Nanomaterials toxicity **Dr.Neihaya Heikmat**

- **Nanotoxicology** – Science of engineered nanodevices and nanostructures that deals with their effects in living organisms.

- Potential NM exposure routes include:

-Inhalation

-Dermal contact

-Ingestion

- There are three ways are the most likely points of entry for natural or anthropogenic nanoparticles, there are:

- -Human skin

- -lungs

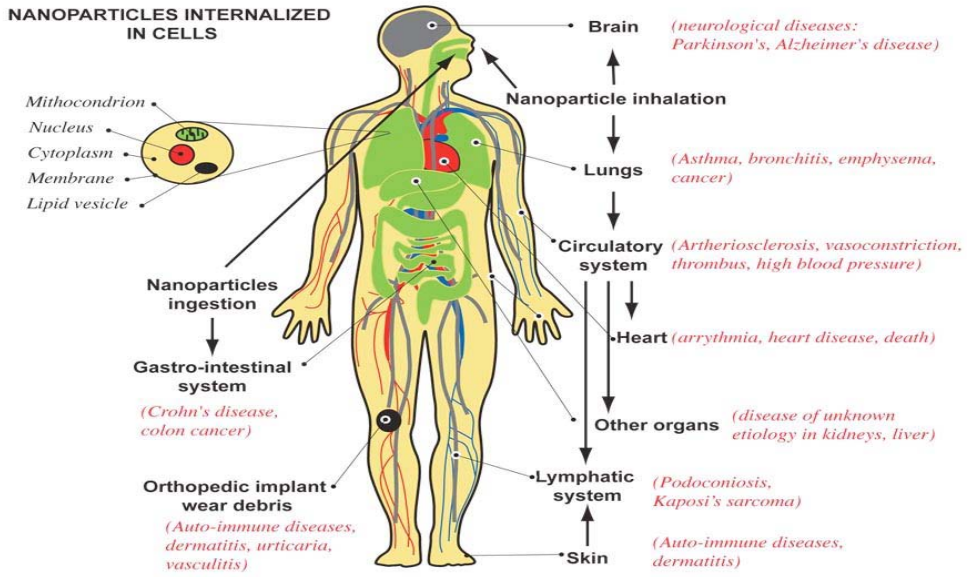
- -the gastro-intestinal tract .

- Injections and implants are other possible routes of exposure.

- Human skin, lungs, and the gastro-intestinal tract are in constant contact with the environment.

- While the skin is generally an effective barrier to foreign substances, the lungs and gastro-intestinal tract are more susceptible.

- Injections and implants are other possible routes of exposure, primarily limited to engineered materials.



- Due to their small size, nanoparticles can translocate from these entry portals into the circulatory and lymphatic systems, and ultimately to body tissues and organs.

- Some nanoparticles, depending on their composition and size, can produce irreversible damage to cells by oxidative stress or/and organelle injury.

Research Approaches to Understand NM Toxicity

- *In vitro* and *in vivo* approaches allow study of the mechanisms and biological effects of NM on cells and tissues under controlled conditions.

- ***Respiratory tract uptake***

- After inhalation, nanoparticles deposit throughout the entire respiratory tract, starting from nose and pharynx, down to the lungs.

- Smaller particles have a higher toxicity than larger particles, and they generate a consistently higher inflammatory reaction in the lungs.

- Smaller nanoparticles are correlated with adverse reactions such as: inflammation, accumulation of particles, and epithelial cell proliferation, followed by fibrosis, and the appearance of tumors.

- **Translocation/Bioaccumulation of Nanomaterials**

-Nanoparticles can cross alveolar wall into bloodstream.

-Absence of alveolar macrophage response.

-Distribution of NM to other organs and tissues.

-Inhaled nanoparticles may reach brain through olfactory nerve.

Cellular interaction with nanoparticles

nanoparticles are able to enter cells and interact with subcellular structures.

Cellular uptake, depend on nanoparticle chemistry, size, and shape.

This type of uptake and free movement within the cell makes them very dangerous by having direct access to cytoplasm proteins and organelles.

Depending on their localization inside the cell, the nanoparticles can damage organelles or DNA, or ultimately cause cell death.

Nervous system uptake of nanoparticles

In addition to nanoparticle uptake due to inhalation, nervous system uptake may occur via other pathways (such as dermal).

the initiation and promotion of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, Pick's disease, are associated with oxidative stress and accumulation of high concentrations of metals in brain regions associated with function loss and cell damage.

Nanoparticles translocation to the circulatory system

Metallic nanoparticles with size smaller than 30 nm pass rapidly into the circulatory system.

 From the circulatory system long-term translocation to organs (such as the liver, heart, spleen, bladder, kidney, bone marrow) is possible, depending on the duration of exposure.

 nanoparticle fast translocation into circulation may be enhanced by pulmonary inflammation, and increased microvascular permeability.

 Ingestion Pathway

 Ingestion exposures can occur through direct intake of food or materials containing NM and secondary to inhalation or dermal exposures.

 Some evidence suggests that ingested NM may pass through to lymphatics.

 Little research to date about Ingestion exposures and the potential for distribution of NM to other tissues.

 Gastro-intestinal tract uptake of nanoparticles

 Endogenous sources of nanoparticles in the gastro-intestinal tract are derived from intestinal calcium and phosphate secretion.

 Exogenous sources are particles from food.

 Also, a small fraction of inhaled nanoparticles was found to pass into the gastrointestinal tract.

 Nanoparticles have been constantly found in colon tissue of subjects affected by cancer, Crohn’s disease, and ulcerative colitis.

 Nanoparticles translocation to the lymphatic systems

 Nanoparticles that are able to enter the circulatory system can also drained through the lymphatic system to the lymph nodes as free nanoparticles and/or inside macrophages.

- nanoparticle uptake by lymphatic system may lead to oxidative stress created by certain types of nanoparticles and lead to damage of lymphocytes, lymph nodes, and/or spleen.

- **Liver, spleen, kidneys uptake of nanoparticles**

- In the presence of inflammation the permeability of the endothelium is increased, allowing a larger passage of particle.

- accumulation of nanoparticles in these organs, potentially adverse reactions and cytotoxicity may lead to disease.

- intestinal absorption of NPs can lead to severe health conditions, including fever, enlarged spleen and liver, suppression of bile flow, and acute renal failure.

- **Assessing Risks of Nanomaterials**

- -Identify and characterize potential NM hazards.

- -Assess potential exposure scenarios.

- -Evaluate toxicity.

- -Characterize risk and uncertainty.

- -Communicate about risks.