Neutrons reveal potential dangers of gold nanoparticles—pharma's drug delivery agent of the future

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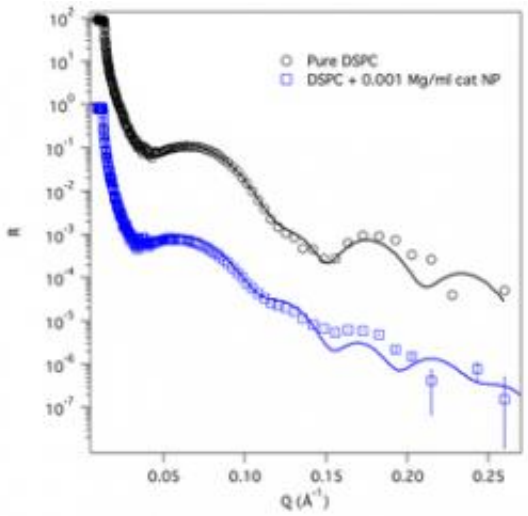

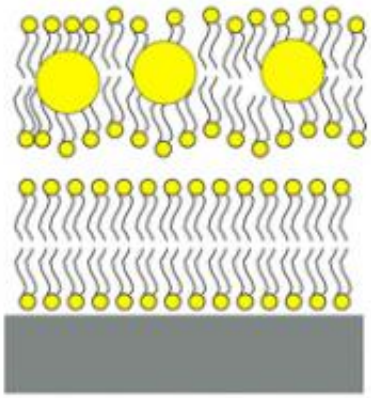

Scientists working at the Institut Laue-Langevin have shown that the charge of gold nanoparticles, identified by major pharmaceutical companies as a drug delivery agent of the future for the treatment of cancer, affects how they interact with our cell's protective outer wall. These crucial insights, published in *Langmuir*, provide a first step in the effective design of safe nanoparticles for biomedical applications and the practices and procedures for their secure handling in a variety of other consumer products.

The growing use of nanoparticles, tiny flakes of material, 1 millionth the size of a grain of sand, in a wide range of commercial products, such as clothing, food storage containers, pharmaceuticals, cosmetics, tyres, electronics and optical devices, is controversial. Common nanoparticles, such as gold, silver and copper, easily penetrate organic membranes, (cell walls, ...) creating potentially significant impacts on human health and the environment. However, there is one area where their toxicity might prove useful and even life-saving.

A major challenge in modern medicine is finding delivery agents capable of targeting and penetrating cells to transport drugs directly inside the infected tissue. The search for the right vehicle has led to a new field of research, 'nanomedicine', where nanoparticles could be programmed to target cancerous cells for example, reducing or even eliminating the need for surgery.

Of all the nanoparticles available to medical science, one in particular has become a focus of research amongst major pharmaceutical companies – gold. AstraZeneca last year announced a new research project to look at a new nanomedicine, CYT-6091, based on gold nanoparticles.

Gold nanoparticles make particularly good delivery vehicles because:

- They are easy to 'load-up' with other molecules, such as existing cancer drugs
- They are easy to produce
- They are chemically stable inside the body
- They offers a unique set of optical, electronic and thermal properties, which means they can be 'switched on' inside the body very easily when they arrive at the right location.

However, at present we don't understand in any detail the interaction

mechanisms between nanoparticles and our cell's outer defences – the cell membrane. Without this it is impossible to determine how dangerous they are and whether their ability to penetrate and destroy cells can ever be harnessed for good ends, such as in the fight against cancer.

One thing that is known is that there is a complex set of parameters that influence this interaction, including the nanoparticle's shape, size, composition and charge. But a systematic study that shows how the interaction depends on these parameters at a molecular level has up until now been lacking.

To start to address this, a research team from the Institut Laue-Langevin (ILL), the University of Illinois and the Australian Nuclear Science and Technology Organization used the ILL's neutrons and world-leading neutron scattering instruments to investigate, on a molecular level, the physical changes undergone by our cell walls as they come into contact with gold nanoparticles of different charge.

2 nm diameter gold nanoparticles had either cationic (positively charged) or anionic (negatively charged) groups added to their surface. To mimic the cell membrane, the research team used two double layers of fatty lipid molecules held 20-30 Å on top of each other that together produced the dynamic properties seen in cell membranes. The scientists then applied neutron reflectometry techniques at the ILL to accurately model the nanoparticle - cell membrane interaction on a fraction of a nanometre scale.

What they found was that the nanoparticle surface charge does indeed play a significant role in determining their interaction with our cells membranes. Cationic nanoparticles pass straight through the lipid membrane and embed themselves deeply within the floating bilayer, destabilising the entire membrane structure sufficiently to completely destroy the cell at higher concentrations. In contrast, anionic

nanoparticles do not penetrate the lipid membrane at all. Rather, at given concentrations they hinder membrane decomposition helping it withstand the sort of extreme conditions, such as elevated pH, that would normally significantly destabilise it.

Provided by Institut Laue-Langevin