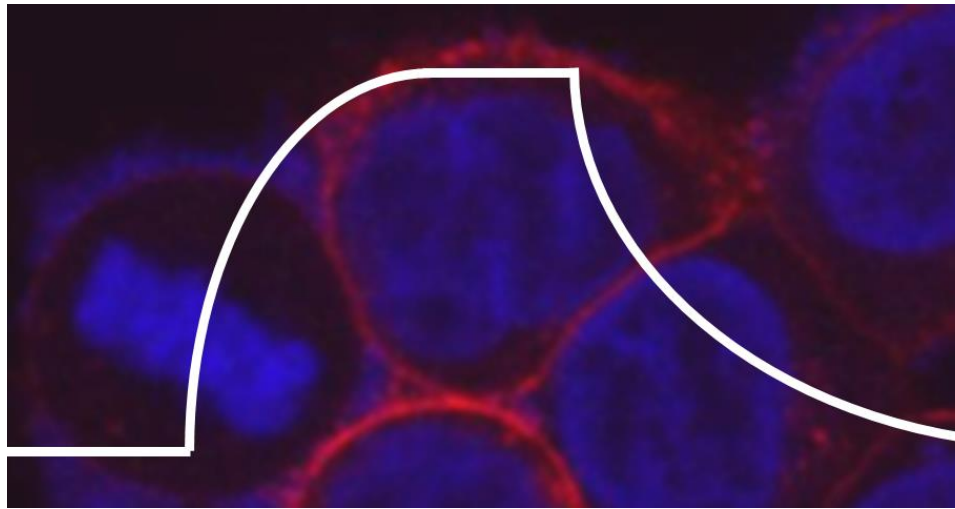


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Towards prediction of *in vivo* behavior of nanoparticles: A quartz crystal microbalance platform for characterization of nanoparticle - cell interactions in a complex biological milieu



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T. Aastrup, K. Dawson**

**Attana AB, Stockholm**



# Agenda

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- Attana - the company
- Attana technology
- Assay development
- Results; biochemical / cell-based assays
- Summary; towards a mechanism for NP grouping and even for predicting NP behavior *in vivo*

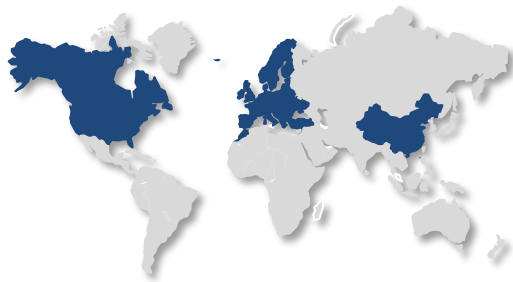


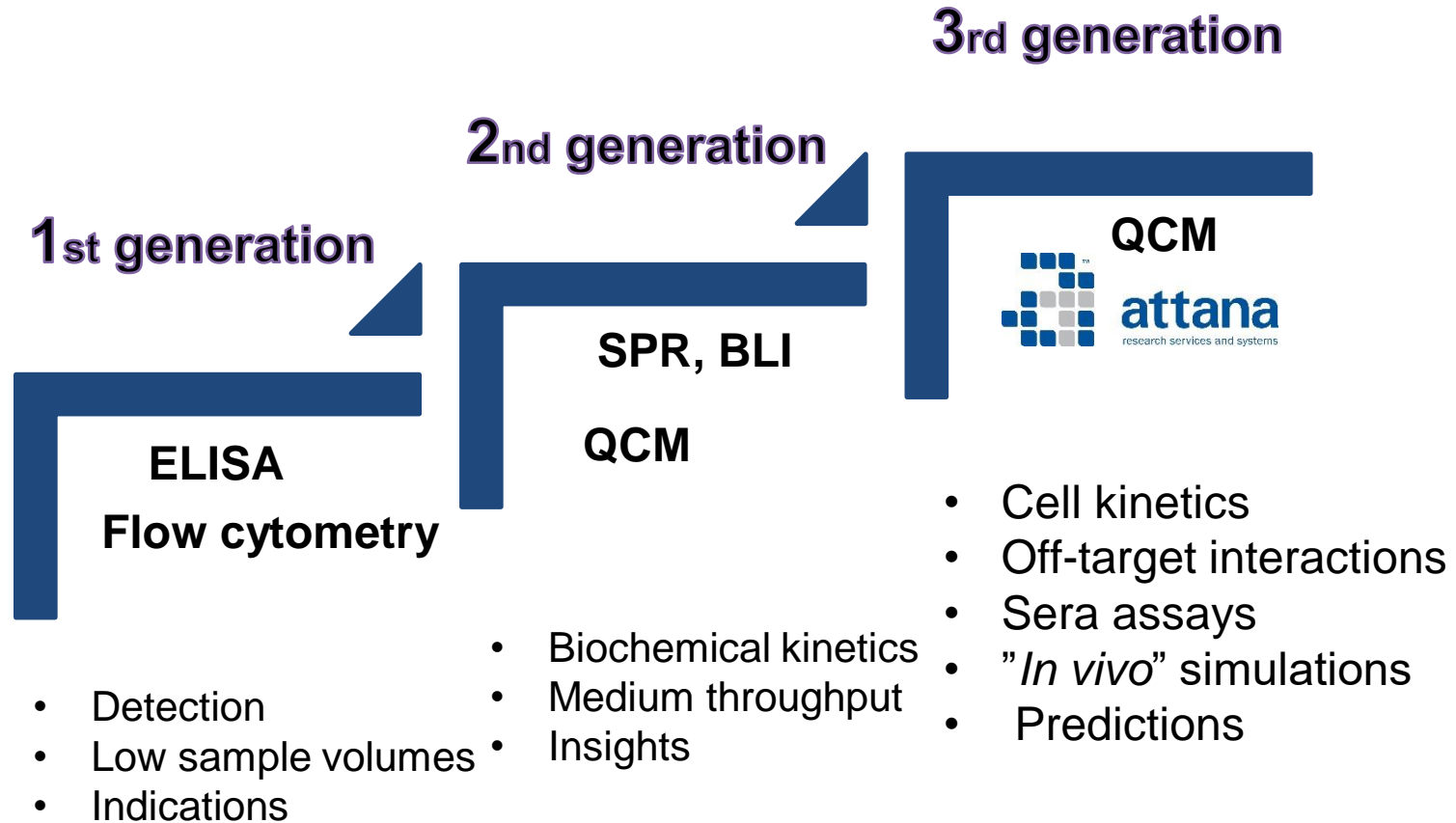
## History and background

### Attana history and biosensor systems

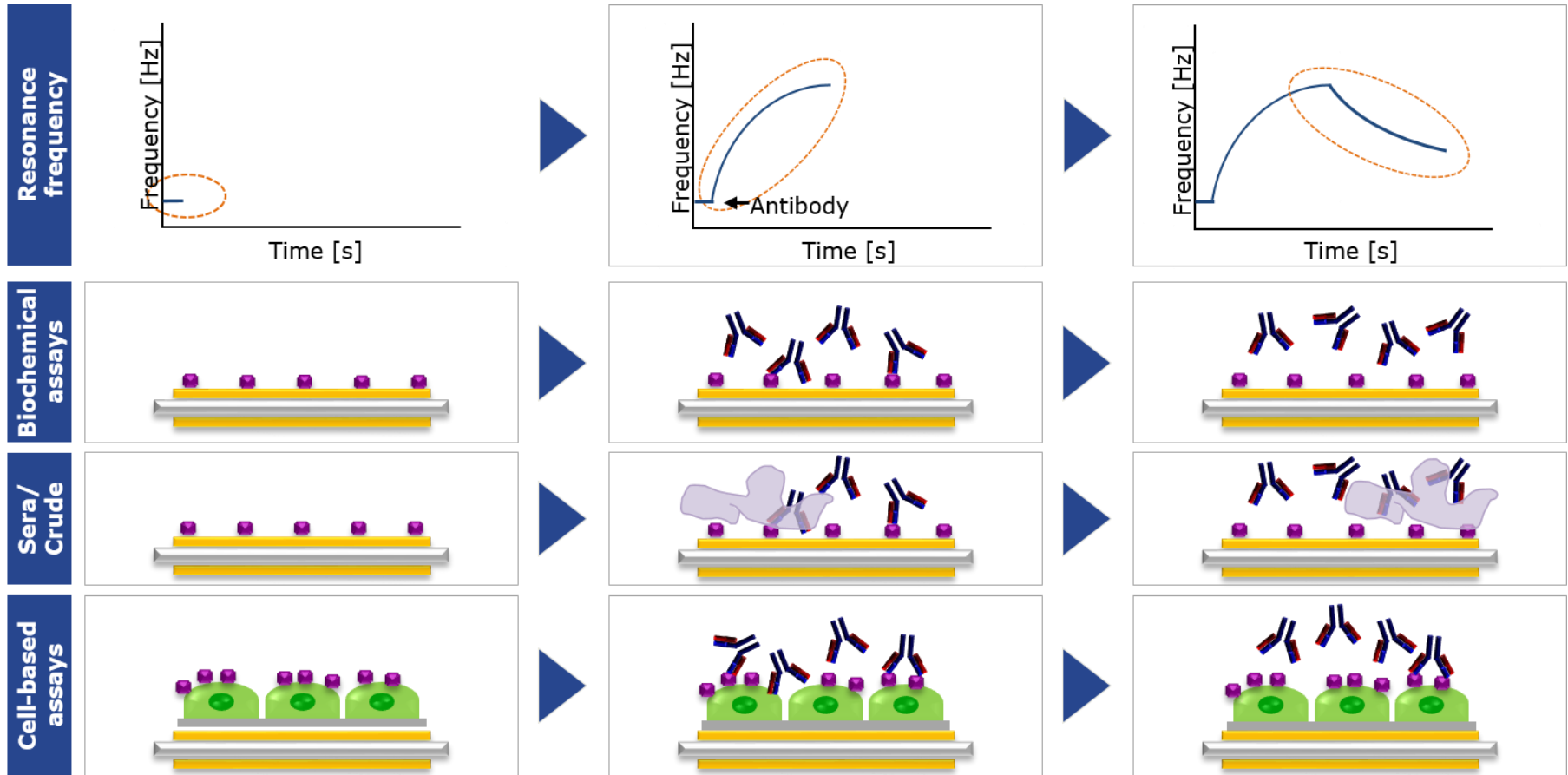
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- Founded 2002 in Stockholm, Sweden
- Based on research from KTH, Royal Institute of Technology
- Products on market since 2003
- Contract Research since 2013
- Attana contract research labs in Stockholm, London and Copenhagen



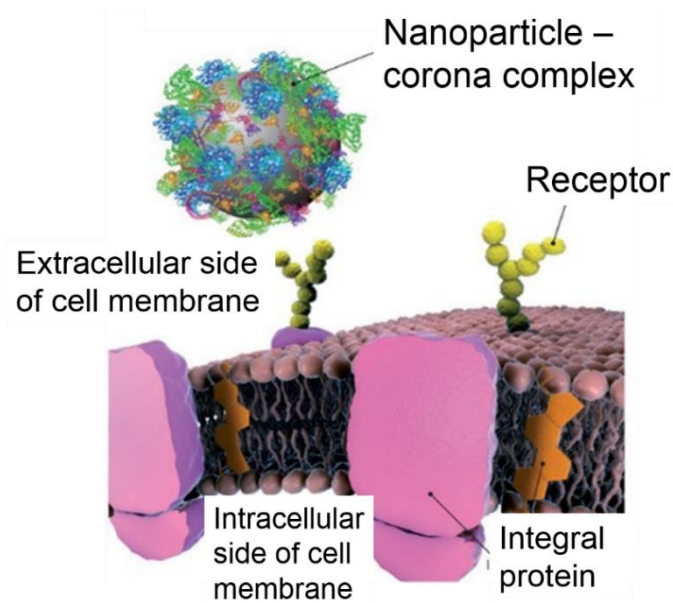


### Full binding profiling providing *in-vitro* biology



### Objectives

- Label-free *in situ* detection of functional epitopes on the nanoparticles biological surface
- To profile the actual binding partners for nanoparticles in complex biological milieu

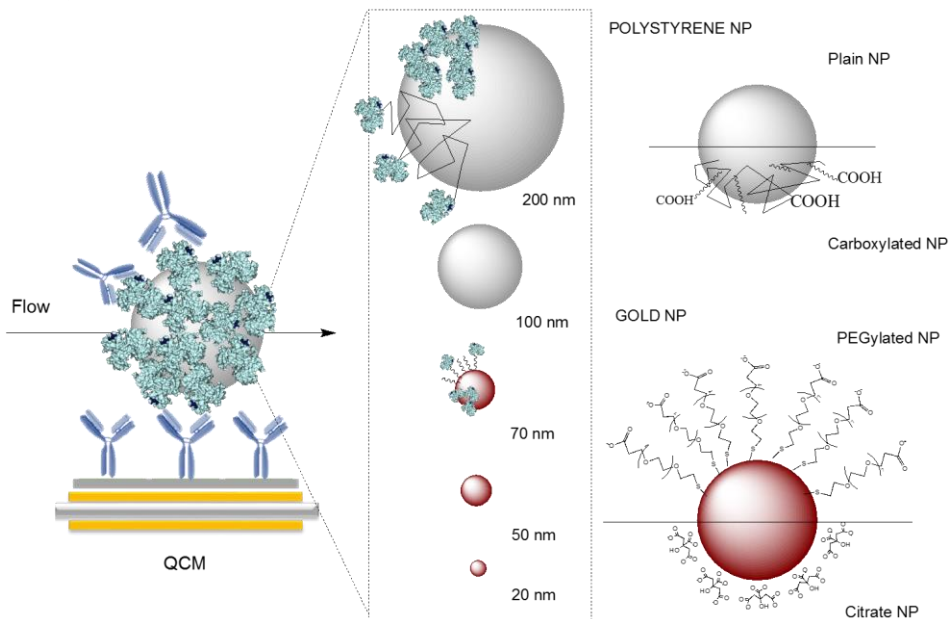


Monopoli *et al*, 2014

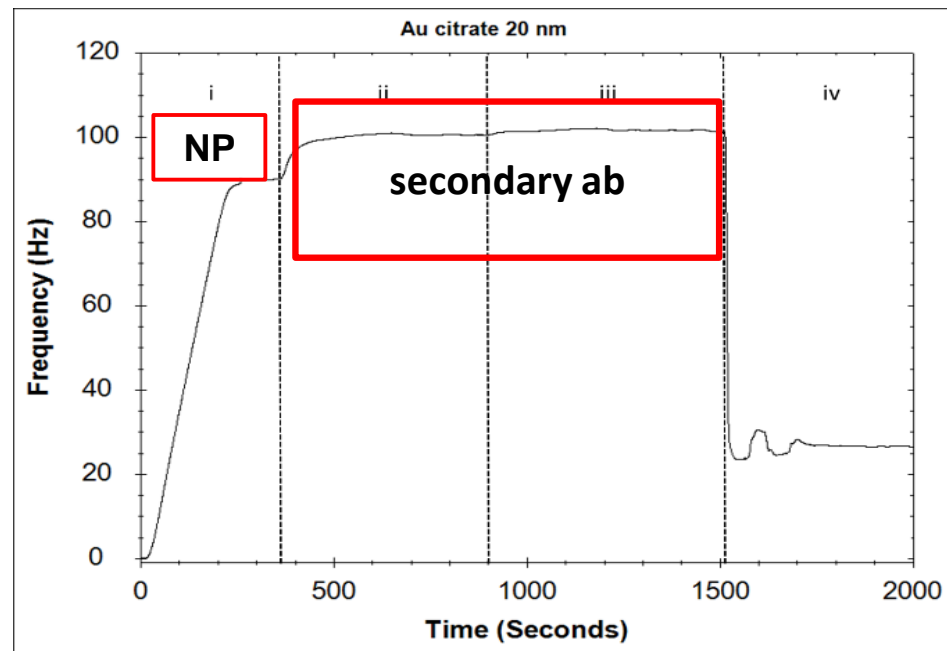
# Assay Development

## Workflow – Biochemical assays

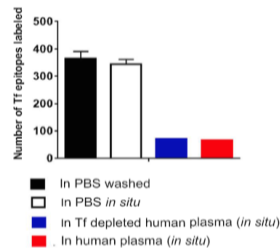
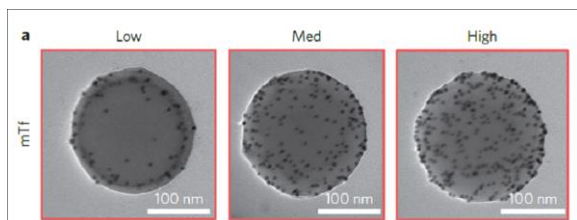
### Experimental set-up



### QCM sensorgrams



### Validation - Comparison



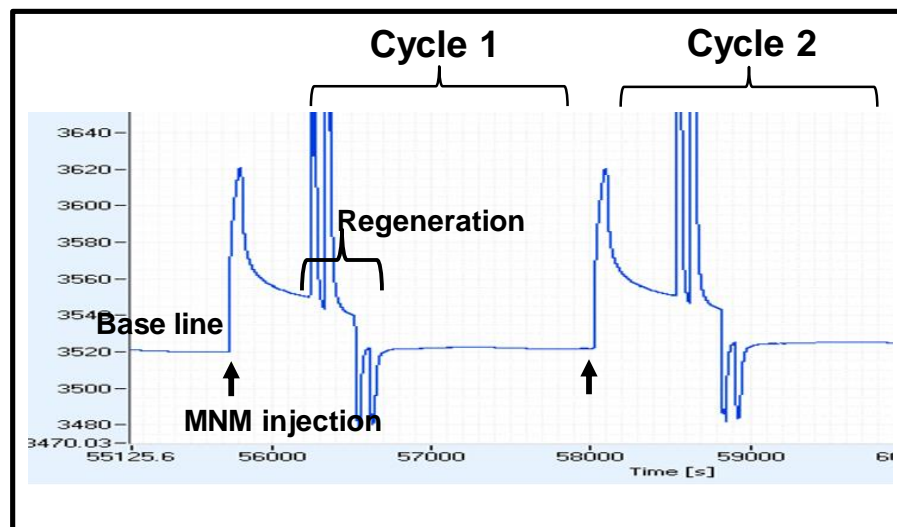
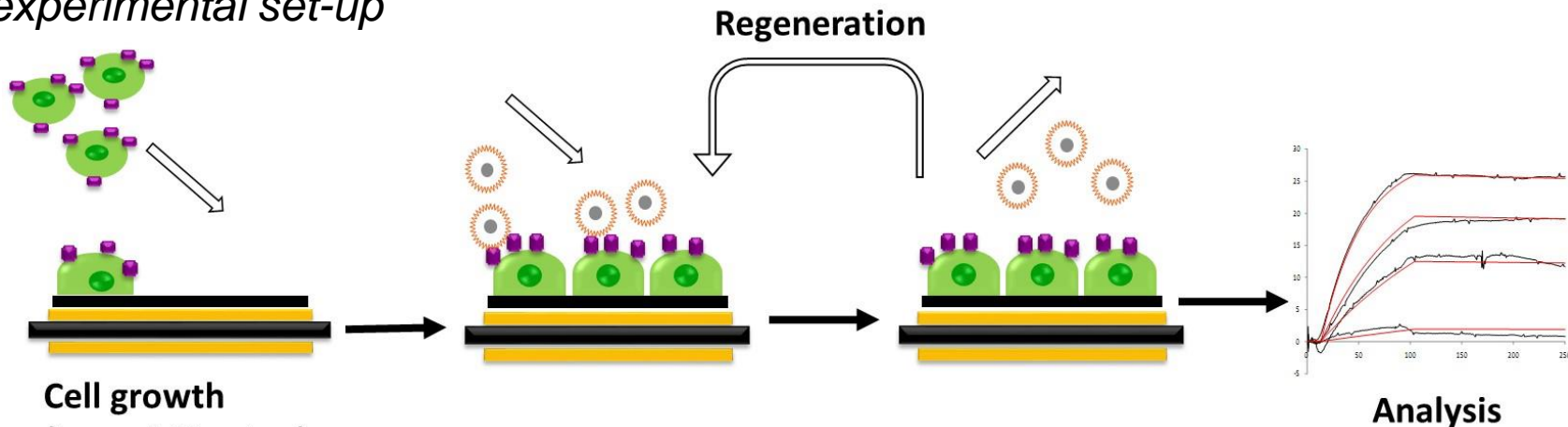
- Kelly et al., Nature Nanotechnology 2015
- MCL Giudice et al., Nature Communications 2016



# Assay Development

## Workflow – Cell-based assays

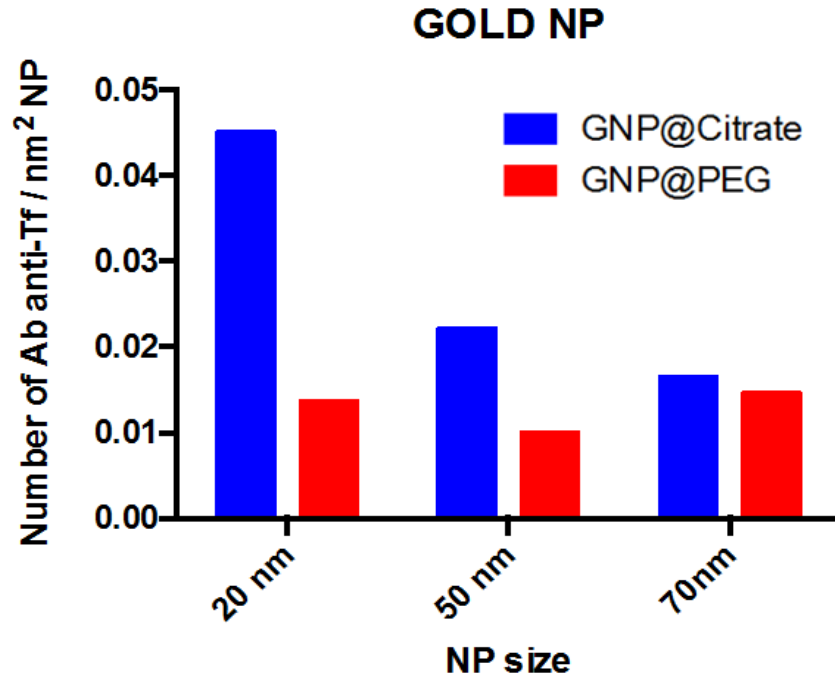
*experimental set-up*



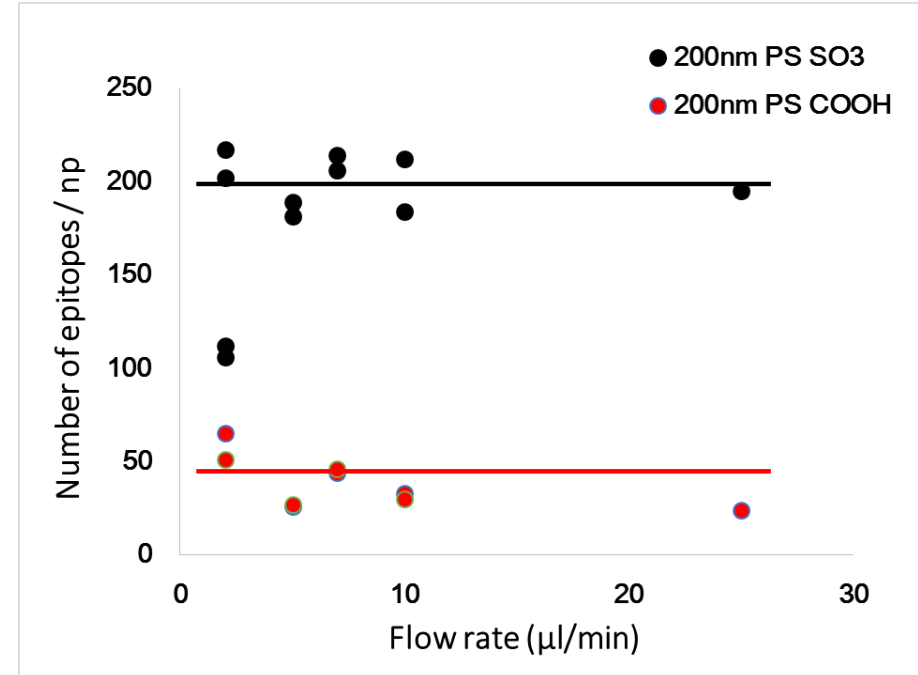


## Results

# Mapping protein binding sites on the NP biomolecular corona



- Number of anti-transferrin antibodies / nm<sup>2</sup> NP
- 2 different materials; Au, PS
- Influence of size
- Influence of functionalization

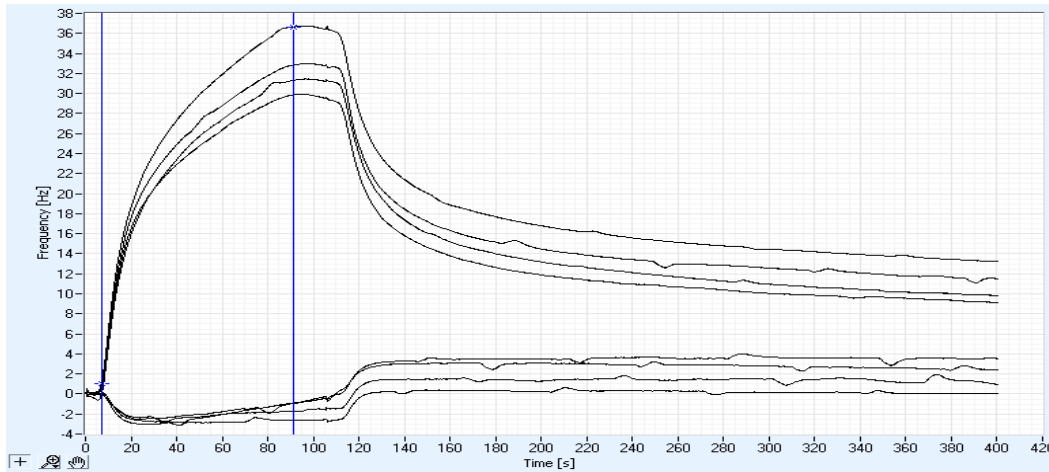
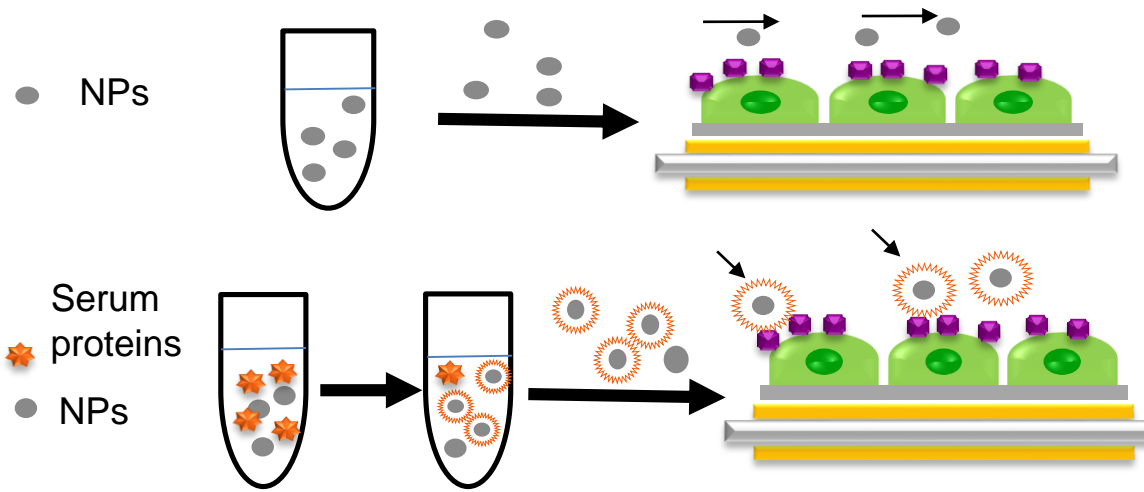


- Effect of flow rate of secondary ab
- No influence on number of counted abs in that range
- Accessibility of functional transferrin epitopes



# Results

## Clear impact of sera-formed corona on the interaction properties

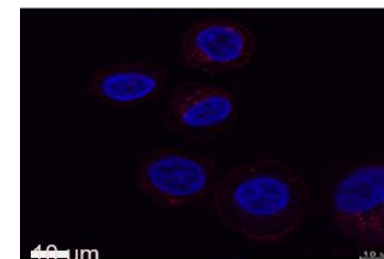
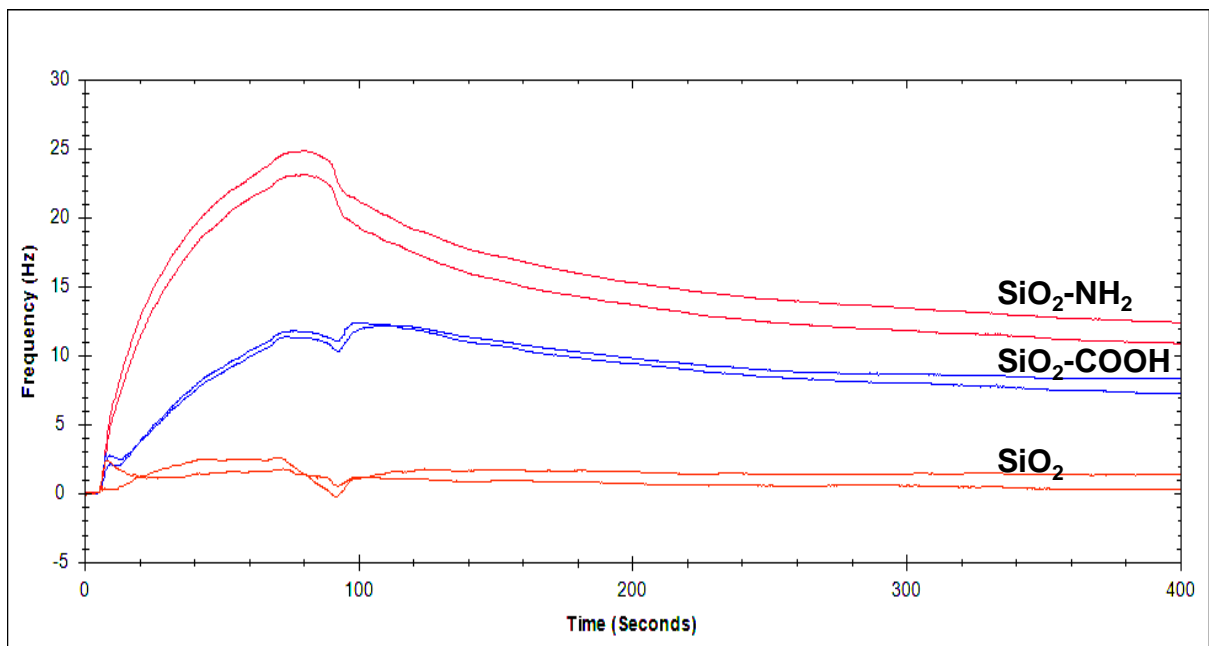


} TiO<sub>2</sub> incubated in 10 % FCS

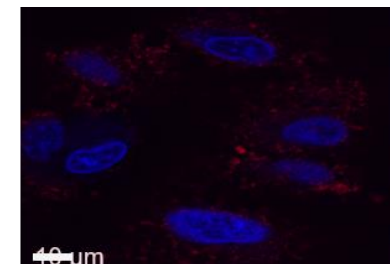
} TiO<sub>2</sub> dispersed in PBS (No FCS)

# Results

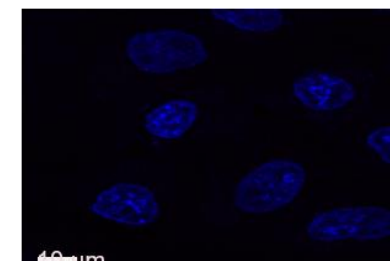
## Effect of surface modifications on interaction properties



SiO<sub>2</sub>-NH<sub>2</sub>



SiO<sub>2</sub>-COOH



SiO<sub>2</sub>

particle type	dissociation rate constant ( <i>kd</i> )	maximum response at 200 sec.
SiO <sub>2</sub> -NH <sub>2</sub>	18.3E <sup>-4</sup>	15 Hz
SiO <sub>2</sub> -COOH	2.17E <sup>-4</sup>	8 Hz



## Results

### NP screening

Particle	A549 cells		Caco2 cells	
	10% FCS	PBS	10% FCS	PBS
TiO <sub>2</sub>	√	—	√	—
Ag-cit	√	√	√	√
CeO <sub>2</sub>	—	—	—	—
SiO <sub>2</sub>	—	—	—	—
Printex 90	—	—	√	—
FeOx	√	—	√	—
SiO <sub>2</sub> - COOH	√	—	√	—
SiO <sub>2</sub> - NH <sub>2</sub>	√	—	√	—



# Summary

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- Label-free *in situ* detection of functional epitopes on the nanoparticles biological surface
  - ❑ Biochemical assays
  - ❑ Correlate NP properties (size, shape, surface chemistry) to biological identity
  
- To profile the actual binding partners for nanoparticles in complex biological milieu
  - ❑ Cell-based assays
  - ❑ NP interaction experiments performed in serum
  - ❑ Influence of corona formation on interaction properties
  - ❑ Influence of functionalization on interaction properties – kinetics profiling



research services and systems

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## Where to find us

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# THANK YOU !!



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