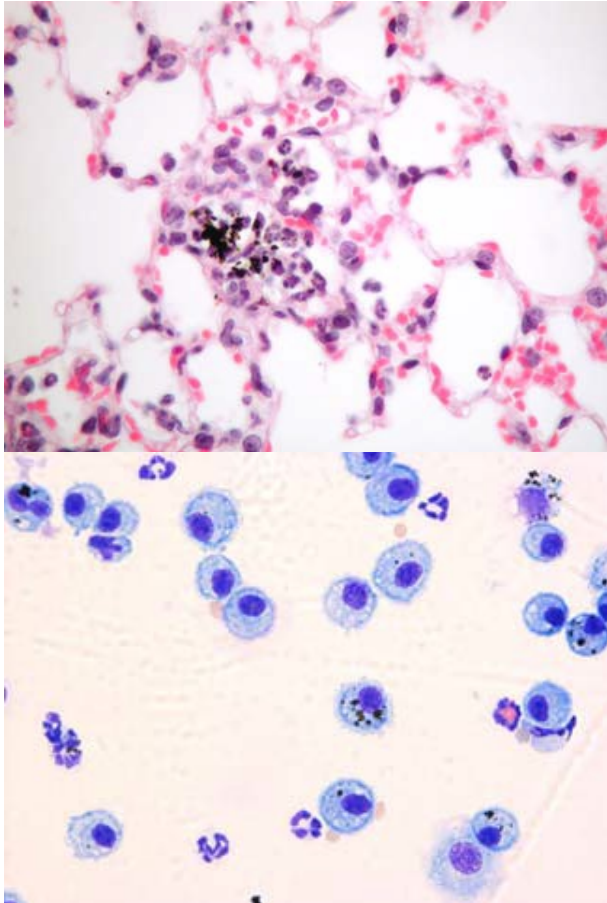
Microbial effects



Enseignements tirés des études humaines et animales (in vivo) relatives aux dangers des nanoparticules inhalées

Particules ultrafines et poumon

Exposition intranasale – souris (Balb/c) Effet immunologiques (LBA)



de Haar C, Hassing I, Bol M, Bleumink R, and Pieters R. Ultrafine carbon black particles cause early airway inflammation and have adjuvant activity in a mouse allergic airway disease model. *Tox. Sciences* 2005, 87, 409-418.

Particules de polystyrène et poumon

Exposition intranasale – souris (Balb/c) Effet immunologiques (LBA)

PSP 0.0588 μm

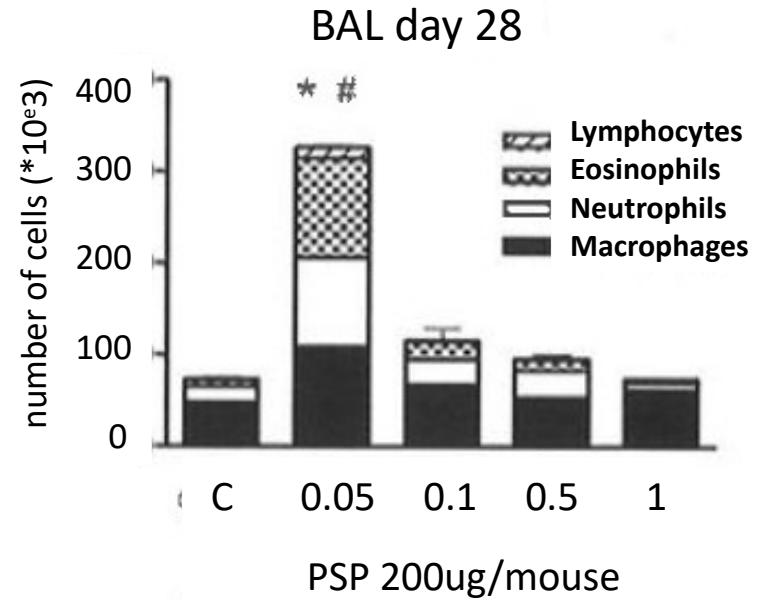
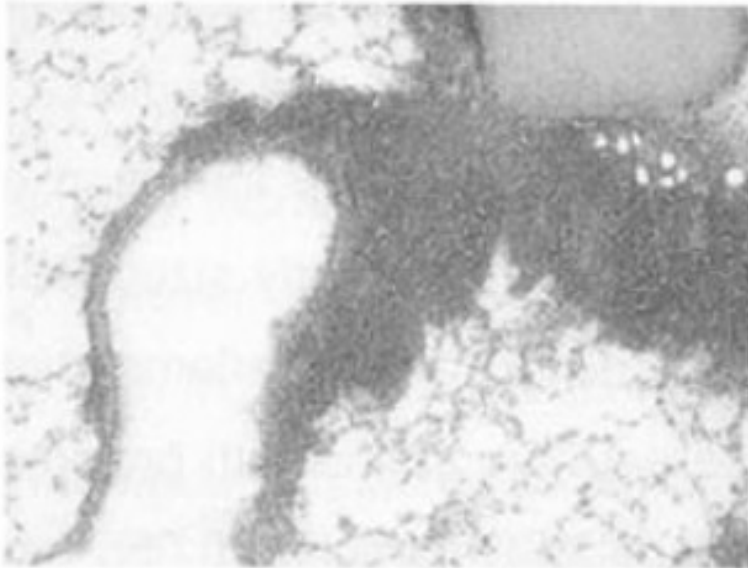


Table 1. Polystyrene particle characteristics

Particle size (μm)	Number of particles in 200 μg PSP	Total surface area of 200 μg PSP (cm^2)	% protein bound
0.0588	$1.77 \cdot 10^{12}$	192	97
0.107	$2.94 \cdot 10^{11}$	106	26
0.585	$1.80 \cdot 10^9$	19.3	23
1.053	$3.08 \cdot 10^8$	10.7	7
4.64	$3.61 \cdot 10^6$	2.44	5

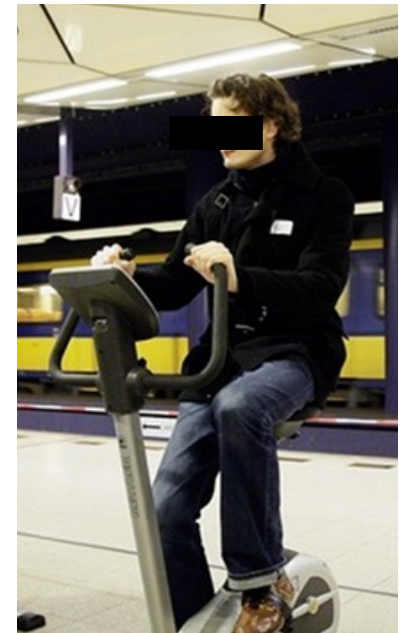
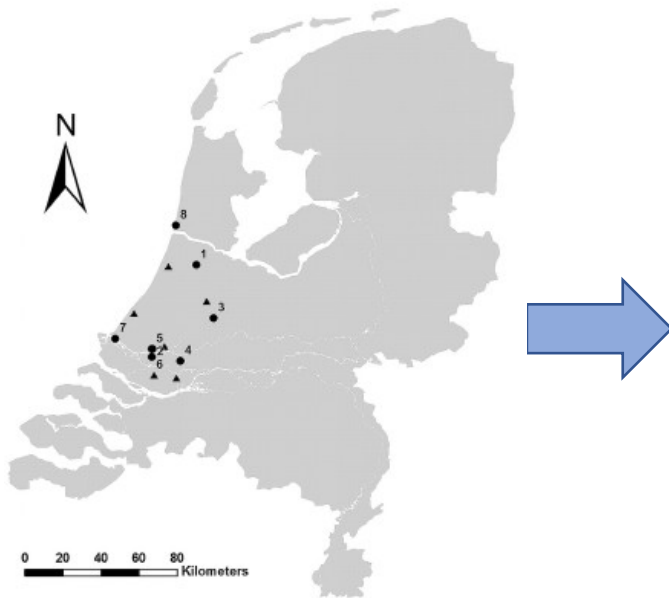
Etudes humaines

RESEARCH ARTICLE

Inhal Toxicol, 2014; 26(3): 141–165

Air pollution exposure affects circulating white blood cell counts in healthy subjects: the role of particle composition, oxidative potential and gaseous pollutants – the RAPTES project

Maike Steenhof¹, Nicole A. H. Janssen², Maciej Strak^{1,2*}, Gerard Hoek¹, Ilse Gosens², Ian S. Mudway³, Frank J. Kelly³, Roy M. Harrison^{4,5}, Raymond H. H. Pieters¹, Flemming R. Cassee^{1,2}, and Bert Brunekreef^{1,6}



Volontaires sur ergocycle

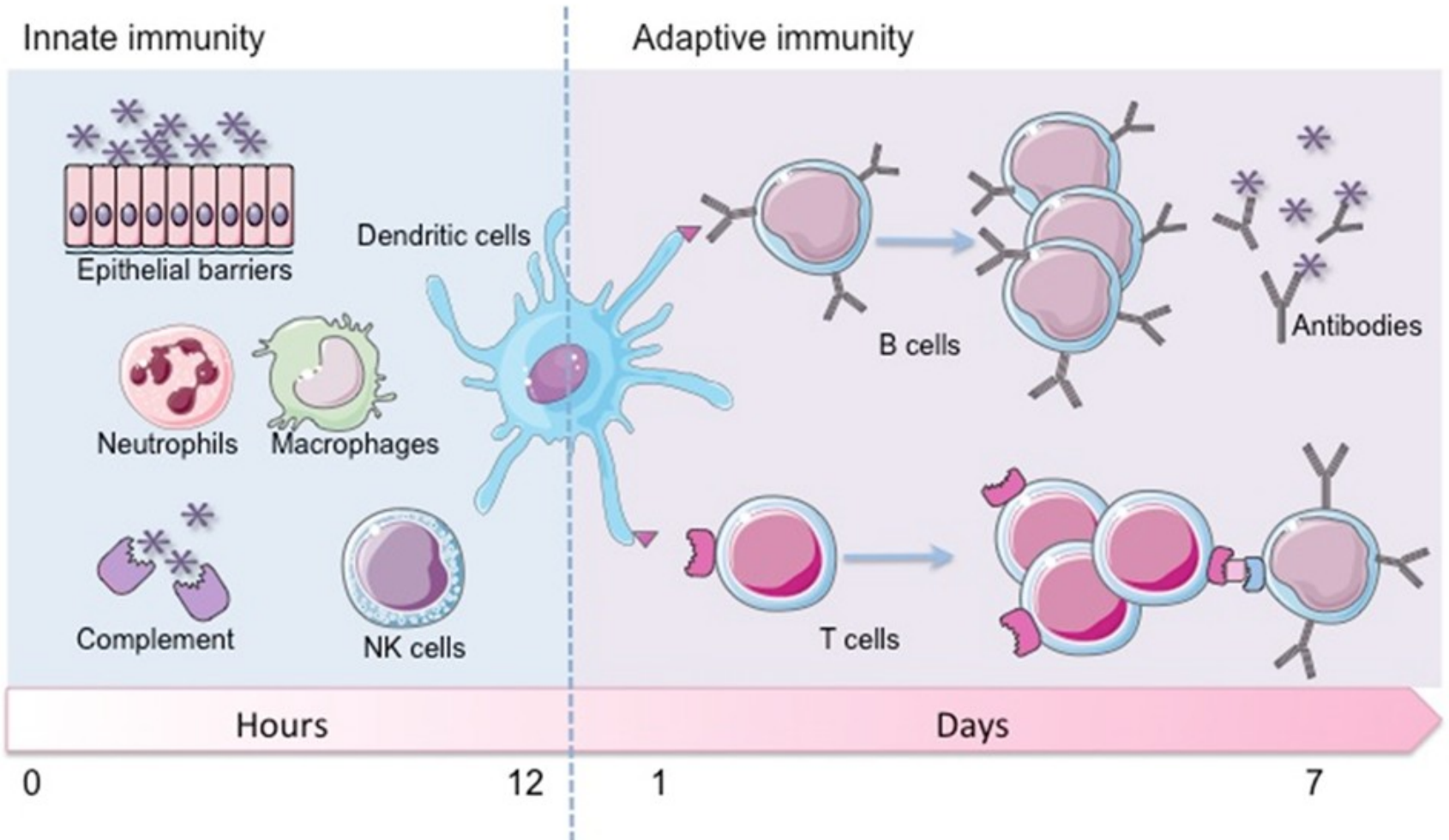
Outdoor: Urban background; Continuous traffic; Stop-and-go; Farm...

Table 4. Descriptive statistics: percentage change in blood cell counts over baseline.

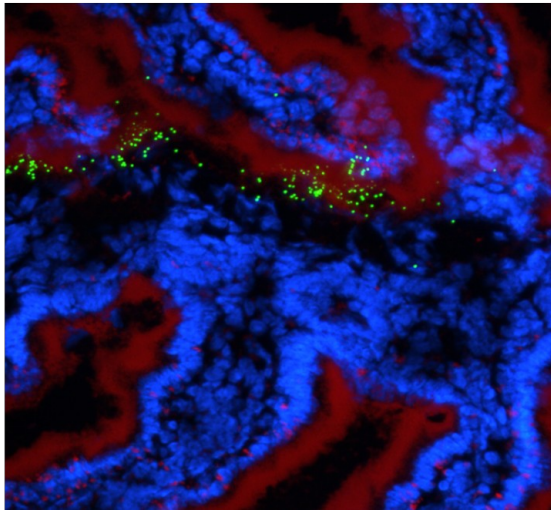
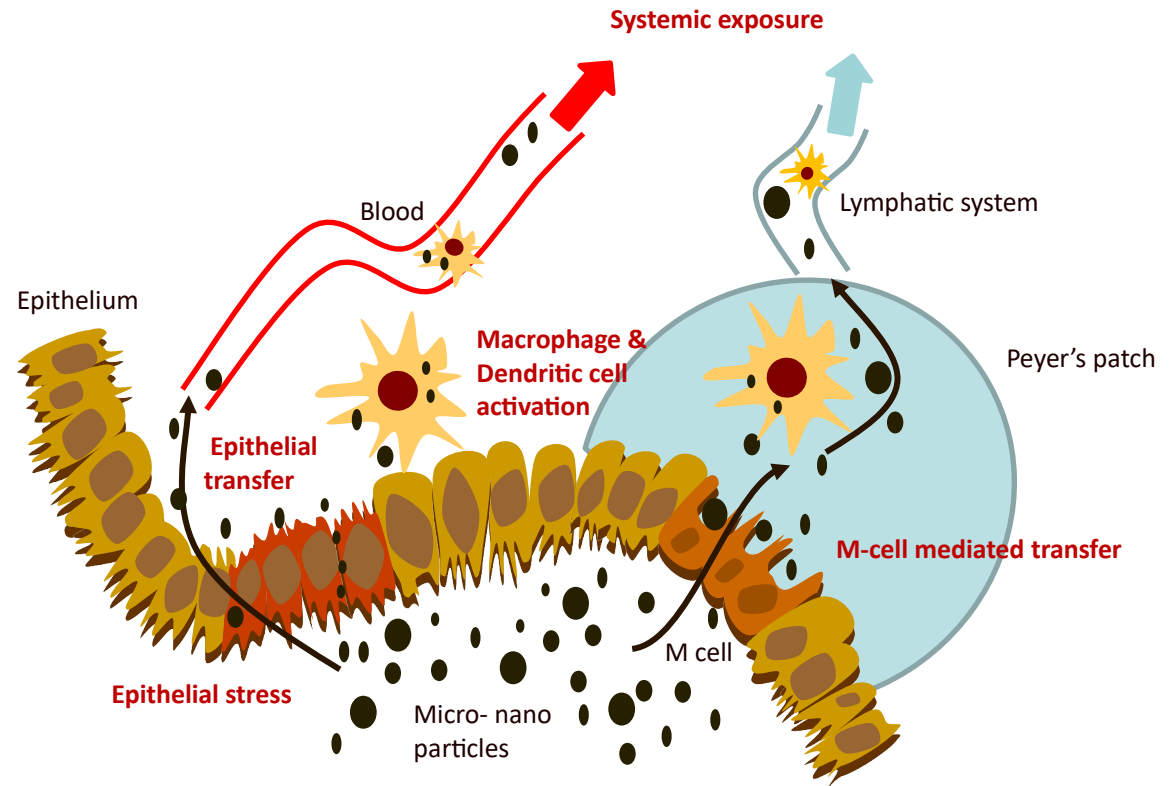
	Percentage change over baseline ^a (95% CI)		
	All sites (<i>n</i> = 167/166)	Outdoor sites (<i>n</i> = 124/122)	Underground (<i>n</i> = 43/44)
Total WBC			
2 h PE	15.0 (11.8; 18.4)	10.5 (7.1; 14.1)	25.9 (18.6; 33.6)
18 h PE	-10.4 (-12.7; -8.1)	-12.2 (-14.3; -10.0)	-4.9 (-10.6; 1.2)
Neutrophils			
2 h PE	35.0 (29.3; 41.0)	31.0 (25.1; 37.2)	49.2 (34.8; 65.2)
18 h PE	-2.0 (-5.5; 1.7)	-3.0 (-6.8; 1.1)	1.0 (-7.6; 10.4)
Monocytes			
2 h PE	-11.3 (-19.8; -1.9)	-15.6 (-25.4; -4.6)	4.1 (-10.4; 20.9)
18 h PE	-12.2 (-14.8; -9.5)	-13.9 (-16.9; -10.8)	-6.8 (-12.0; -1.2)
Lymphocytes			
2 h PE	-6.8 (-10.0; -3.4)	-6.8 (-10.2; -3.2)	-5.8 (-14.4; 3.6)
18 h PE	-21.3 (-23.5; -19.1)	-22.9 (-25.2; -20.5)	-17.3 (-21.7; -12.6)
Eosinophils			
2 h PE	-35.6 (-43.4; -26.8)	-36.9 (-46.1; -26.1)	-31.6 (-42.9; -18.0)
18 h PE	-12.2 (-16.8; -7.3)	-13.9 (-19.5; -7.9)	-5.8 (-12.8; 1.7)

CI = confidence interval; h = hours; *n* = number of observations for total cell counts 2 h PE/18 h PE; PE = post exposure; WBC = white blood cells.

^aCalculated by using log-normalized cell counts. Cell counts are expressed as 10⁹ cells/L.

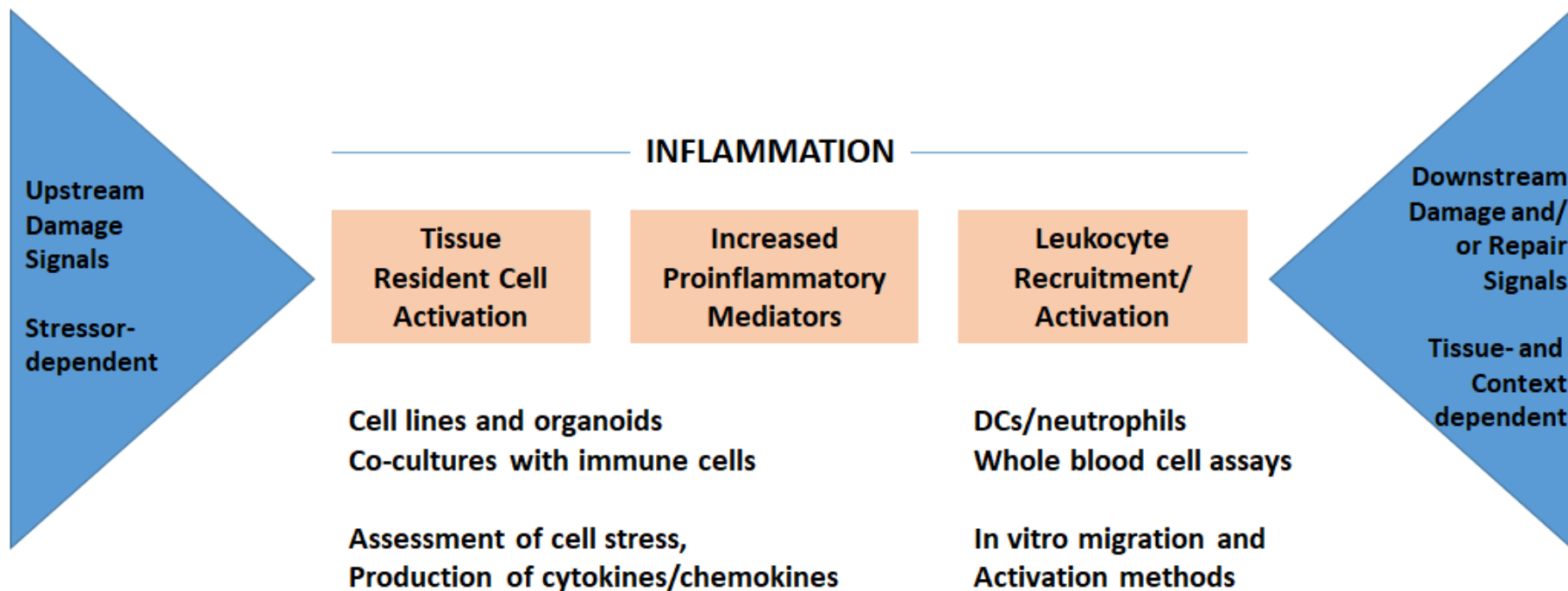
WHAT ARE KEY EVENTS PREDICTIVE FOR INFLAMMATION?

Eposition d'épithéliums aux micro-et nanoplastiques



Fluorescent PSP









EVENEMENTS CLE CENTRAUX D'EFFETS INFLAMMATOIRES ADVERSES

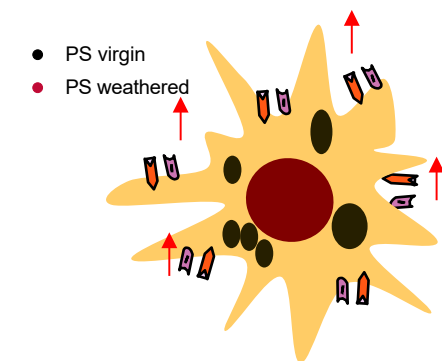
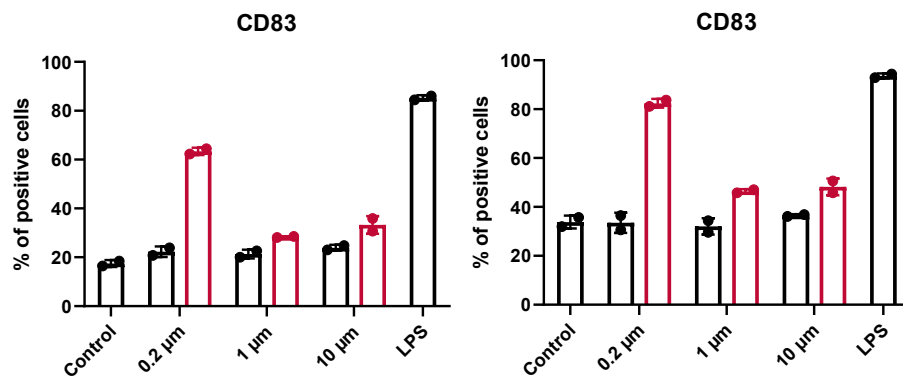
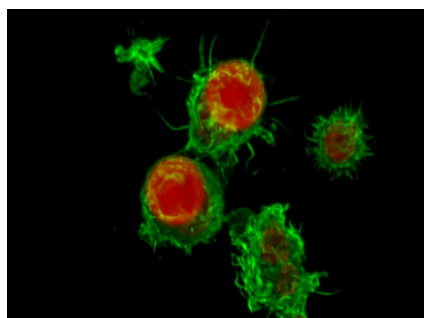
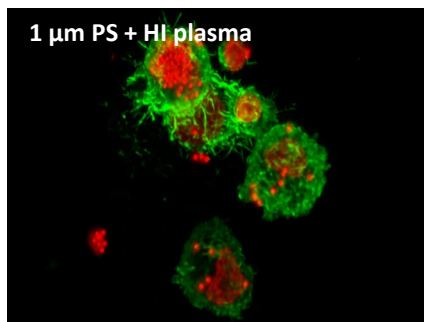
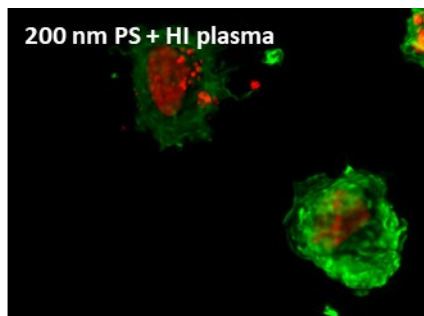


Representing the Process of Inflammation as Key Events in Adverse Outcome Pathways

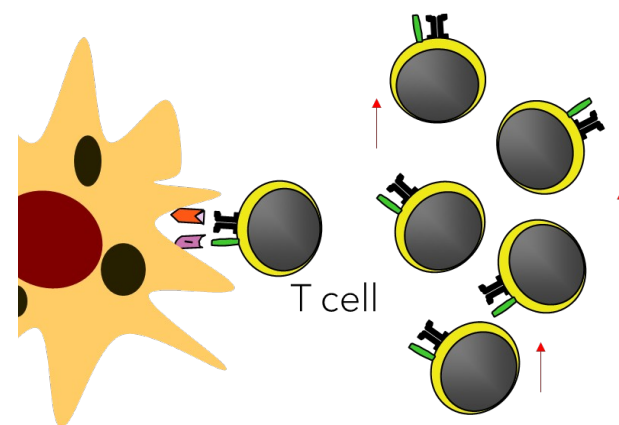
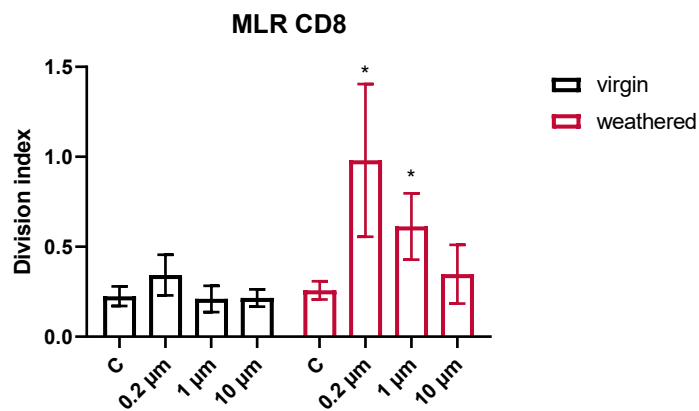
Daniel L. Villeneuve,^{*,1} Brigitte Landesmann,[†] Paola Allavena,[‡] Noah Ashley,[§]
Anna Bal-Price,[†] Emanuela Corsini,[¶] Sabina Halappanavar,^{||} Tracy Hussell,^{|||}
Debra Laskin,^{|||} Toby Lawrence,[#] David Nikolic-Paterson,^{**} Marc Pallardy,^{††}
Alicia Paini,[†] Raymond Pieters,^a Robert Roth,^b and Florianne Tschudi-Monnet^c

Environmentally weathered polystyrene particles induce phenotypical and functional maturation of human monocyte-derived dendritic cells

Annemijne E. T. van den Berg^a , Maud Plantinga^b , Dick Vethaak^{a,c} , Kas J. Adriaans^a , Marianne Bol-Schoenmakers^a , Juliette Legler^a , Joost J. Smit^a  and Raymond H. H. Pieters^a 

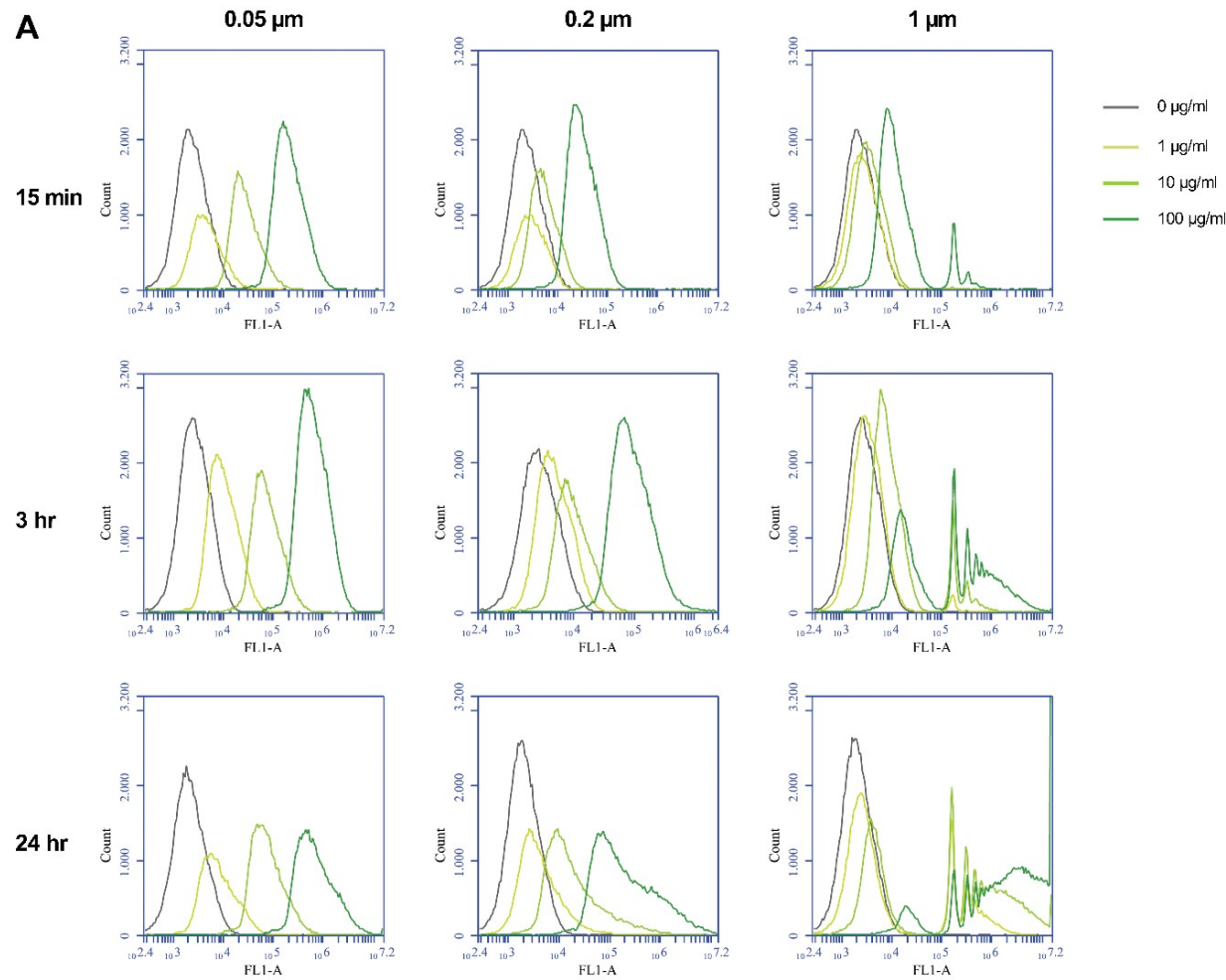
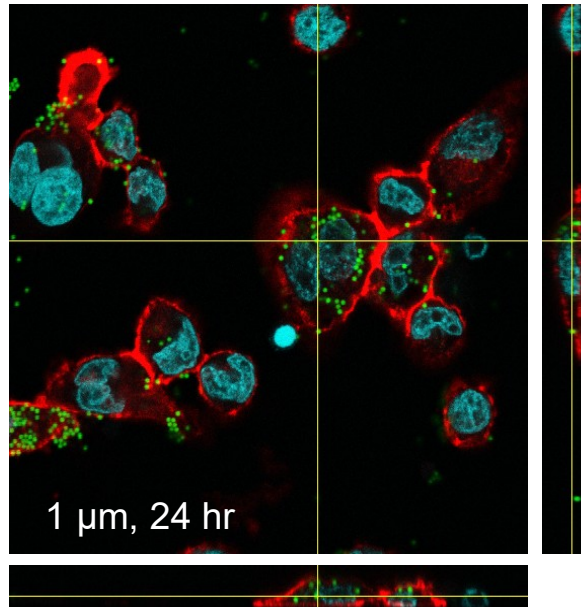


Effect of virgin and weathered PS particles on the presence of co-stimulatory molecules on the membrane of MoDCs



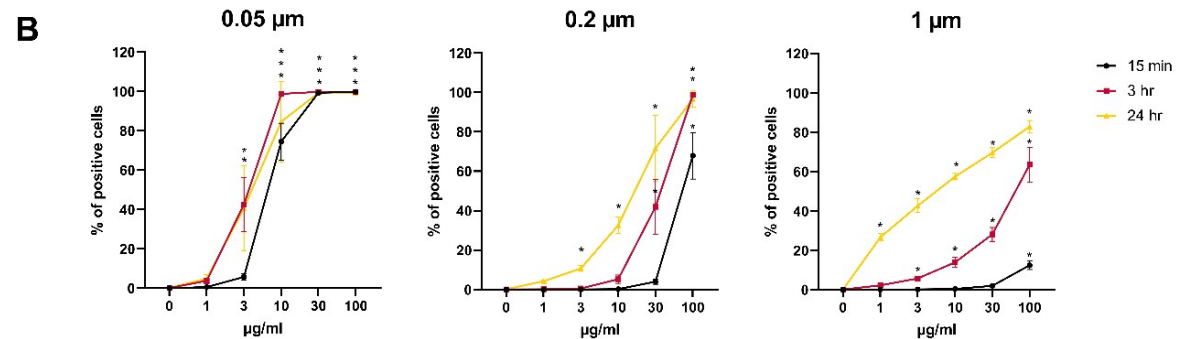
Effect of virgin and weathered PS particles on T-cell activation

Internalisation de particules de PS par des macrophages (cellules THP1)



10 µg/ml
50 nm: =1,46E+11 p/ml
200 nm: =2,27E+09 p/ml
1 µm: =1,82E+07 p/ml

Van den Berg et al,
manuscript in prep



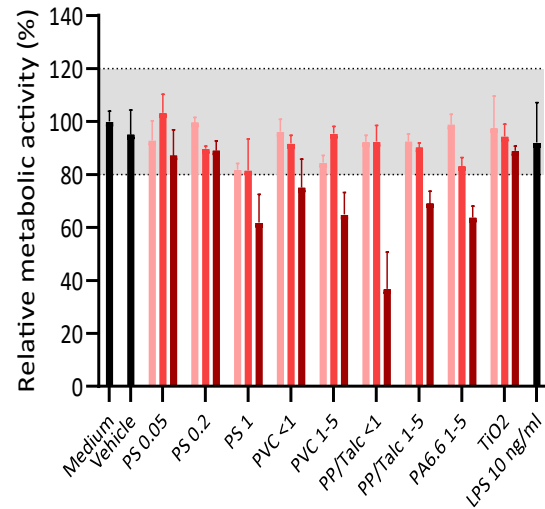
Effets des MNP sur macrophages THP1:

- viabilité cellulaire affectée à forte [],
- pas d'effet sur laproduction cytokinique

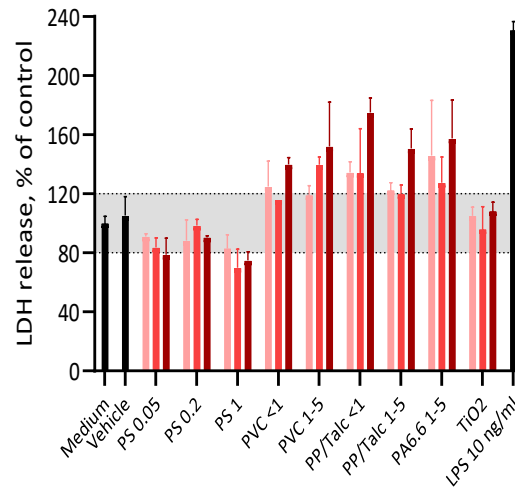


Annemijne van den Berg
Utrecht University

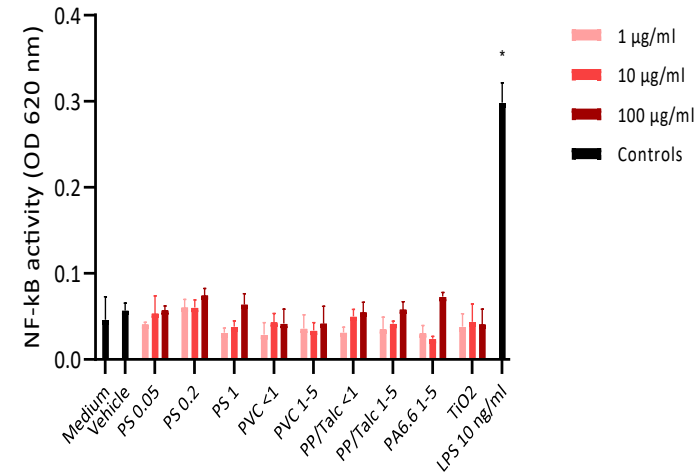
Mitochondrial activity (alamar blue)



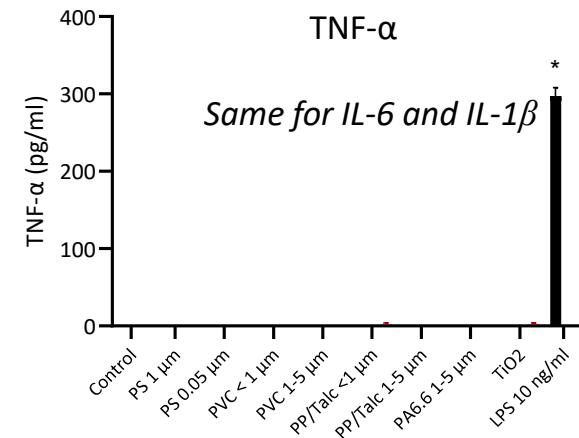
LDH leakage



NF-kB activation

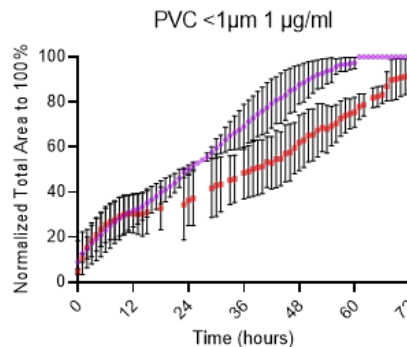
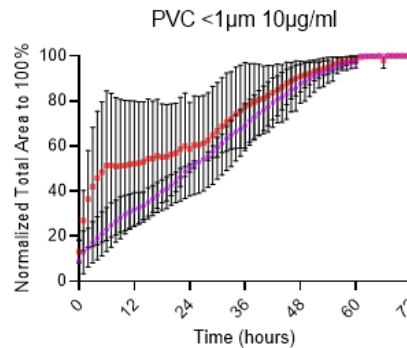
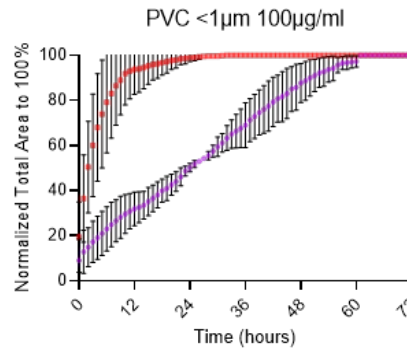
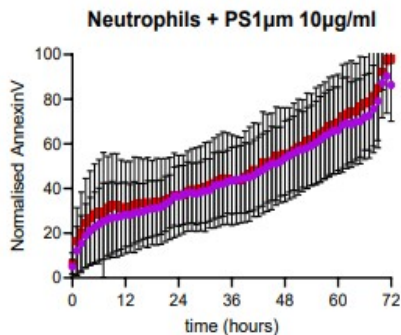
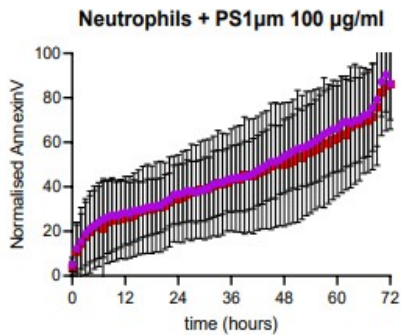
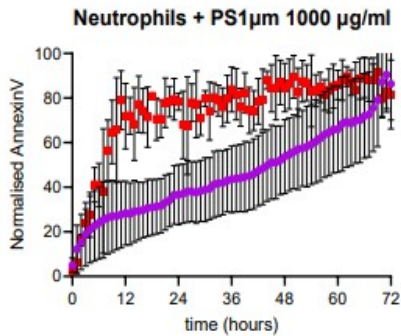


Particle type	Size (µm)
PS (polystyrene)	0.05, 0.2 and 1
PVC (polyvinylchloride)	<1 and 1-5
PP (polypropylene)/Talc	<1 and 1-5
PA (polyamide/Nylon-6,6)	1-5
TiO2 (Titanium oxide, reference particle)	0.35
LPS (10 ng/ml, positive control)	



Effets de MNP sur neutrophiles humains

- cinétique d'expression de l'annexine V



• Neutrophils only
• PVC <1µm 100µg/ml

• Neutrophils only
• PVC <1µm 10µg/ml

• Neutrophils only
• PVC <1µm 1µg/ml

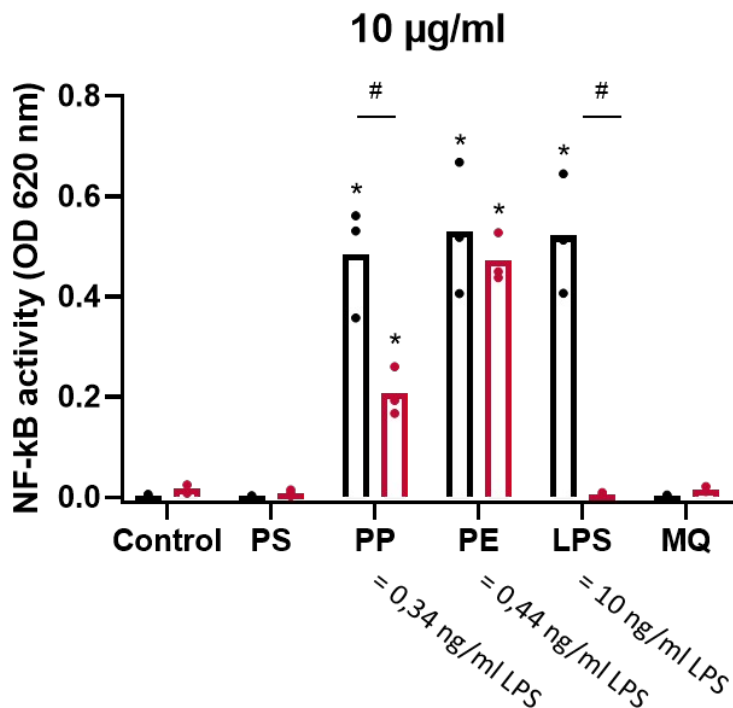
Tim Skrabanja
Utrecht University

Effects on cell viability at high concentrations
>100 µg/ml PVC (1 µm, 1-5µm)
>1000 µg/ml PS (1 and 10 µm)
10 µg/ml PP (180 nm)

No effects of
-PA6.6 (1-5 and 6-10 µm),
-PE (BAM particles, 350 nm,
at 10 µg/ml)



Effet de nano-PE et nano-PP vieillis sur l'expression NF-kB par des macrophages THP1



Similar effects on cytokine production: TNF, IL-6, IL-1β

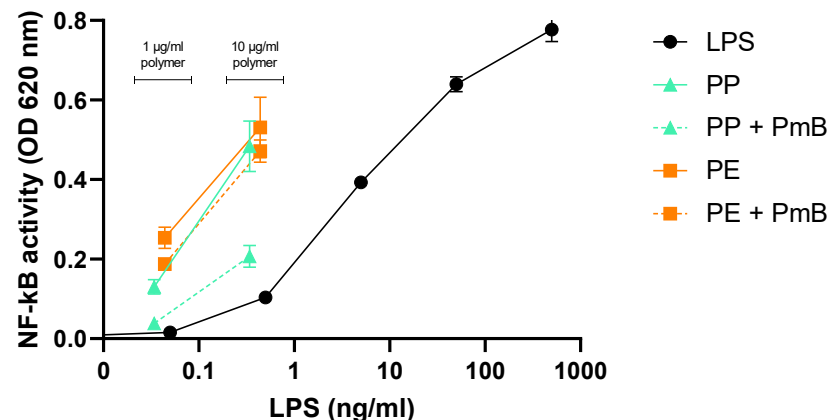
c=O groups detected on both PP and PE

XPS data from BAM (Korinna Altmann)

Estimation of LPS content based on LAL assay

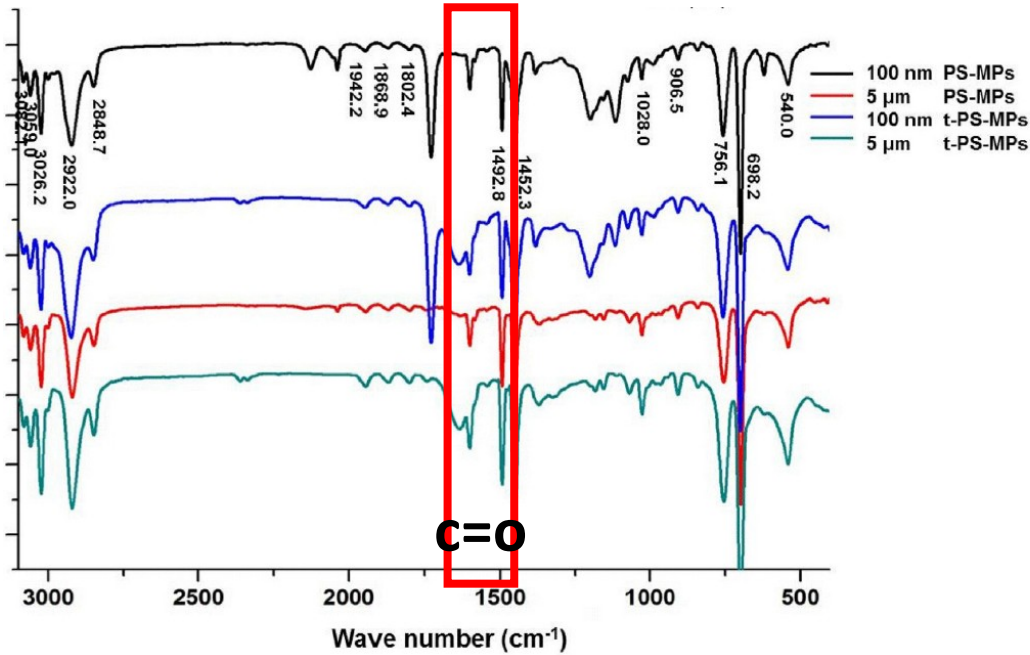
	Polymer in stock (µg/ml)	LPS in stock (ng/ml)	Exposed polymer concentration (µg/ml)	Exposed LPS concentration (ng/ml)
PP	41	1,404	10	0,34
PE	82	3,598	10	0,44

Effects on NFkB of PE, PP relative to LPS

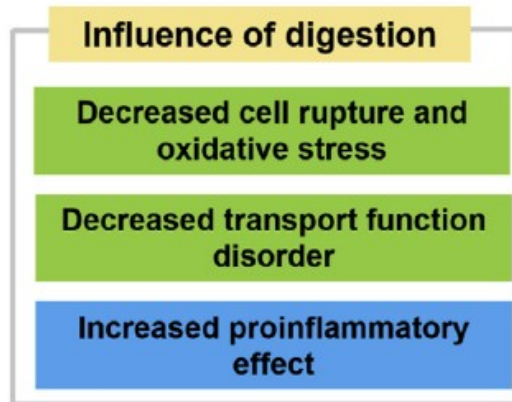
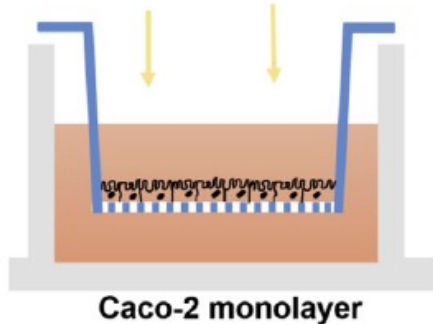


Influence of the digestive process on intestinal toxicity of polystyrene microplastics as determined by *in vitro* Caco-2 models

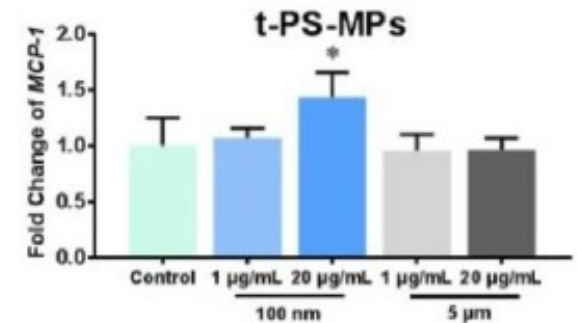
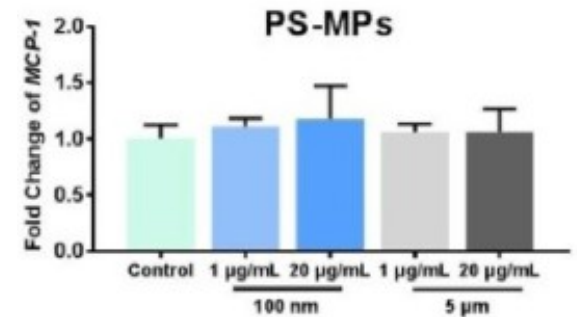
Su Liu ^{a, b}, Xiaomei Wu ^a, Weiqing Gu ^a, Jing Yu ^a, Bing Wu ^{a, *} *Chemosphere* 256 (2020) 127204



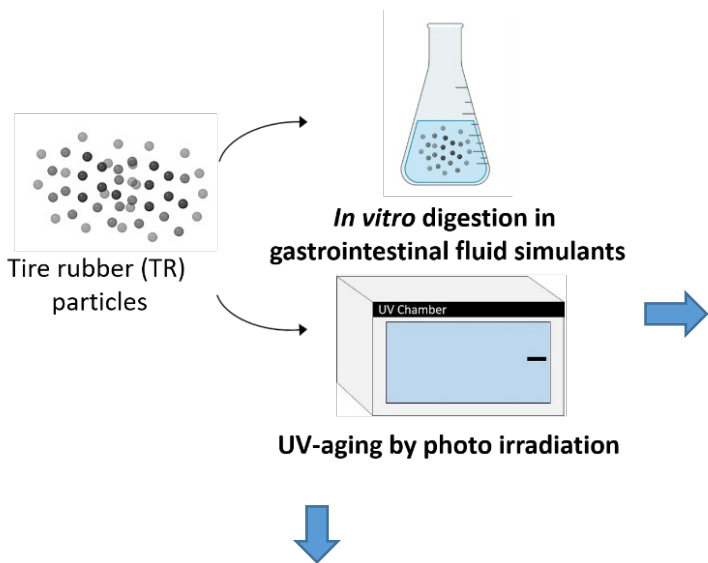
Original PS-MPs Transformed PS-MPs
in digestive tract



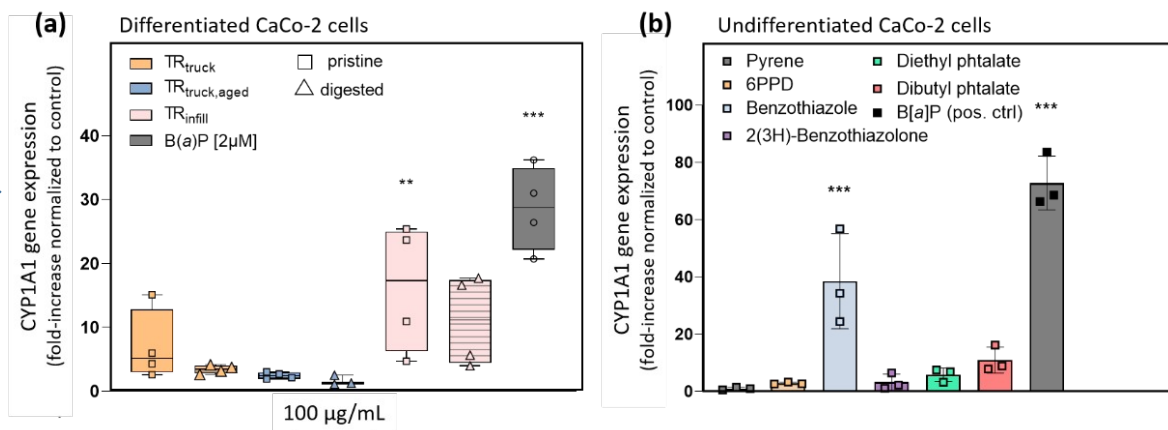
Gene expression of MCP1



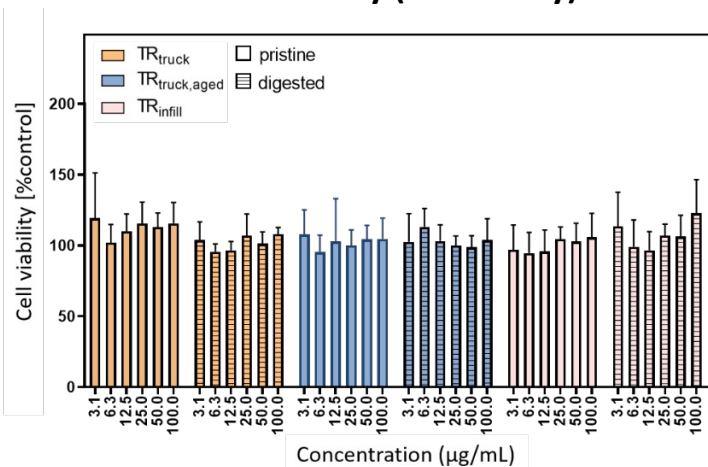
Effets cellulaires de particules de pneumatiques sur des cellules CaCo-2 après vieillissement UV et digestion in vitro par des simumants de liquide gastro-intestinal



Cytochrome P450 1A1 (CYP1A1) gene expression



Cell viability (MTT assay)



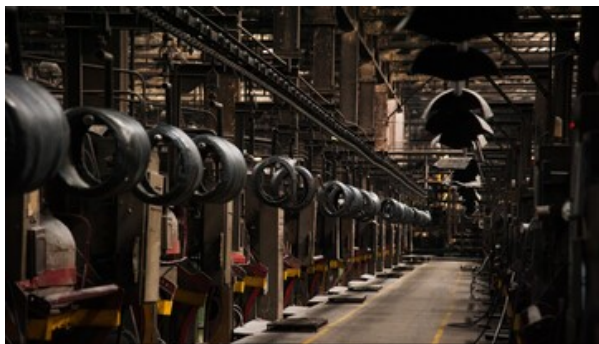
- Identification and quantification of released additives by GC-MS (Emeka Emecheta)
- Selected additives were individually tested for their CYP1A1 induction

Amelie Vogel
Federal Institute for Risk Assessment,
Germany



Scénarios d'exposition reels – Projet POLYRISK

Exposition interne/externe Effets sur les fonctions immunitaires



Air exposure at tire rubber refurbishing workplaces



Textile fibre workplace exposure



MNP in bottled drinking water



Utrecht
University



Norwegian Institute of Public Health



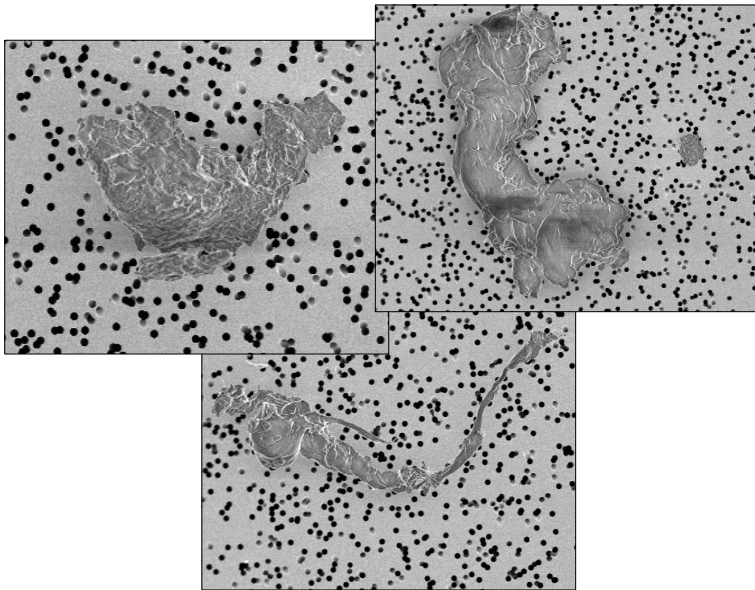
Urban and rural outdoor air ambient MNP



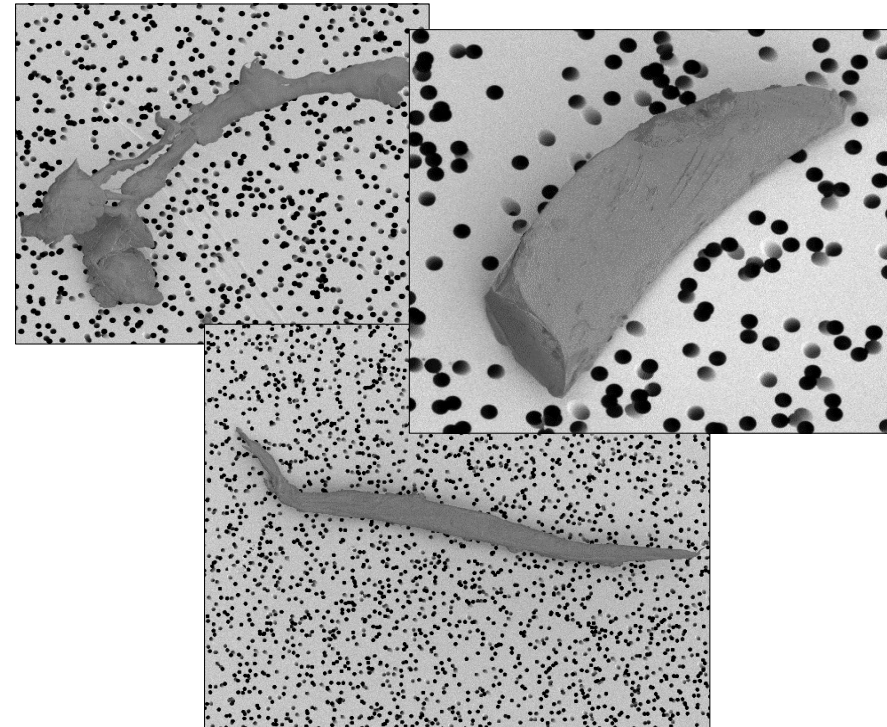
Indoor Soccer Players exposure to rubber granulate-MNP

Exemple d'images MEB (gazon synthétique)

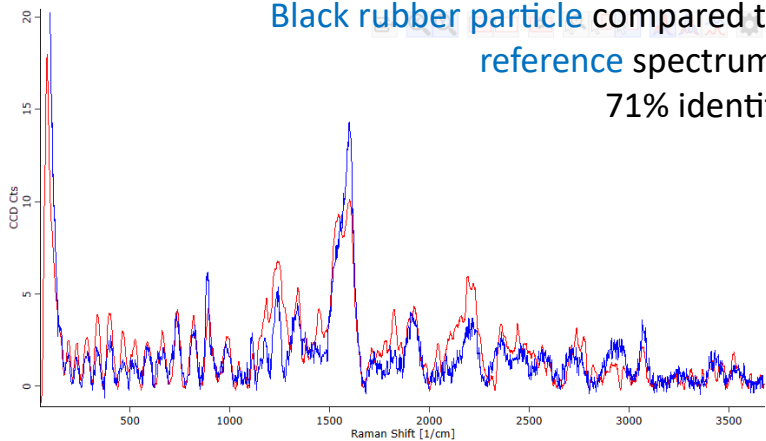
Tire Rubber particle sampled



Olive stone particle sampled



Black rubber particle compared to
reference spectrum:
71% identity



Développement de méthodes d'échantillonnage et d'analyse

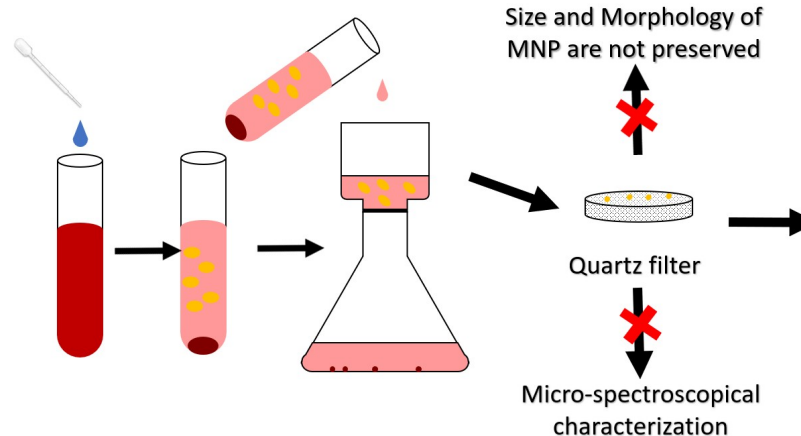
Protocoles pour

- 1) Analyses dans le sang
- 2) Analyses dans l'air
- 3) Analyse de liquides filtrés (différents types de filtrations)



Figure: Digestion and filtration protocol for blood analysis.

Based on:
Leslie et al., *Environment International*, 163, 2022, 107199.



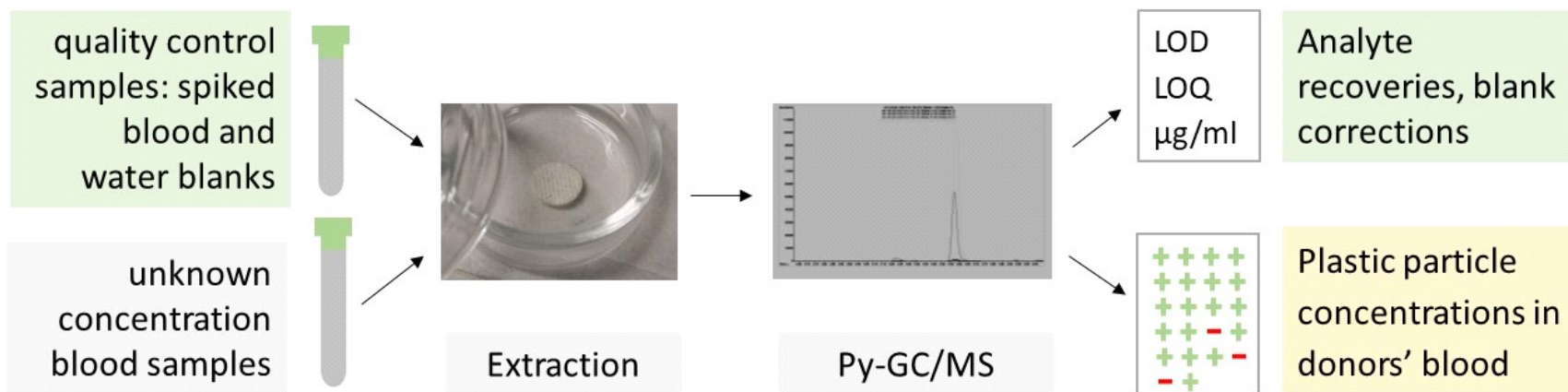
- Blood
- Digested blood
- MNP
- Organic residue



Py-GC/MS

Concentrations sanguines humaines

Analyse par Py-GC/MS: 1.6 µg polymères/ml sang
Polymères détectés : PMMA, PP, PS, PE, PET



Full length article

Discovery and quantification of plastic particle pollution in human blood



Heather A. Leslie^a, Martin J.M. van Velzen^a, Sicco H. Brandsma^a, A. Dick Vethaak^{a,b}, Juan J. Garcia-Vallejo^c, Marja H. Lamoree^{a,*}

^a Dept. of Environment and Health, Faculty of Science, Vrije Universiteit Amsterdam, De Boelelaan 1108, 1081 HZ Amsterdam, the Netherlands

^b Deltares, Delft, the Netherlands

^c Cancer Center Amsterdam and Amsterdam Infection and Immunity, Amsterdam University Medical Center (VUmc location), De Boelelaan 1108, 1081 HZ Amsterdam, the Netherlands

Eau potable

- Données POLYRISK : 15,000 mp (>1 mm)/l
- Etude récente : 240,000 np/l
- Particles utilisées in vitro (cellules THP1):
 - PSP (200nm) 10-100 µg/ml/200,000 cells= 2.3 e9-e10
 - PSP (1 mm) 10-100 µg=1.8 e7-e10

PNAS






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Rapid single-particle chemical imaging of nanoplastics by SRS microscopy

Naixin Qian^a , Xin Gao^a , Xiaoqi Lang^a, Huiping Deng^b, Teodora Maria Bratu^b, Qixuan Chen^c, Phoebe Stapleton^d , Beizhan Yan^{b,1} ,
and Wei Min^{a,e,1} 

Résumé et conclusions

- L'évaluation des dangers, des risques et des expositions aux micro- et nanoplastiques (MNP) est complexe et nécessite de relever de nombreux challenges
- Les MNP natifs semble peu actifs sur le système immunitaire. Les phénomènes de vieillissement (chimie de surface, lixiviation) pourraient rendre les MNP plus actifs/toxiques
- L'évaluation des risques pour l'Homme n'est pas possible en raison du manque de données et de connaissances. Cependant, les MNP appartenant à la famille des particules, il est important d'appliquer le principe de précaution





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Thank you for your attention.

