Gene Expression Changes in Secondary Organs of Rats Intratracheally Exposed to Silver Nanoparticles.

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Studies in rats have demonstrated the ability of silver nanoparticles (AgNP) to translocate to secondary target organs (e.g. liver or kidney) after administration by respiratory route (Takenaka et al, Environ Health Perspect, 2001). In this study, the expression profile of genes involved in oxidative stress (Gpx1, SOD, Gss, FMO2, Gsr, Txnrd1), metal toxicity (mt1), apoptosis/cell cycle (Casp3, p53), and protein folding (Hsp70) was investigated in liver and testis of rats at different time intervals after i.t. instillation of AgNP. $AgNO_3$ was used as a positive control.

Groups of adult male Sprague-Dawley rats received 50 μg/rat of AgNP (20 nm), 7 μg/rat of $AgNO_3$ or 100 μL aqueous solution/rat (control). At days 7 and 28 post-administration, the transcriptional profile of selected genes was examined in tissues by cDNA microarray analysis coupled with bioinformatics and functional gene annotation studies. Semiquantitative followed by Real Time PCR was performed to quantify gene expression changes.

At day 7, changes in gene expression that selectively involved antioxidant enzymes were observed in both liver and testes. In particular, Gpx1, FMO2 and SOD genes were upregulated. No changes were seen for the other genes. At day 28 the AgNP-treated animals exhibited a tissue gene expression profile similar to control. None of the investigated genes was shown to be affected by treatment with $AgNO_3$ at both time points considered. The results suggest the potential of AgNPs to cause, at low doses, subtle molecular changes in secondary target organs, in contrast with Ag ions, possibly reflecting the strong tendency of Ag ions to form inert complexes with cellular or blood components or be neutralized by defense mechanisms.

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