The possibility that nanomaterials could perturb the normal course of an inflammatory response is a key issue when assessing nano-immunosafety. The alteration of the normal progress of an inflammatory response may have pathological consequences, since inflammation is a major defensive mechanism and its efficiency maintains the body’s health. We can thus consider as pathology-related inflammation those inflammatory reactions that, instead of eliminating foreign agents, lack down-regulation and cause tissue damage. To assess the ability of nanoparticles to initiate and modulate inflammatory reactions, an in vitro model was used that recapitulates all the stages of infection-induced inflammation, from initiation to resolution, based on human primary blood monocytes. A parallel model reproducing pathological chronic inflammation shows that the differences between resolving and persistent inflammation are subtle and evident only upon kinetic analysis of gene expression profiles and production of inflammatory factors. Rigorously endotoxin-free Au and Ag nanoparticles have been assessed for their ability to directly initiate in vitro inflammation and for their capacity to modulate the course both physiological resolving inflammation and pathological persistent inflammation. In no case significant effects were observed, with the exception of a transient increase of the inflammatory response in the presence of Ag nanoparticles. An important issue in the regulation of monocyte/macrophage inflammatory functions is the capacity of innate “memory”, i.e., the ability of respond differently to a challenge if previously primed with the same or a different agent. How nanoparticles can impact innate memory was assessed by using Au nanoparticles as priming and challenge agent with and without LPS and zymosan. Priming with LPS and zymosan could drastically decrease the response of monocytes (production of TNF-α) to a challenge with any stimulus, given 7 days after the first. The presence of Au nanoparticles did not influence such behaviour. Likewise, Au nanoparticles did not directly induce memory, i.e., did not influence the response of monocytes to subsequent stimuli. We conclude that Au and Ag nanoparticles, at the size and concentrations used, are taken up by monocytes without this causing any notable interference with their capacity to mount an adequate defensive responses to microbial challenges, either immediate or after some time from exposure.

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