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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When nanoparticles (NPs) enter a biological milieu, they come into contact with a huge variety of biomolecules including proteins. These proteins immediately coat the NP surface and form a protein corona. As a consequence, the original "synthetic identity" of the NPs is covered by the corona and a distinct "biological identity" is acquired. This new corona identity governs how the NPs are "seen" and subsequently interact with cells and other bio entities. Yet, it is not clear how the physical and chemical properties of NPs affect the composition and structure of the protein corona and, in turn, cellular interactions. Improved understanding of the interaction mechanisms and the response of living systems to NPs can accelerate the implementation of nanotechnologies in medicine. We have developed a label free dynamic flow QCM-based platform and methodology for characterization of the bio-nanointerface. This enables identification of key molecular details for NP interactions with cells. A "library" of core and functionalised nanoparticles has been employed to understand the link between NPs physicochemical properties (size, shape, surface chemistry and functionalisation) and the functional protein epitopes of the corona that generate the biological recognition on the surface of the particles. The platform allows studies of the effect of surface modifications of NPs on the interactions with cells grown on QCM sensor surfaces. The results highlight fundamental relationships between NP design, the protein corona, and cellular interactions and

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demonstrate the potential of the platform to predict NP-cell interactions within a biological system.

References

- [1] Kelly et al., Nature Nanotechnology 10 (2015), 472
- [2] Peiris et al., Eurolab 06 (2015), 63

Figures



Figure 1. Experimental set-up



Figure 2. PS NPs modified with sulphonated groups (upper) and carboxylic groups (down) coated with transferrin by physical adsorption