Title *

Nanoparticles and persistent virus infection - a dangerous liaison for the development of chronic lung disease(s)?

Abstract *

Both inhalation of ambient nanoparticles (NP) as well as persistent herpesvirus-infection have been implicated to contribute to the development of chronic lung disease. Here we asked the question whether NP exposure during a latent virus infection may disrupt the anti-viral immune control and induce virus reactivation. We conducted in vitro studies with latently infected cell lines, and in vivo studies with mice, using the murine gammaherpesvirus 68 (MHV-68) model system.

Our results show that exposure of latently infected murine or human cells with spherical carbon nanoparticles (CNP) or double-walled carbon nanotubes (CNT), induced lytic virus production and expression of the viral transactivators Rta and BZLF1. In the lungs of latently infected mice (28 days after infection), immunohistochemistry demonstrated an increase in lytic viral proteins 24h after exposure to CNP or CNT, a response usually observed during the acute lytic phase (6 days after infection). Likewise gene expression analysis of lung homogenates revealed a pro-inflammatory signature with considerable parallels the pattern seen during the acute lytic phase. Analysis of the lung metabolome demonstrated an enrichment of phospholipids in the lungs of latently infected mice after exposure to CNP, matching profoundly with the pattern observed during acute virus infection.

Taken together, our results indicate that the combination of NP exposure and persistent herpesvirus infection restores a molecular signature found in acute virus infection, boosts production of lytic viral proteins, and induces an inflammatory response in the lung – a pattern which might finally result in severe tissue damage and even fibrotic alterations.

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