A breakthrough in nanotoxicology

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Whereas resistance to antibiotics complicates certain treatments, antimicrobial silver nanoparticles (AgNP) are gaining popularity for medical use. These particles are toxic for certain bacteria, but what about for humans? Researchers at INRS-Institut Armand-Frappier Research Centre have taken a step toward understanding the cellular and molecular mechanisms that affect these particles. In an article published in The *Journal of Biological Chemistry*, Denis Girard's team established for the first time that AgNP induce stress in the endoplasmic reticulum (ER), which is one of the signs of nanotoxicity.

In their experiment, the researchers used 15 nm AgNP on human monocytes and macrophages, which are among the first cells to interact with foreign bodies. At low concentrations, the AgNP induced stress in the ER, but did not cause cell death. However, higher concentrations did cause a type of programmed cellular death, which is characteristic of certain inflammatory responses.

The research team's results suggest that the AgNP cause degradation of the ER's ATF-6 sensor and activation of the NLRP-3 protein complex. It is the first time that an inflammatory response to AgNP particles in this protein complex has been reported.

Following up on these results, Professor Girard's team will study the ATF-6 molecule more closely in order to better understand the mode of action of various nanoparticles with respect to myeloid cells.

Professor Girard believes these research results using THP-1 cells also

open up other research possibilities: "We used leukemia cells throughout most of the study. The question is, could we achieve the same results with other types of cancer cells? If so, it may be possible to use nanoparticles to kill cancer cells without the use of drugs, which would be very promising."

More information: *Journal of Biological Chemistry*, DOI: 10.1074/jbc.M114.610899

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