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HUMAN HEALTH
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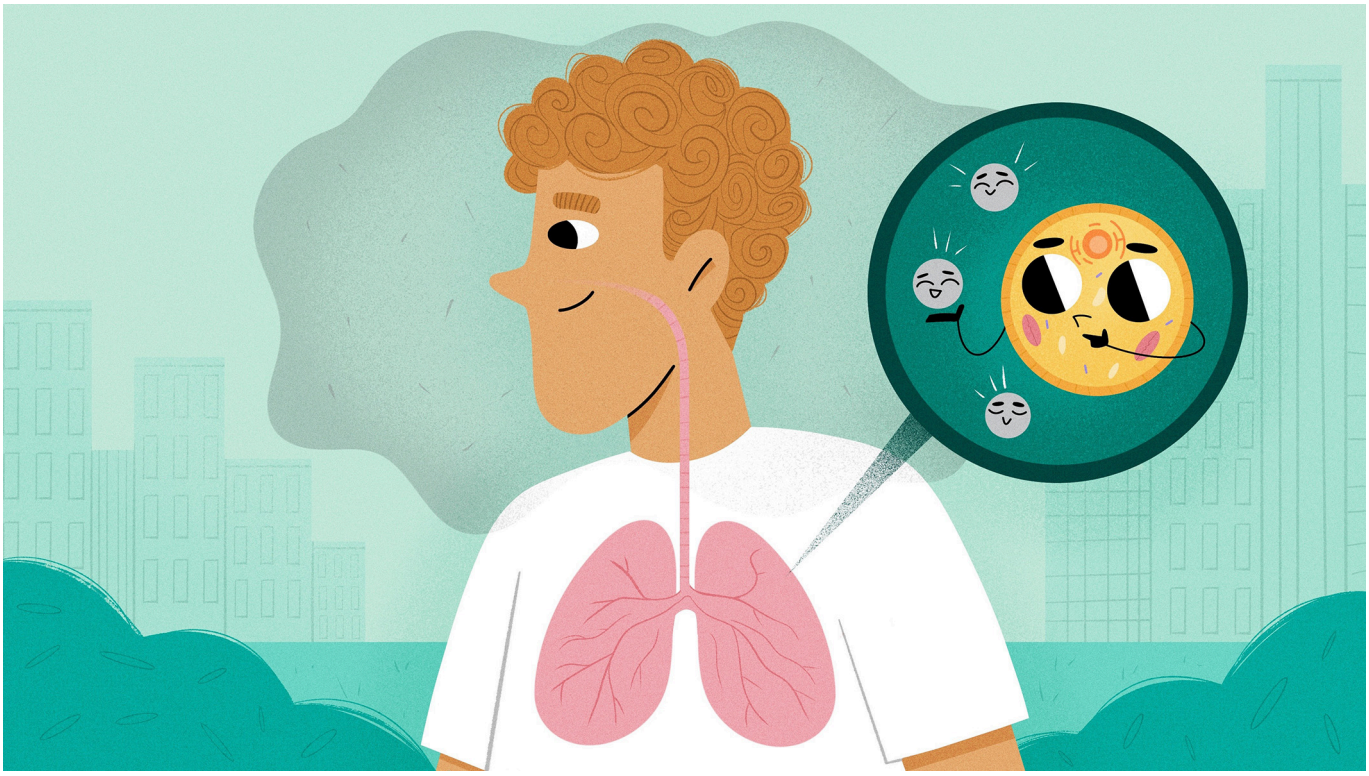

IS "SMALL" SAFE? EXPLORING THE GOOD AND BAD OF NANOMATERIALS

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YOUNG REVIEWERS:

KONSTANTIA
AGE: 10

MIDDLE SCHOOL PARINI-MERELLO
AGES: 12–14

"Small" does not necessarily have a clear meaning... is a ball big or small? A ball might be small compared to the entire planet, but it is absolutely huge compared to tiny "nano" particles! If you look at 1 mm on a ruler, one *million* nanometers can fit into that millimeter. Nanomaterials—the general name for materials made from tiny particles in the nanometer range—are so small that they have properties that can be quite different from "normal" materials. Nanomaterials may have a number of helpful functions. For example, they can be useful in medicine, helping our bodies to fight infections from bacteria and viruses. Nanomaterials can also be included in some products, to make them stronger or longer lasting. However, despite their advantages, we must be cautious with nanomaterials

because they can sometimes get past the barriers in the human body that protect us from foreign invaders, causing damage to cells and potentially making people sick. Let us see how their size changes where they go and what they can do.

THE NANOSCALE

The term "nano" comes from the Greek word "nanos", which means "extremely small". When we say nanoscale, we are referring to a size range of 1 to 100 nanometers (nm)—the ideal range for investigating teeny-tiny particles and materials. To give you an idea of how small this is, consider a single human hair. Even one hair is much larger than anything on the nanoscale! A hair's thickness ranges from 60,000 to 100,000 nm (0.06 to 0.1 mm), and a sheet of paper is ~75,000 nm (0.075 mm) thick. A bacterial cell is 10,000 nm (0.01 mm), a tiny red blood cell is ~7,000 nm (0.007 mm) in diameter, a fungi spore is 500 nm (0.0005 mm) and a virus is just between 20 and 200 nm (0.00002 to 0.0002 mm). Now consider this: the radius of a DNA molecule is only 1 nm!

NANOMATERIALS

These are very tiny materials, so small you cannot even see them with the naked eye.

Nanomaterials, the general name for any material in the nanoscale, can range from 0.7 nm in size, such as graphene and carbon nanotubes, all the way up to 80 nm in the form of nanogold, for example [1]. Does this give you an idea of how small nanomaterials are? Figure 1 shows how big nanomaterials are compared to a dog, its tennis ball, a flea, an animal cell, and a bacterial cell.

Figure 1

How small is the nanoscale? The sizes of the objects shown give you an idea of just how tiny nanomaterials are.

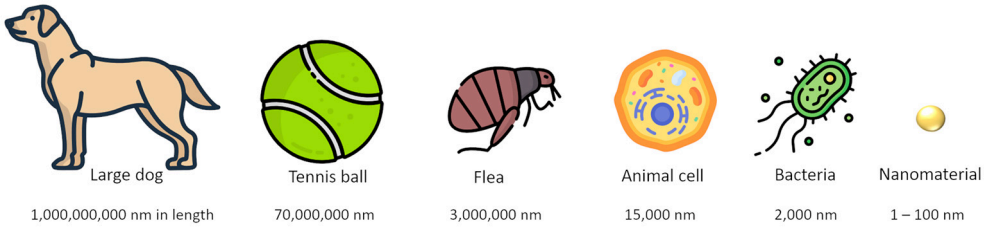

Figure 1

HOW ARE NANOMATERIALS CHANGING THE WORLD?

Because nanomaterials are so small, they have special properties. Figure 2 shows the use of graphene nanomaterials in bulletproof vests, for example. Traditional bulletproof vests are typically made from very strong plastic. Scientists can strengthen these bulletproof vests by adding graphene sheets to the plastic. This is because the graphene sheets are extremely strong but weighs less than a piece of paper. This nanomaterial can absorb the impact of the bullet, so that the person wearing it does not get hurt.

Figure 2

A nanomaterial made of graphene can be used in bulletproof vests. This material can take more impact from a bullet due to its structure.

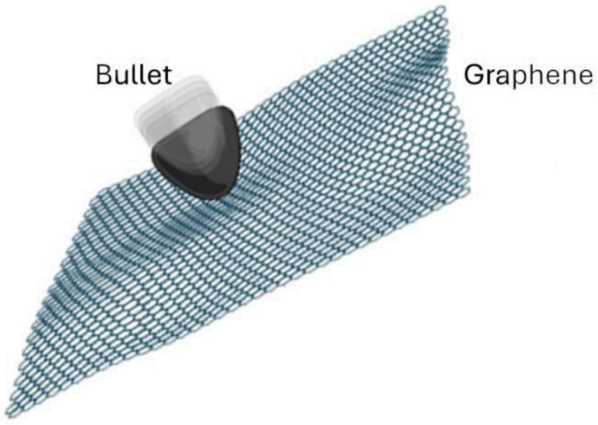

Figure 2

If you think 3D printing is cool, just wait until 4D printing using nanomaterials as tiny building blocks becomes a reality. Regular 3D printers can build awesome toys but imagine if printers could print toys that transform after printing! That is 4D printing—it uses nanomaterials that change shape under different conditions. Scientists design these nanomaterials to react to heat, light, or water, so they can transform for various uses. Imagine clothes that get warmer when you are cold! 4D printing is new, but it has the potential to do amazing things, especially in medicine. Imagine new bandages that changes color to let you know that your body is not healing properly or can alert you to replace the bandage for a new one. Or imagine tiny robots that help you heal from an injury [2, 3].

Nanomaterials have several other uses in medicine, too. For instance, doctors could treat diseases using nano-sized medicines that can reach sick cells in locations that regular medicines cannot get to. Even certain cancers can be treated with tiny nanodrugs that deliver medicine right to the specific part of the body where it is needed [4].

Nanomaterials can also play an important role in vaccines, especially in some COVID-19 vaccines [5]. These vaccines contain nano-sized bubbles called **liposomes**. Scientists can put pieces of the virus (or even instructions telling your body to make its own defenses) inside these liposomes. The liposomes protect the vaccine parts as they travel into your body, and they help the vaccine to get to the right cells to trigger protection. This can make the vaccine more effective and require fewer doses. So, next time you get a vaccine, especially for COVID-19, there is a good chance tiny nanomaterials are helping keep you healthy! Using powerful microscopes, we can "see" nanomaterials and how they interact directly with human cells (Figure 3A).

LIPOSOMES

Tiny bubble-like structures that are made of fat and that carry medicine inside them.

Nanomaterials can also help clean up pollution in water, making our world a healthier place. Finally, as nanomaterials are becoming more

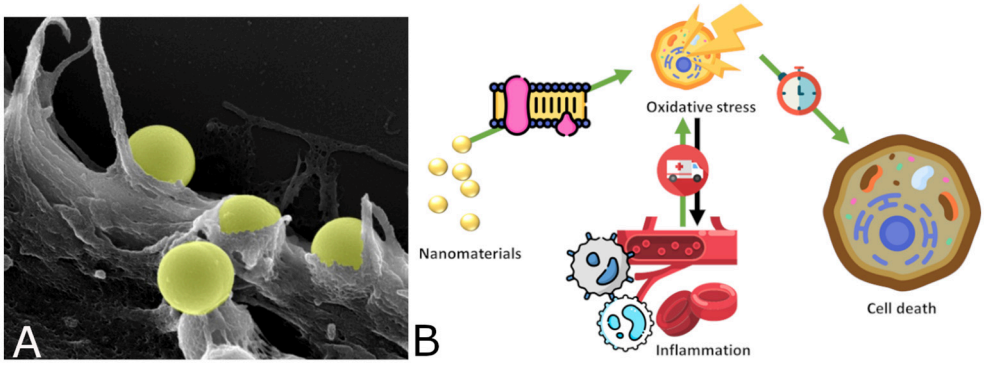

Figure 3

Figure 3

(A) A super-powerful microscope called a scanning electron microscope was used to take a picture of nanobeads made of silica (yellow) on the surface of a human cell (image credit: Matthew Ware and Biana Godin Vilentchouk, Houston Methodist Research Institute, Texas). **(B)** Nanotoxicity can happen when nanomaterials cause uncontrolled inflammation, which leads to a condition called oxidative stress, which can kill cells. Oxidative stress itself can also increase inflammation, making the situation worse (adapted from [6]).

common, they can even be found in some packaged snacks. They are usually part of the packaging, used to make it stronger, or they can even be used as an ingredient of the snack itself, to keep it fresher or even to fight off bacteria [7]. This is an area that is still being researched, so scientists are figuring out the best ways to use nanomaterials safely.

HOW DO NANOMATERIALS ENTER THE HUMAN BODY?

Nanomaterials typically enter the human body in three ways. First, they can enter through the skin. The skin normally functions as a shield, but it cannot prevent the entry of nanomaterials that are found in some sunscreens, for example. Second, if nanomaterials are inhaled, they can enter through the respiratory system [8]. Due to their small size, the body cannot expel them. Currently, scientists are not exactly sure how bad it is for humans to inhale nanomaterials in the long term, but experiments in the laboratory have shown that nanomaterials in the lungs can be very bad—some can even lead to permanent tissue damage. Finally, nanomaterials can enter through the digestive system, when people eat foods containing these materials as additives like colorants or preservatives.

DOES THE HUMAN BODY DEFEND ITSELF AGAINST NANOMATERIALS?

The human body has many defenses against foreign bodies, such as the mucous membranes in the respiratory and digestive tracts, which trap foreign substances, and the acidity (low pH) of the stomach. In an acidic environment, many types of invaders are killed or dissolved. With nanomaterials, this does not always work. In fact, nanomaterials can bind with normal proteins present in the stomach, creating new structures called **biocoronas**. Biocoronas can pass through the body unnoticed, as if wearing an invisibility cloak. Therefore, the body's cells

BIOCORONA

The structure created when molecules from the body, such as proteins, stick to the surface of a non-biological substance, such as nanomaterials, basically disguising them.

specialize in recognizing and killing foreign invaders do not detect the nanomaterials and thus do not attack them.

NANOTOXICITY

This is when nanomaterials can cause harm to living things (people, animals and the environment). Scientists are still learning about this.

INFLAMMATION

The body's reaction to infections and injuries, often appearing as redness and swelling. Too much or long-lasting inflammation can cause cells to die through oxidative stress.

OXIDATIVE STRESS

A process that happens when harmful molecules produced by inflammation damage cells. It can lead to diseases and aging. The body has natural defenses to help protect against it.

WHAT ARE THE NEGATIVE CONSEQUENCES OF NANOMATERIALS IN THE BODY?

The negative effects that nanomaterials can have on the human body are known as **nanotoxicity**. In some cases, cells recognize nanomaterials as dangerous and attempt to eliminate them through **inflammation**. Inflammation may produce toxic by-products which, under normal conditions, do not do much damage. However, if there is lots of inflammation or if it lasts a long time, these toxic by-products can damage the body's cells or even cause them to die through a process called **oxidative stress**. Imagine your body is a playground, and the toxic byproducts of inflammation are like little troublemakers bouncing around. Normally, your body has "playground monitors" called antioxidants that grab these troublemakers before they cause any damage. But if there are too many troublemakers and not enough monitors, things can get out of control! That is kind of like what happens during oxidative stress, which can then lead to even more inflammation, in a vicious cycle (Figure 3B) [3]. Some nanomaterials cannot be removed or destroyed and remain in the body for years. Continuous inflammation may also lead to tumors over time.

CONCLUSION

Nanomaterials offer exciting possibilities, from medical treatments to pollution clean-up. However, their small size presents a double-edged sword. While it gives them special properties, it also allows them to bypass the body's natural defenses, which if out of control can cause inflammation and even cell death. As research into nanomaterials continues, so too must our understanding of their possible risks. By weighing up the potential risk and amazing benefits we can ensure a future where nanotechnology continues to improve our lives without affecting our health.

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CONFLICT OF INTEREST: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

YOUNG REVIEWERS

KONSTANTIA, AGE: 10

Konstantia is a curious 10-year-old girl who loves reading as much as the next person! Her passion for reading excites her whenever she discovers a good book. Having lived in various places around the globe, she has mastered three languages. Konstantia adores interacting with other kids. If it were up to her, she would play all day long!

MIDDLE SCHOOL PARINI-MERELLO, AGES: 12–14

We are 150 students (12–14 years old) from seven classes (2A, 2B, 2C, 2E, 2F, 2I, 3G) of the Parini-Merello Middle School of Genova. Thanks to our teachers, the school is involved in many projects, and we are lucky to have many exciting experiences! The Frontiers for Young Minds project was one of the best: we thought that it would have been a very challenging job, but once we started working all together, we had so much fun, and our curiosity helped us in carrying out the review work!

AUTHORS

CHARLENE ANDRAOS

My work centers on the development and refinement of testing methodologies in the laboratory, specifically aimed at assessing the mechanisms of toxicity of particles, particularly nanomaterials. In addition, my research delves into the potential health risks associated with nanomaterial exposure. As a toxicologist specializing in airborne particles, I am particularly intrigued by understanding how the unique characteristics of nanomaterials may result in potential human health implications. This work excites me as it requires knowledge from many scientific fields including biology, human anatomy, and chemistry, among others. *charlenea@nioh.ac.za

KAILEN BOODHIA

What intrigued me into becoming a scientific researcher? My curiosity about how do things work and the fact that I like working with my hands. I like to understand how testing methodologies work, and then combine or modify them to try something new. Most of my research career has focused on the assessing the toxicity of nanomaterials, considering inhalation as one of the major routes of exposure. I started exposing lung cells in a tissue culture dish, and now I am working on one of the first nano aerosol exposure systems in South Africa.

TARRYN LEE BOTHA

My research is curiosity driven; "we are only limited by our imagination" is a philosophy I live by. I studied zoology and biochemistry, which led me to become an expert in aquatic health. I study how safe water is to drink and whether we can sustain a high level of biodiversity in aquatic systems. Nanotechnology is an

emergent field and rather than waiting to see whether it poses a risk, it is better to develop products with potential risks in mind—we call this safety by design. We work in complex teams that involve chemists, biologists, ecotoxicologists, inhalation experts, and policy makers.