Maturation Effect of Engineered Nanoparticles on Human CD34$^+$ Progenitor-derived Dendritic Cells

Nelissen I.[1], Verstraelen S.[1], Leppens H.[1], Ooms D.[1], Casals E.[2], Puntes V.F.[2], Witters H.[1], Van Den Heuvel R.[1], Schoeters G.[1]

[1]VITO N.V. (Flemish Institute for Technological Research), Center of Expertise in Environmental Toxicology, Boeretang 200, BE-2400 Mol, Belgium; inge.nelissen@vito.be; Phone: +32 14 33 52 11
[2]ICN (Institut Català de Nanotecnologia), Campus de la UAB, Barcelona, Spain

The EU funded project DIPNA aims to develop an integrated platform to assess the toxicity and ecotoxicity of nanoparticles (NP). VITO N.V. mainly contributes to workpackage 2 which focuses on the impact of engineered NP on human immune cells, such as T cells, macrophages, dendritic cells and epithelial cells, by assessment of cytotoxicity, genotoxicity, carcinogenicity, inflammatory and immunological parameters. The goal of our study was to assess the effect of NP on dendritic-cell maturation.

To study the potential immune-stimulating effect of engineered NP, human primary CD34$^+$ progenitor-derived dendritic cells (CD34-DC) were exposed to spherical gold (4.3 and 13 nm), iron oxide (6 nm) or cobalt (4 nm) NP for 24 and 48 hours. Mono-dispersed NP in solution and freshly resuspended nanopowders were used at the same concentration per type of NP. The maturation response of CD34-DC was measured by determination of cell surface expression of the DC surface markers HLA-DR, CD86, CD83 and CD54 using flow cytometry. Additionally, potential inhibition of cellular growth by the NP was analysed by means of the alamarBlue™ and WST-1 assays.

Microscopically, freshly resuspended nanopowders were observed to be more likely to form aggregates, compared with NP in dispersion. No reduction of CD34-DC growth was observed in response to all NP tested at different concentrations. At the highest concentration tested, ranging from $2.4*10^{11}$ to $2.0*10^{13}$ NP per ml for the different particle types, no induction of maturation of the CD34-DC was observed after 24 and 48 hours of exposure to either the mono-dispersed or freshly resuspended NP, i.e. no significant increased expression of the DC maturation markers HLA-DR, CD86, CD83 or CD54 was measured when compared to control conditions.

Small spherical, engineered NP were found not to be cytotoxic to CD34-DC when added either as mono-dispersed NP solution or freshly resuspended nanopowders. Furthermore, they were not able to potently trigger DC maturation. Comparison of our data with other toxicological endpoints and different NP (size, composition, surface coating, shape, …) is warranted. Future work may also include the use of transcriptomics (gene fingerprints) to reveal potential changes at multiple sites in cells.

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