Novel silver compounds offer a potential cancer treatment breakthrough

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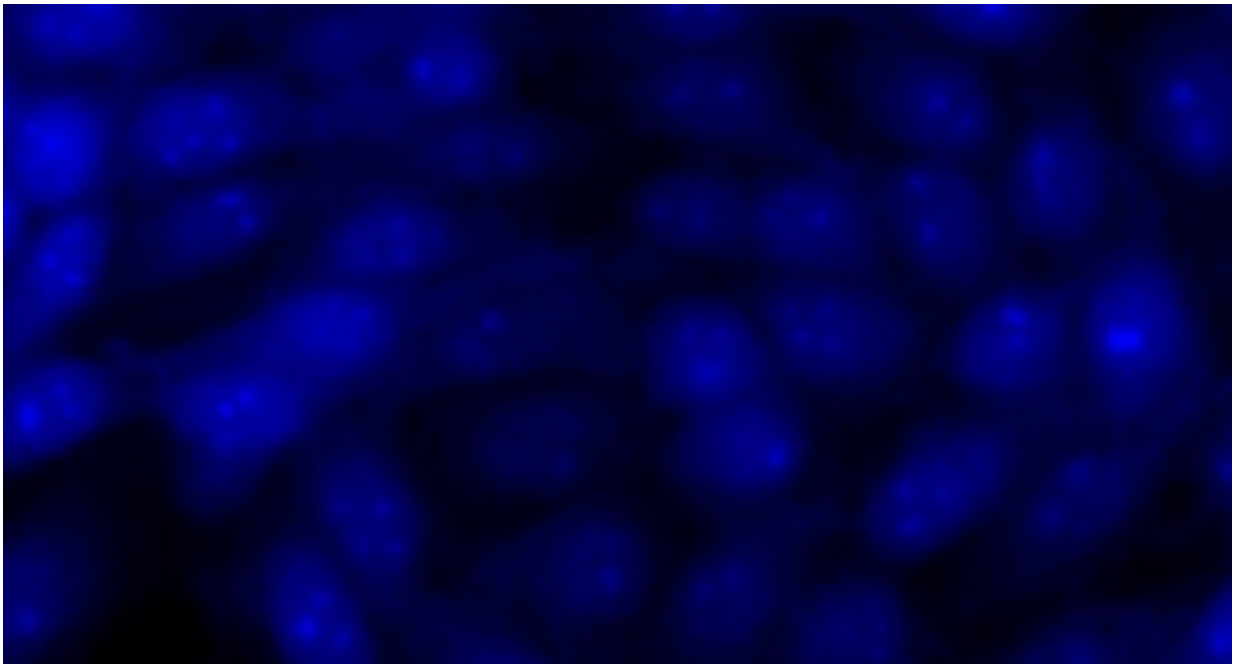

Oesophageal cancer cells before the silver-based compounds have been added.

The development of chemotherapeutic drugs to treat various cancers has been fraught with challenges. One of the toughest is the acute and long-term toxicity of drugs and its severe side-effects on almost all organs in the body.

In the absence of targeted treatments for each cancer patient, oncologists

have accepted these side-effects as the price that has to be paid to try and control a fatal disease.

This, along with the fact that cancer cells can become resistant to treatment, makes the development of drugs with specific targets highly desirable.

Until recently, most chemotherapeutic drugs have targeted DNA, directly or indirectly, either by damaging the DNA or interfering with enzymes that repair or fold the DNA.

But over the past 10 years, efforts to find alternatives have opened up new avenues of research, with one of them focusing on finding compounds that activate the "cell suicide" process to kill cancer cells.

This has also been our area of research for a number of years. Our most recent research involved testing whether a group of silver-based compounds could kill cancer cells in this way. What makes our findings so exciting is that the compounds seem to be able to tackle the energy centre (the mitochondria) of the cancer cells, preventing them from growing and spreading.

And our provisional data, based on studies on human cell cultures and rats, show that the compounds have a lower level of toxicity than at least one chemotherapeutic cancer drug on the market.

Our compound still needs to go to extensive clinical trials before it can become available as a chemotherapeutic agent. But our findings pave the way for a new chemotherapeutic drug that could be more effective but less toxic, with fewer side effects.

This is the first time that our compounds have been proposed as a chemotherapy drug – but its not the only one that can kill cancer cells.

Our findings are also ground breaking because they offer the promise of much cheaper cancer treatments. Some of the industry-standard chemotherapy drugs are derived from platinum based compounds, making them very expensive. But our compounds are based on silver making them more economical.

A promising candidate

Cancer cells have a unique set of properties that make them the ultimate survivors. They can develop their own growth signals and they have the ability to ignore signals that tell them to stop growing. They can also invade tissue and then spread and have a limitless ability to replicate.

Cancer cells are also able to evade a naturally controlled process where cells die, known as apoptosis. This is an essential "cell suicide" process for controlling cells. When they are no longer needed, have to be replaced due to old age or have become dangerous (that is, they've mutated), they receive a signal to die. Cancer cells are problematic because they're resistant to these signals.

As part of our study, we tested various silver-based compounds to see how they affect cells. One of them – a silver thiocyanate phosphine complex (or UJ3 in short) – showed immense potential.

It had the ability to induce apoptosis in a wide range of cancers, including cultures of skin, breast, esophageal, lung, prostate, liver, cervix, colon, pancreas, adrenal glands, bone marrow and blood (leukemia and lymphoma) cells. It also had a minimal effect on normal cells.

A new candidate

Promising anticancer drugs should, ideally, have these characteristics:

- they should be metabolically stable (in other words they must be active for a long period of time after entering the body),
- they must be available, in other words able to be absorbed into the blood stream after administration and reach the tumour site, and
- they should have low levels of toxicity to have the lowest possible side-effects.

Provisional tests on human cells, rats and mice helped us establish that the compound ticked all these boxes.

Aside from the compound accumulating in the tumour and in the blood, there was no evidence of organ damage in rats, even at very high dosages, while the rest of the compound was eliminated from their bodies.

An alternative

The next steps are to put the compounds through clinical trials on humans to see how well they do.

Apart from being cheaper because we used silver and not platinum, the compounds were relatively easy to make and can be synthesised with standard laboratory equipment. This suggests large scale manufacture should be easier.

We remain hopeful that the compound could eventually provide the cure for the most common cancers. And that it can lead to treatment that doesn't debilitate patients.

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