FROM RESEARCH TO INDUSTRY

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# CHARACTERIZATION OF NANOPARTICLES IN URINE FROM RATS EXPOSED TO TITANIUM DIOXIDE NANOPARTICLES

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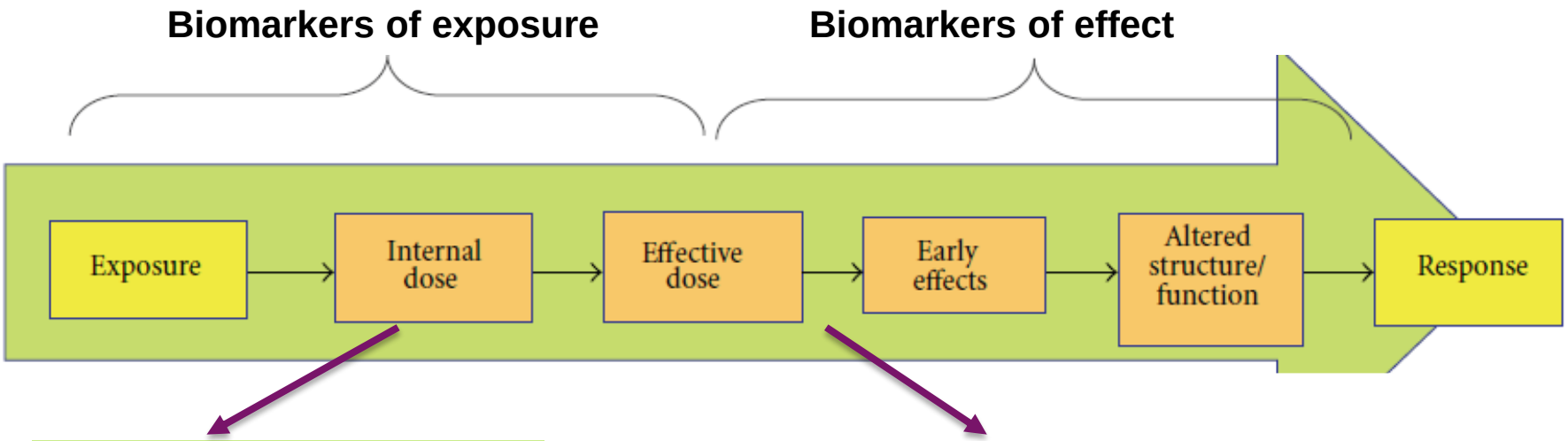
PLATE-FORME NANO SÉCURITÉ

# INTRODUCTION

*Adapted from Bergamaschi E. Journal of Nanomaterials 2012*




**INTERNAL DOSE**

- **Exhaled particles in EBC**
- **Circulating particles**
- Particle uptake
- **Elemental analysis**
- Protein modification
- …

**EFFECTIVE DOSE/EARLY EFFECTS**

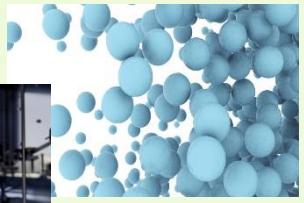
- **Lipid peroxidation in EBC**
- Oxidatively damaged DNA
- Exhaled NO
- Carbonyl compounds in EBC
- **Acute phase proteins**
- Clotting factors
- Vascular adhesion molecules
- …

# Characterization of nanoparticles in biological fluids

**Collaboration with the biomarkers/xenobitics and NP Unit from UdeM (Michèle Bouchard)**

## Toxicokinetics studies *in vivo*

Ag, $TiO_2$



Université de Montréal

**Perfectly characterized exposure scenarios**

## Characterization of nanoparticles (NP)

Better comprehension of biodistribution and elimination of NP

**Main question: particles/ions?**

**Case study**

- Intravenous exposure Sprague-Dawley rats: **1 mg/kg $TiO_2$ anatase 20 nm**
- 14-day kinetics study: focus on urine

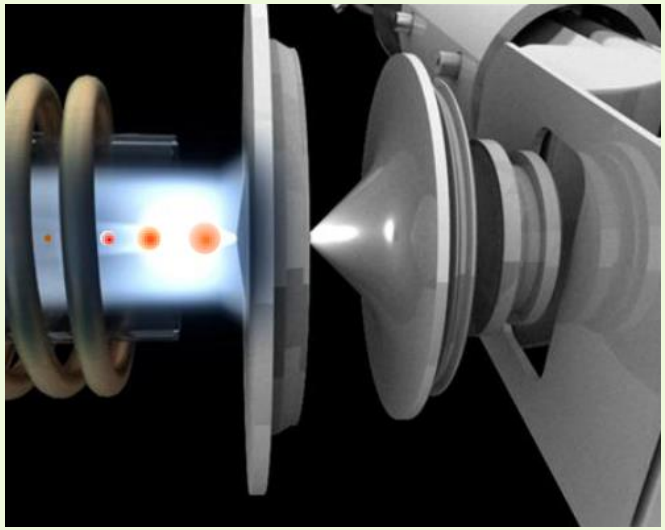
# CHARACTERIZATION OF NANOPARTICLES IN BIOLOGICAL FLUIDS

**Usual methods hardly combine elemental and size characterization**

ICP-MS: a reference method for elemental analysis

No information in terms of particulate contents

Evaluation of coupling strategies

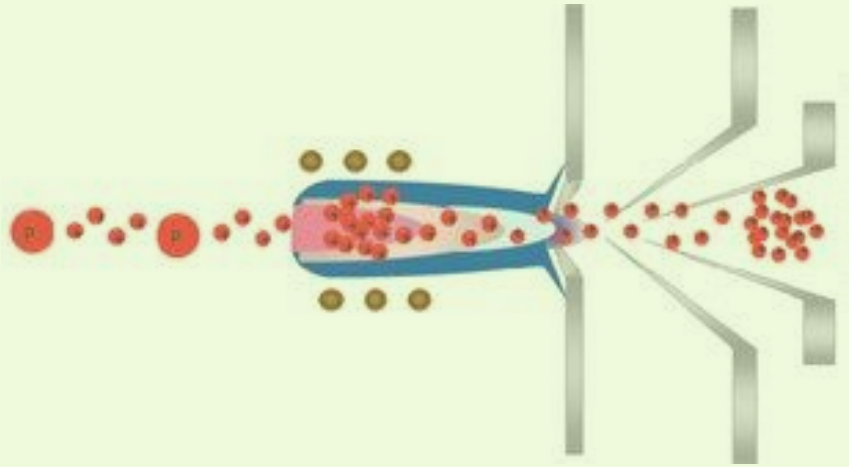


⇒ **Single Particle – ICPMS**

⇒ **Electrothermal Vaporisation – ICPMS**

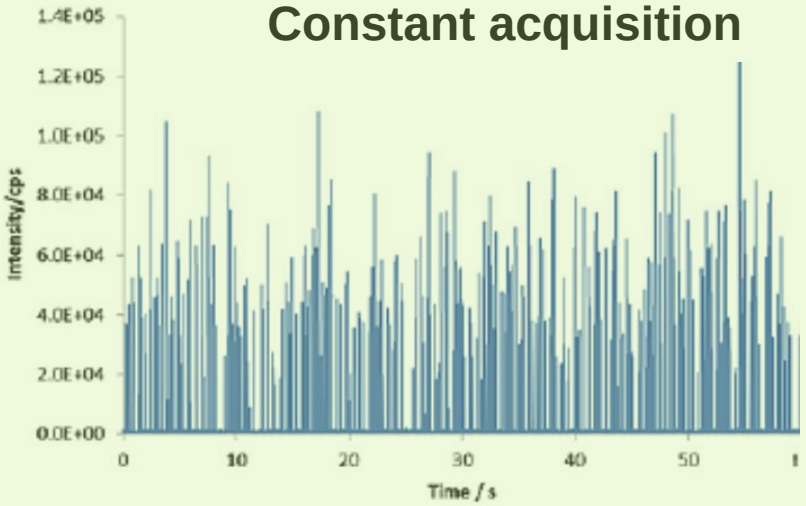
*in collaboration with* PerkinElmer *For the Better*

## Detection of nanoparticles and ions



**Discontinuous signal**

**Constant acquisition**



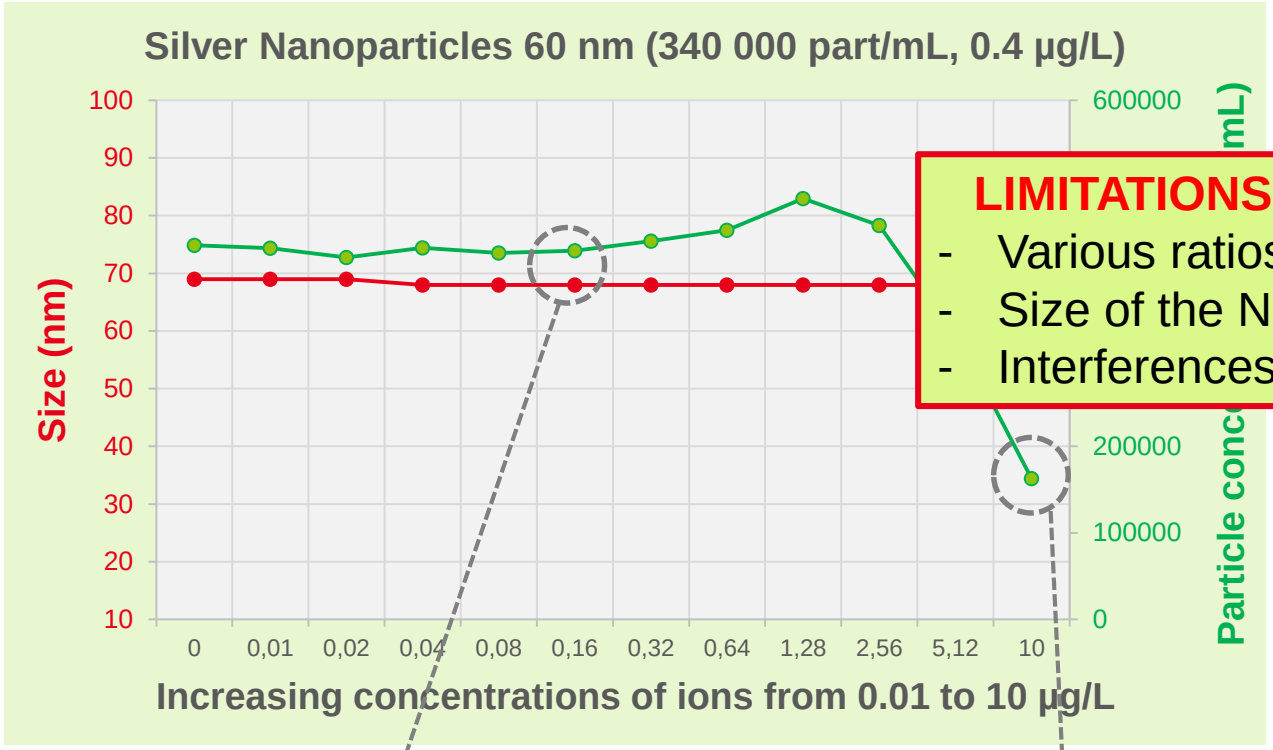

Number of pulses ⟹ Particle number concentration

Intensity of pulses ⟹ Size of particles

# SP-ICPMS: from theory to practice

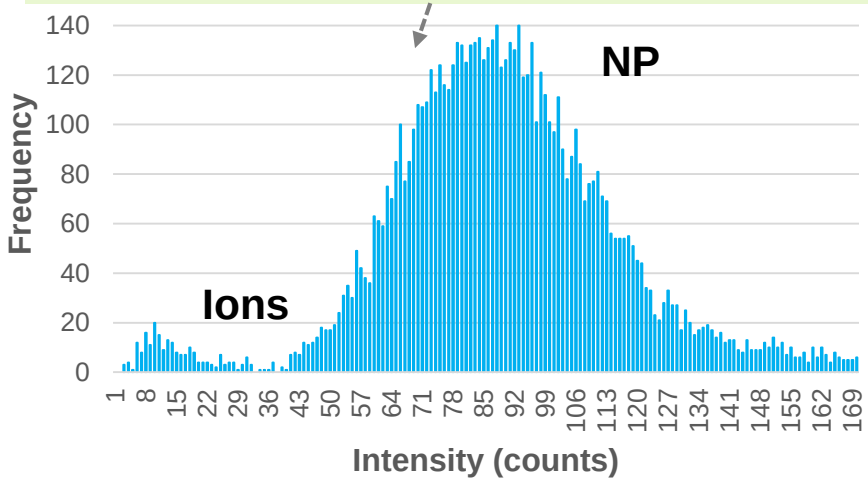


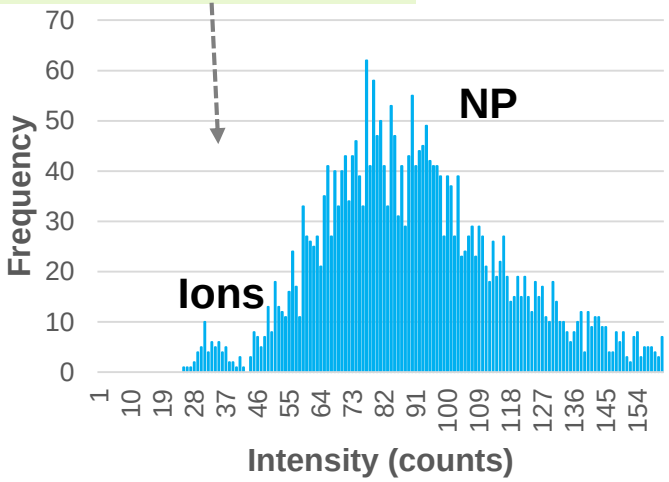
Scan time 100 s - Dwell time 100 µs




**LIMITATIONS for $TiO_2$ 20 nm in urine**

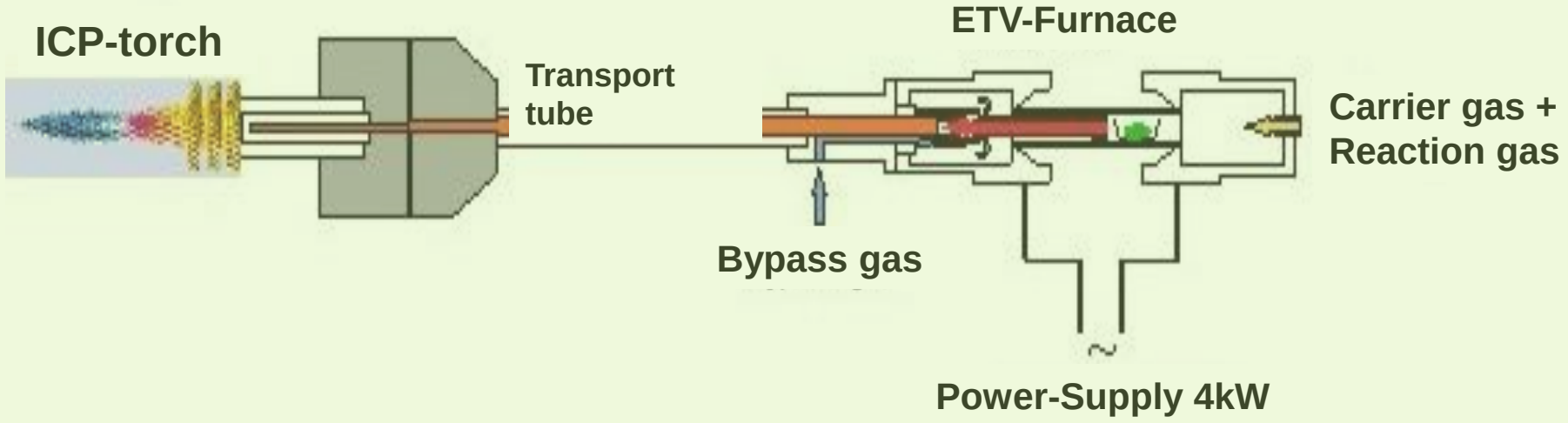
- Various ratios ions/NP
- Size of the NP: near the LOD ~ 20 nm
- Interferences of the matrix



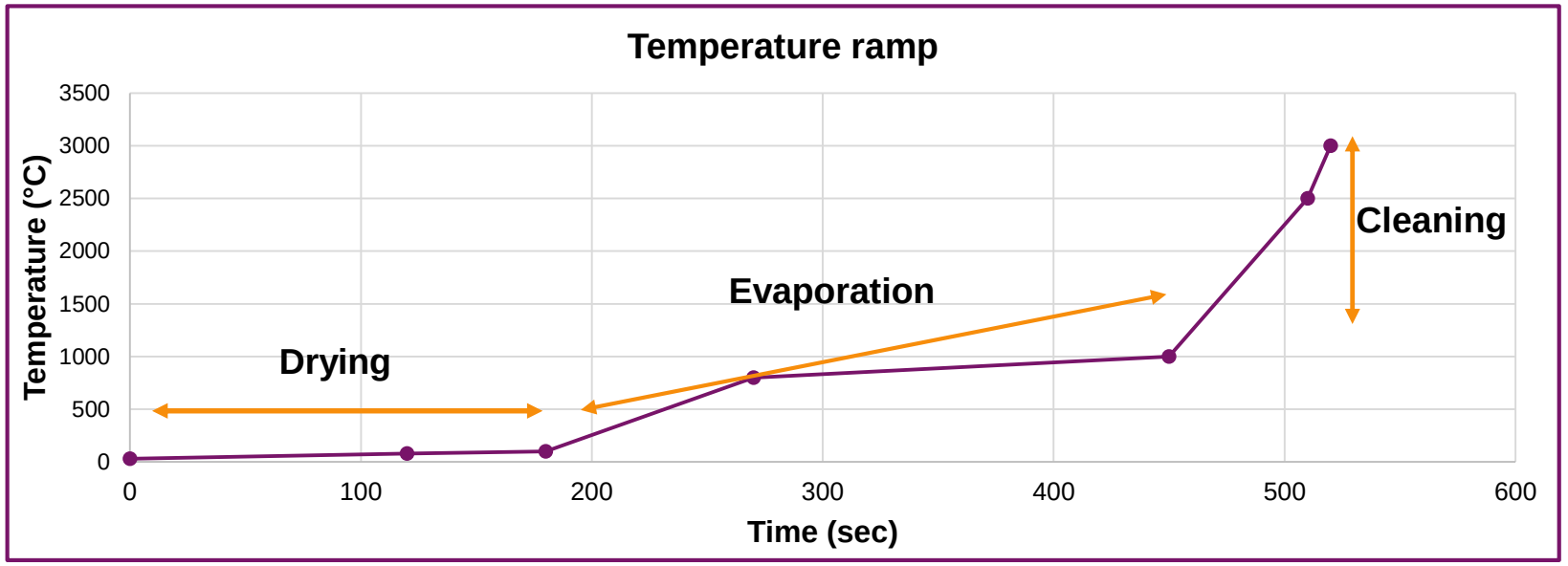



# ELECTROTHERMAL VAPORISATION (ETV) - ICPMS

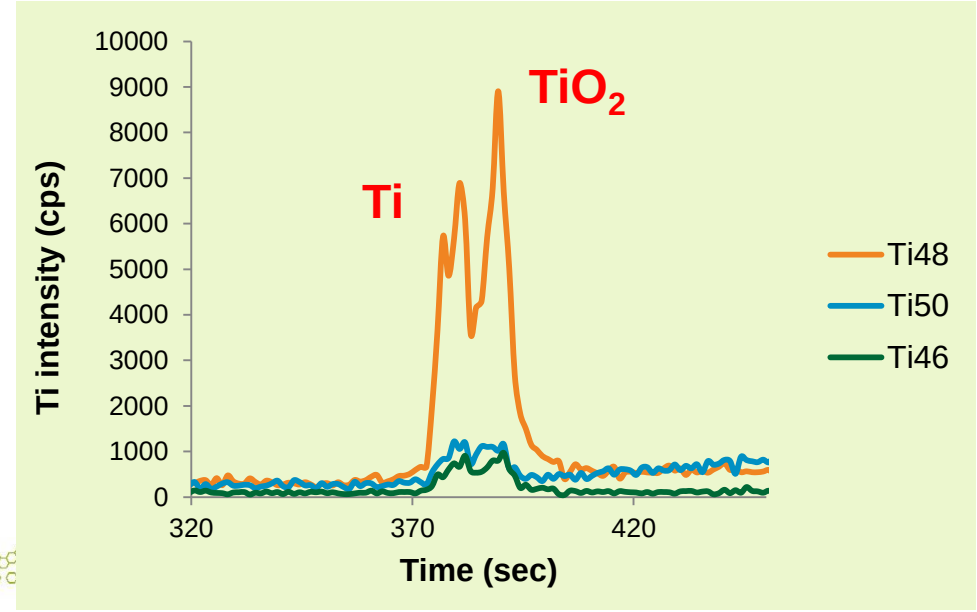
- Graphite furnace up to 3000°C
- Selective evaporation by temperature programs
- Transformation of metal-ions into volatile halogenides



# ETV – ICPMS




**250 ng Ti + $TiO_2$ 20 nm**
In water - KED mode



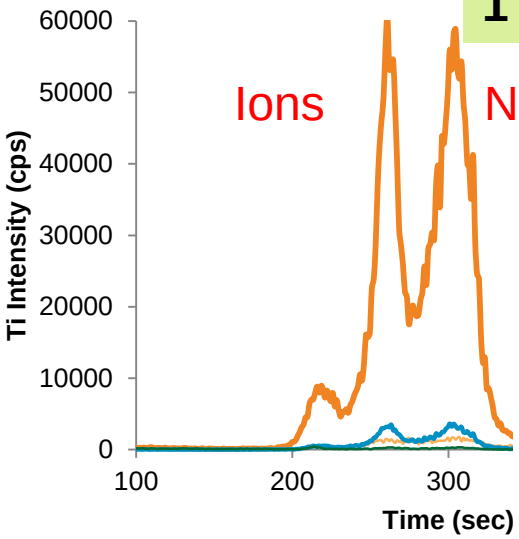
# ETV-ICPMS: CHARACTERIZATION OF URINARY SAMPLES

**ON THE BASIS OF ELEMENTAL ANALYSIS OF Ti**

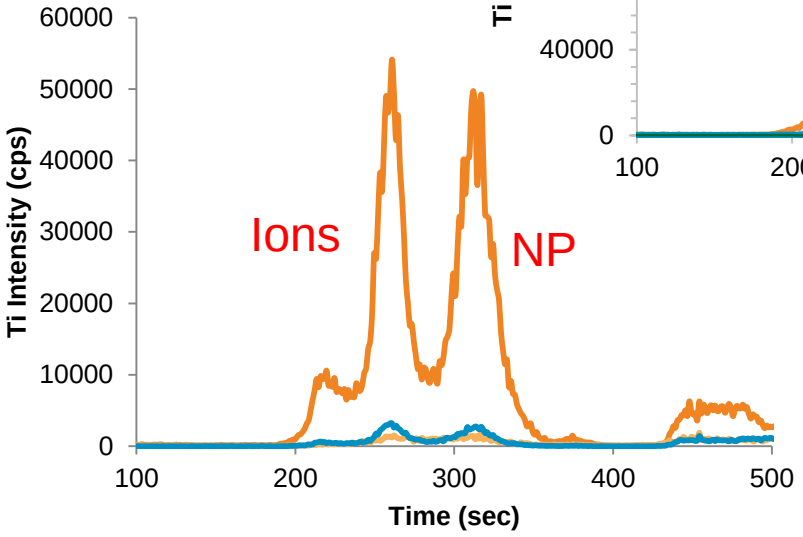
Mean cumulative urinary excretion over 14 days: **3.6 ± 1.0 % ID**

Maximal excretion rate (µg/h) : **2 h post-IV with continuous excretion up to 14 days**

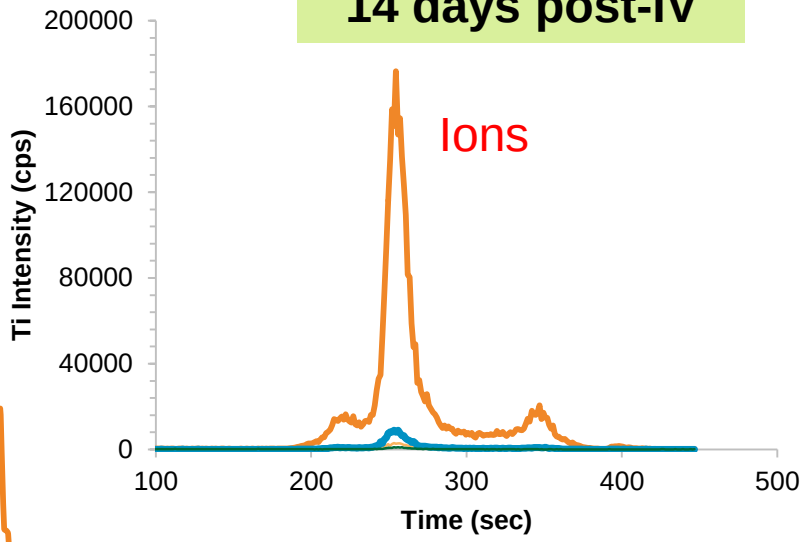
**1 day post-IV**




**2 days post-IV**

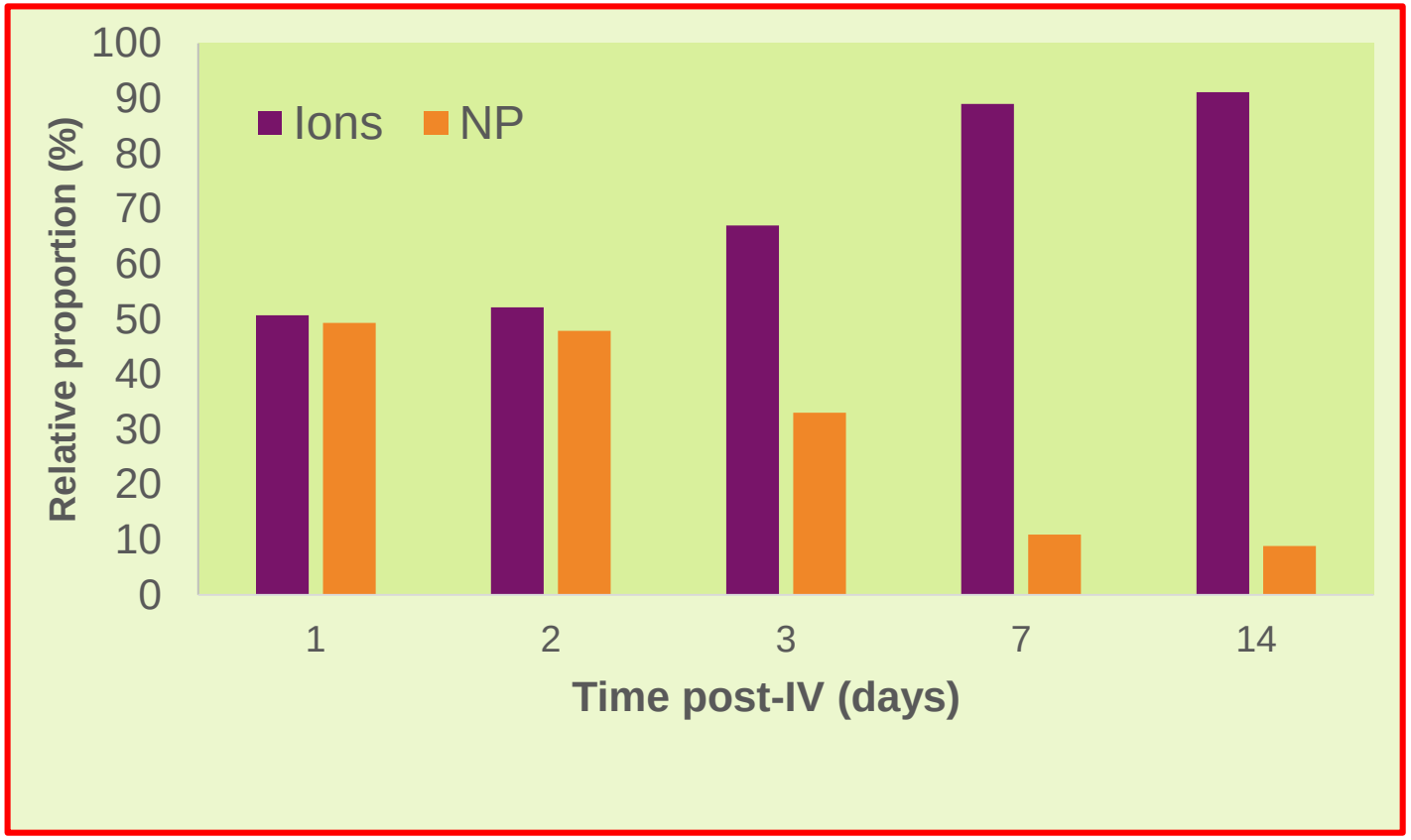



**14 days post-IV**

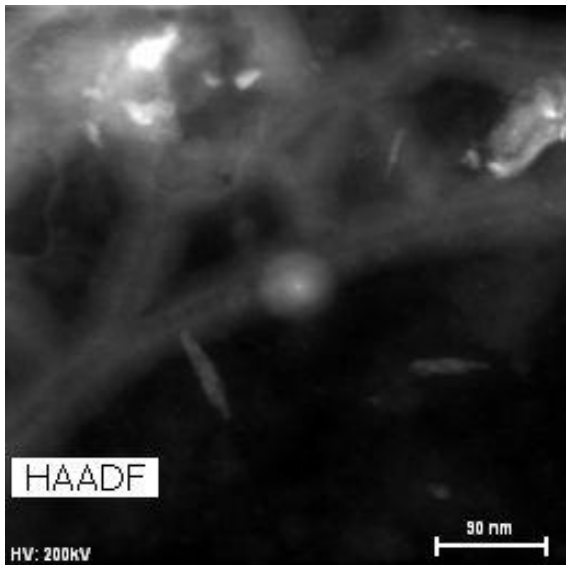


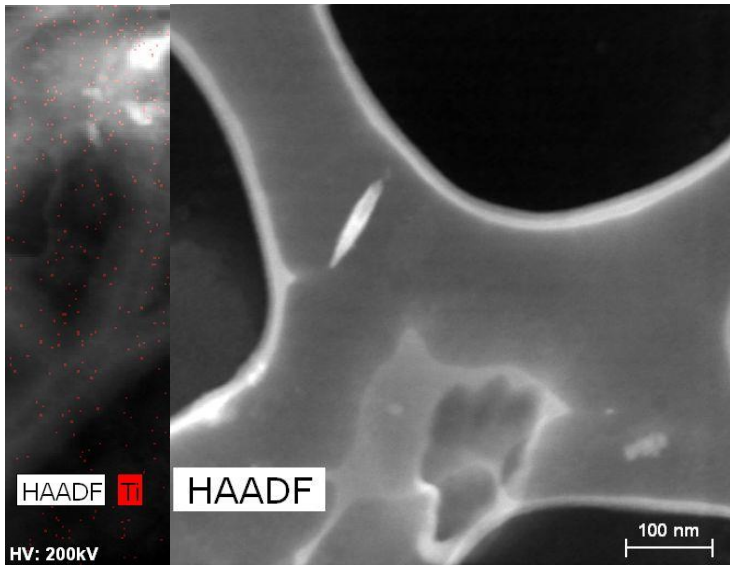
# ETV-ICPMS: CHARACTERIZATION OF URINARY SAMPLES

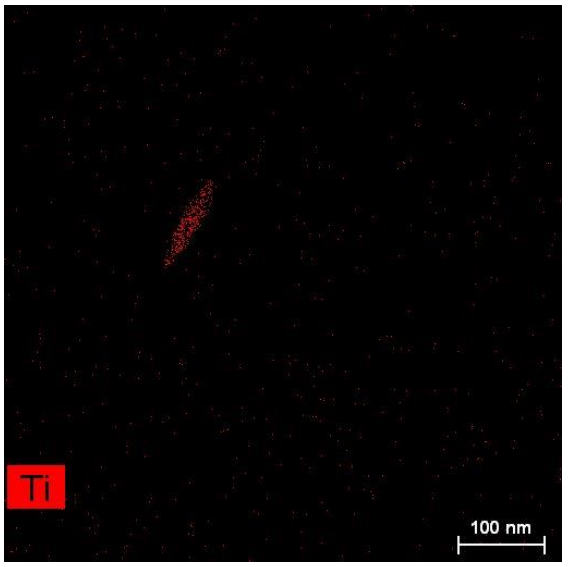
## Composition of titanium urinary excretion

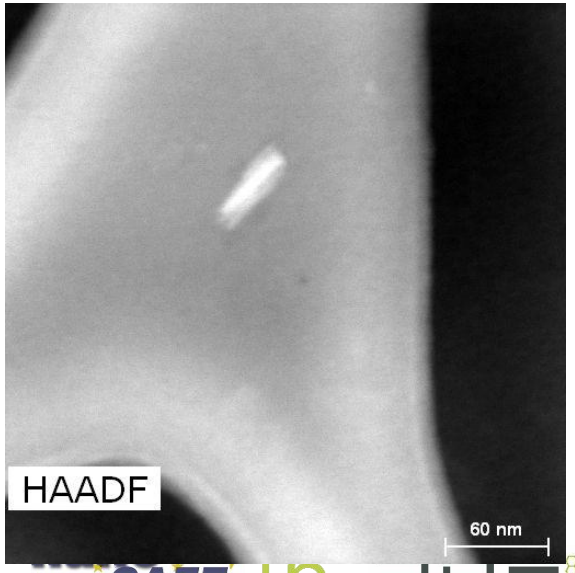


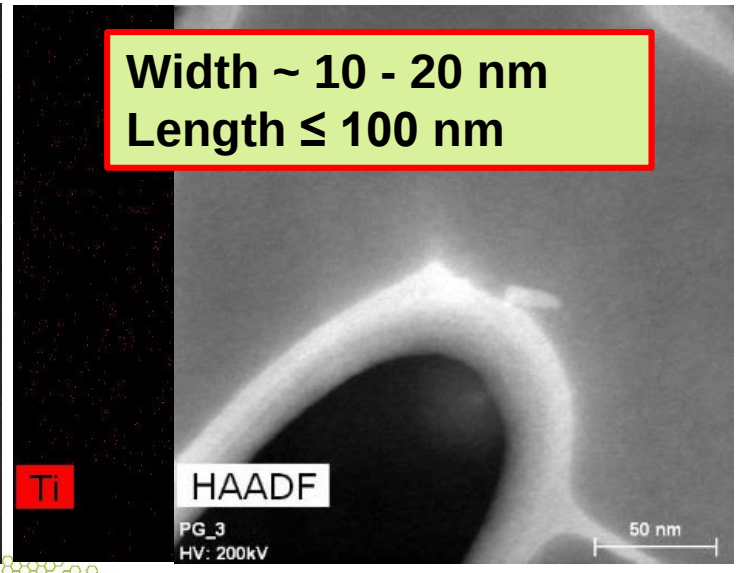
# STEM-EDX explorations: 1 day post-IV



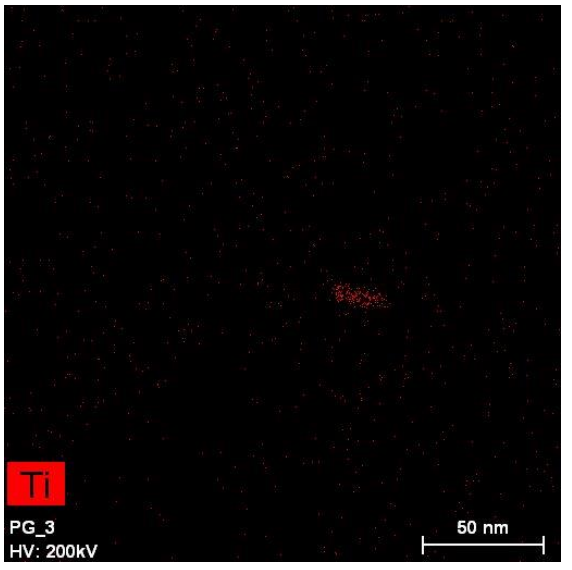



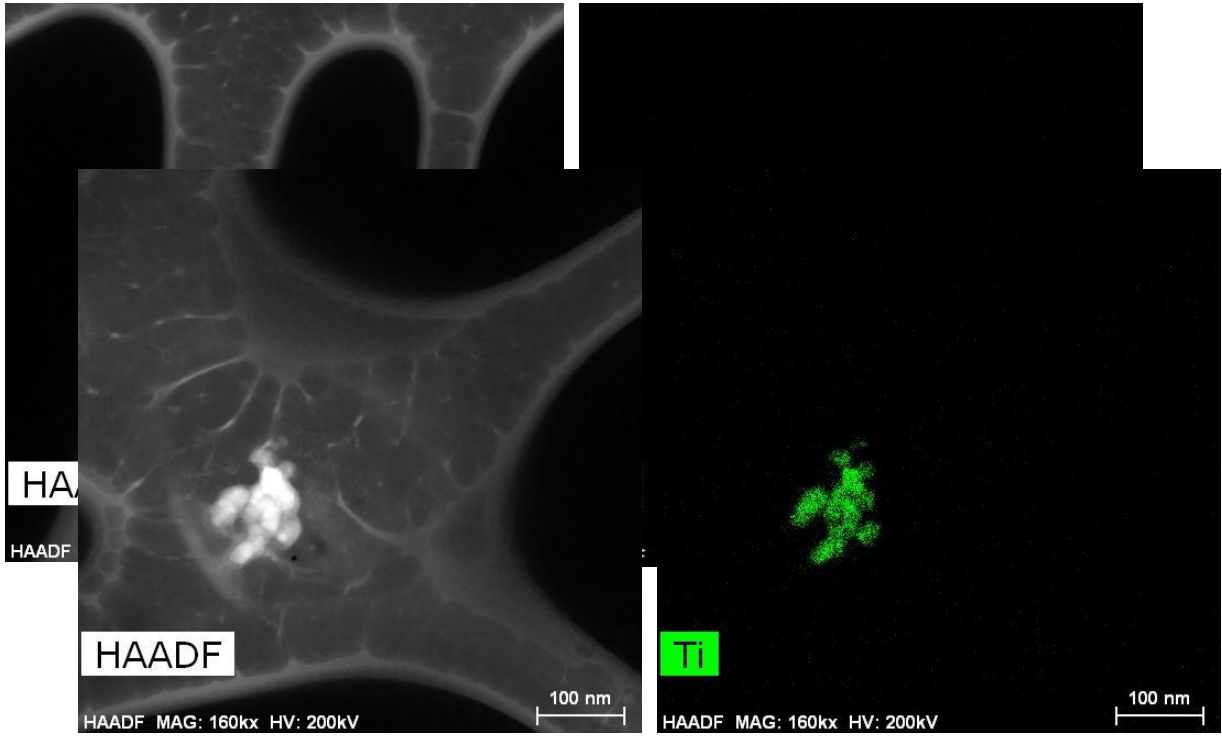




**Width ~ 10 - 20 nm**
**Length ≤ 100 nm**



# TEM-EDS EXPLORATIONS

**Control urine + 100 µg/L $TiO_2$ 20 nm anatase**




**Shape of urinary agglomerates?**

- in accordance with data on the cutoff size for renal excretion *(Choi et al. 2007) :* internal arranging to get through the endothelium?
- de novo formation? As shown for silver (*Van der Zande et al. 2012, Juling et al. 2016*).

# CONCLUSION

**METHODS**

- **SP-ICPMS:** + : size and elemental detection along with quantification, sensitivity, distinction of ions/particles under certain conditions.
  - : for NP > 20 nm, mono-elemental, influence of matrices.

- **ETV-ICPMS:** + : Elemental detection along with quantification, distinction of ions/particles, no influence of the matrix, for liquid or solid samples.
  - : no size detection, sensitivity.

**IN VIVO STUDY**

- Application of ETV-analysis to more samples
- Evaluation of the quantitative aspect of ETV-ICPMS
- Exploration of samples originating from the early times of the kinetics, inhalation exposure, lower doses, different sizes..
- Comparison with a « no-particle » Ti exposure

**APPLICATION**

- Potential recommendations towards human biomonitoring

# Thank you for your attention !

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PLATE-FORME NANO SÉCURITÉ

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