

## Theranostics: A Better Alternative to Surgery?

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The good news for breast cancer patients with refractory tumours is that, researchers at UT Southwestern Medical Center and Oklahoma State University's College of Veterinary Medicine are teaming ultrasound with nanoparticles to ablate or cavitate difficult to reach tumours!

Dr. Ashish Ranjan and his colleagues at Oklahoma State University can now guide liposome nanoparticles directly to the tumour site. This opens up a wealth of opportunities for those designing nanoparticles. For example, finding the perfect chemical drug load to deposit on refractory tumours is our present challenge, one I'm sure that will continue to be met with outstanding efforts! Further, HIFU (High Intensity Focused Ultrasound), which results in a higher temperature treatment that melts the liposomes to release the drug load could also be investigated as a mode of tumour treatment, itself [1].

How does it work? The ultrasound apparatus is equipped with an acoustic lens that operates similarly to how our eyes use their lenses to focus light upon our optic nerves. Sound waves are guided to a very specific point, the tumour site, leaving tissue between the tumour and the instrument unharmed. This novel theranostic therapy is already in use to treat canine tumours at Oklahoma State University's College of Veterinary Medicine! [2].

What does this novel ultrasound therapy mean for a breast cancer patient who is nearing Stage 4 or has already entered it? Once theranostic ultrasound becomes available for human intervention, it will eliminate the need for surgery in smaller tumours. Instead of general anesthesia and a long recovery, ultrasound treatments could be administered on an outpatient basis!

Further, ultrasound is much more cost effective than radiation therapy, and depending upon the nanoparticle administered, can be designed with less systemic toxicity!

Sounds too good to be true? Presently, this technique is being investigated to determine any abscopal (other site) effects. Dr. Nandhini Sethuraman of Oklahoma State University is investigating any immune responses that may be initiated by theranostic ultrasound. Eventually, we may be able to stimulate positive or therapeutic immune responses, but this is still in early development [3].

Still, most primary refractory breast cancer tumours established as xenografts in murine models, are resistant to the most chemotoxic chemotherapies. This has been demonstrated by Dr. Helen Piwnica-Worms in her laboratory [4].

This is why communication through the journals is so important, to spread the news that novel nanoparticle drug loads should be investigated. However, we now understand, through watching breast cancer metastasis in Piwnica-Worms models, the locations where the metastasis tends to spread. If we can intervene more quickly with theranostic ultrasound, we should be able to save lives!

Clearly, Dr. Piwnica-Worms studies demonstrate the need for combinatory therapy. Because of this, synergy investigations should be performed that identify chemotherapy regimens which reduce drug resistance yet are not too toxic for co-administration. Fortunately, there is an abundance of signaling information in the literature, with years of studies performed to identify pathways active in breast cancer and in other cancers. This fund of knowledge should assist in the design of effective pharmacological solutions for loading into the nanoparticles.

While the aforementioned studies are honing in on the etiology of breast cancer metastasis, other researchers have been working to develop novel therapeutic strategies that are not associated with etiology. For example, the non-ABC-type transporter, RLIP76, was identified in 2009 as an excellent drug target in the fight against drug-resistance of prostate and breast cancers to present chemotherapies. Still, translational studies have not been funded. This is unacceptable, as RLIP76 has proven to be elevated in PC-3 cells such that blocking antibodies administered to murine models cause a log-fold reduction in tumour xenografts. Singhal, *et al.* also showed that RLIP76 protein and activity are greater in cancer cells compared to normal controls [5]. Leake, *et al.* proved log-fold reductions in MCF7 breast cancer tumour xenografts as well with RLIP76 inhibition [6].

So, breast cancer patients can hold out hope that even if their disease is triple negative, theranostic solutions are in development!

And, finally, once RLIP76 blocking antibodies are combined with nanoparticle chemotherapy in clinical trials, even breast cancer's drug resistance should be defeated.

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