Principles of Nanotoxicology

Ivan PACHECO, MD, PhD (1), Robert VANNER, MSc (2), Cristina BUZEA, PhD Eng (3)

(1) Queen's University, Department of Pathology and Molecular Medicine, Kingston General Hospital, 76 Stuart Street, Kingston, Ontario K7L 2V7, Canada, e-mail: 7bip@queensu.ca

(2) University of Toronto, faculty of Medicine, Toronto, Ontario M5S 1A8, Canada

(3) Queen's University, Department of Physics, Engineering Physics, & Astronomy, Kingston, Ontario K7L 3N6, Canada

This presentation summarizes the most significant aspects of nanoparticle toxicity and identifies the major sources of nanoparticles. The sources of nanoparticles on Earth are varied (**Figure 1**), encompassing natural as well as anthropogenic causes.

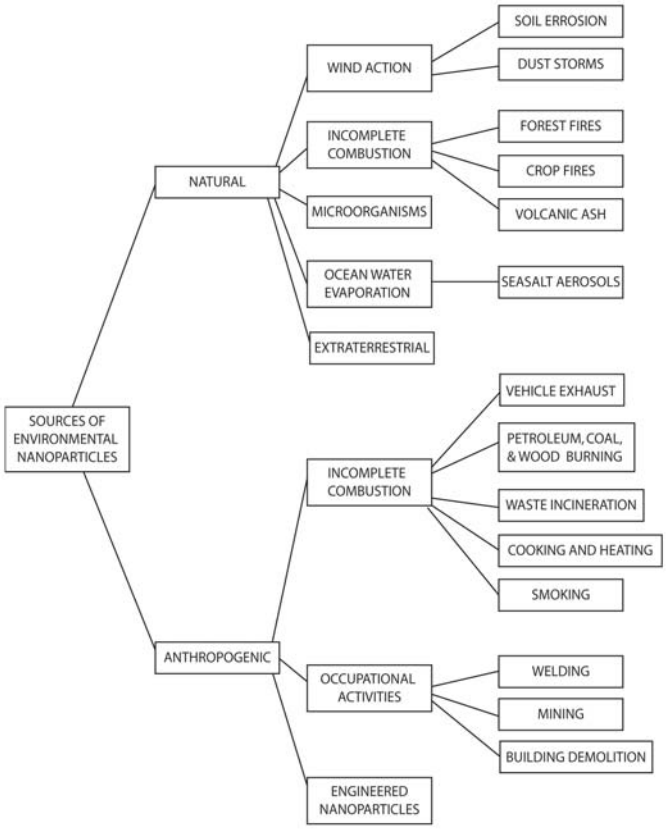

Figure 1. *Schematic indicating sources of environmental nanoparticles*

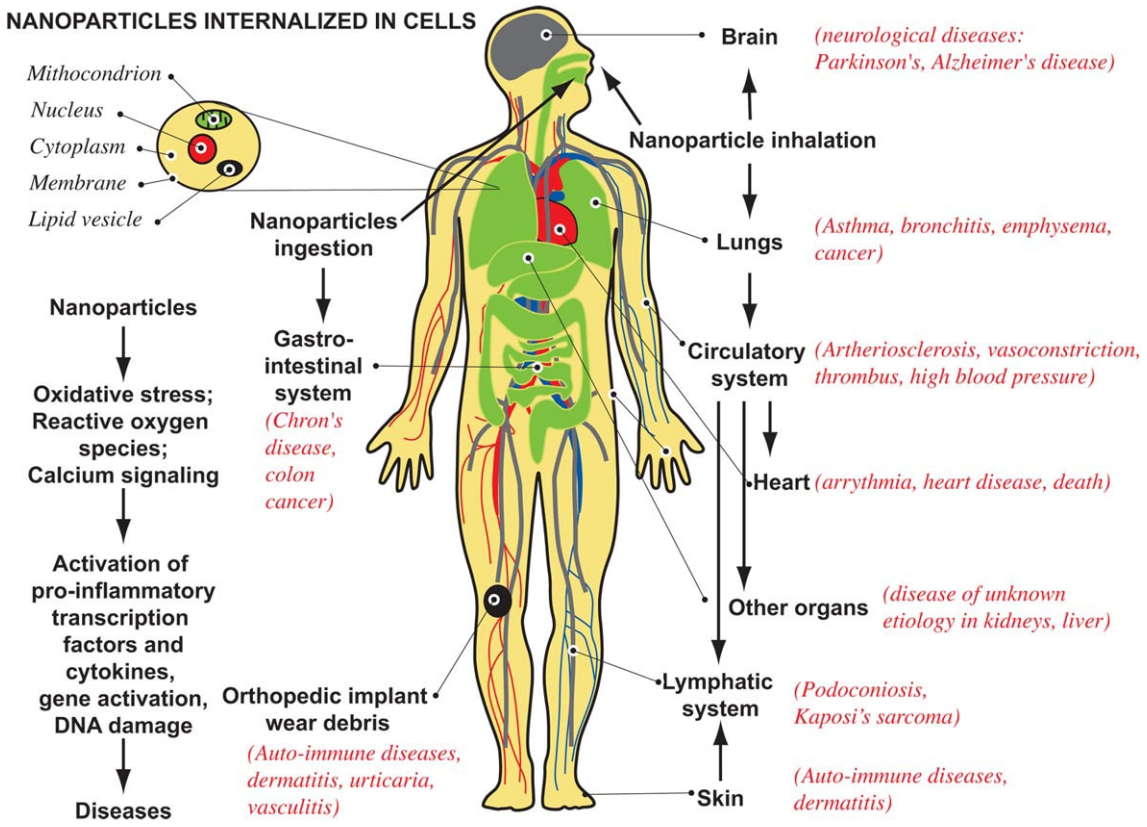

Figure 2. *Schematic of the human body detailing pathways of exposure to nanoparticles, affected organs, and associated diseases.*

In vivo and *in vitro* studies indicate that, as a result of their minute size, nanoparticles are able to enter the body, migrate to organs via the circulatory system, even enter cells and alter basic cellular processes, such as cell proliferation and cell death. Exposure pathways together with the most severe adverse health effects associated with nanoparticle exposure are summarized in **Figure 2**. Diseases associated to nanoparticle's exposure encompass respiratory, cardiovascular, lymphatic, autoimmune, gastro-intestinal, and nervous system diseases. Interestingly, specific nanoparticles seem to be linked to some diseases with unknown etiology (origin), such as: autoimmune, Crohn's, Alzheimer's and Parkinson's disease.

The current knowledge of nanoparticle toxicity indicates that most materials in nanoparticle form are potentially toxic. The extent of their toxicity is largely dependent on their physico-chemical properties, such as composition, crystalline structure, agglomeration, and shape (**Table 1**).

Table 1. The relative cytotoxicity index (RCI) of nanoparticles with different composition on murine macrophage cells (SWCNT – single wall carbon nanotubes, MWCNT- multiple wall carbon nanotube, AR- aspect ratio, D- diameter)

Material	Mean particle size (nm)	Mean aggregate size (μm)	Relative Cytotoxicity Index (at 5 μg/ml)	Relative Cytotoxicity Index (at 10 μg/ml)
Ag	30	1	1.5	0.8
Ag	30	0.4	1.8	0.1
Al_2O_3	50	0.7	0.7	0.4
Fe_2O_3	50	0.7	0.9	0.1
ZrO_2	20	0.7	0.7	0.6
TiO_2 (rutile)	Short fibres 5-15 nm D	1	0.3	0.05
TiO_2 (anatase)	20	2.5	0.4	0.1
Asbestos crysotile	Fibres 20 nm D, up to 500 AR	7	1	1
Carbon Black	20	0.5	0.8	0.6
SWCNT	100 nm D	10	1.1	0.9
MWCNT	15 nm D	2	0.9	0.8

Experimental and epidemiological evidence suggests that exposure to specific nanoparticles from natural and anthropogenic sources can be extremely detrimental to human health It is noteworthy that eight of the top ten leading causes of death in developed countries are diseases to which nanoparticles have been related to etiologically: various cancers, cardiovascular, Alzheimer's, respiratory, kidney diseases, and/or the demographics with this disease are more susceptible to the toxic effects of nanoparticles (heart, respiratory diseases, diabetes). **Figure 3** summarizes the top ten leading causes of death in the United States during 1998-2006 and their possible relationship to nanoparticle exposure.

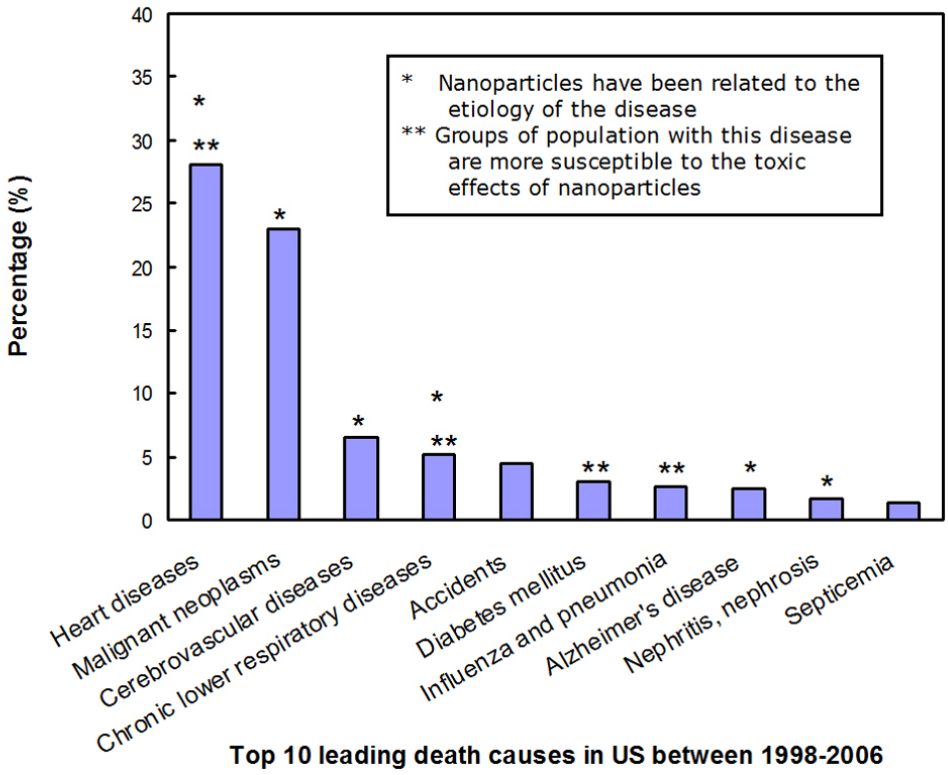

Figure 3. *The average percentage of total death for the ten leading causes of death in the United States of America between 1998 and 2006.*

While today nanoparticles resulting from incomplete combustion are the main anthropogenic nanopollutants associated to adverse health effects, engineered nanoparticles in consumer products are likely to become an important source of toxicity in the near future if not properly handled and recycled. Despite the fact that many nanoparticles prove to be toxic, many consumer products containing engineered nanoparticles are commercially available (in cosmetics, sunscreens, toothpaste, food additives, stain-resistant clothing, sporting goods, and tires, among others) as a result of the lack of specific safety guidelines for the production and use of nanoparticles. There are currently more than 300 products on the market containing nanomaterials.