

# Are nanotextures enough to kill cancer cells?

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## Nanotextures on nanoparticles and implants to kill cancer cells in a more targeted manner may just be the key to tackling resistance to traditional cancer drugs

Is our fight against cancer complete? Consider that although for many cancer diagnoses, while people are living longer, the rate of cancer metastasis is still increasing.<sup>(1)</sup> Further, consider that prostate and some other select cancers remain persistent with only a few new approaches, and even those are not working.<sup>(2)</sup> In fact, most oncologists only look to the drug industry (a.k.a., Big PHARMA) to develop new drugs to help them. Does anyone believe this is the best we can do? Are chemotherapeutics really the answer? Have drugs worked for eradicating infection (e.g. antibiotic-resistant bacteria) or for treating chronic pain (e.g. opioid addiction)?

Talk to the patients. Talk to the MDs. Talk to me. Today's drugs are not the answer. I (and many others) am here to say that they are all wrong. Developing new drugs takes enormous time and resources (thus limiting innovation and silencing other approaches), and it is abundantly clear that cancer cells are resisting our old chemotherapeutic approaches<sup>(3)</sup> – we need more imaginative new approaches. Can't we do better? I think we can.

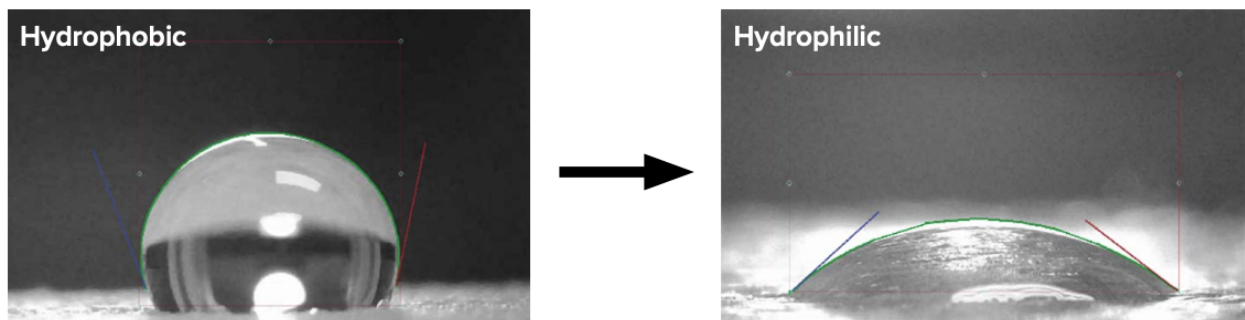


Figure. 1: The power of nanotechnology: Nanotextures can change surface energy to change initial protein adsorption<sup>(7)</sup> and can kill cancer cells (and inhibit infection,<sup>(8)</sup> limit or accelerate immune cell function, and promote tissue growth).<sup>(9)</sup> This can all be accomplished without changing chemistry, which can accelerate regulatory approval (certainly much faster than new drug development).<sup>(9)</sup>

## Using nanoparticles to kill cancer cells

While the use of nanoparticles to prevent, diagnose, and kill cancer cells has been well underway for the past half a century (or perhaps even longer, before the term 'nanotechnology' ever came along),<sup>(4)</sup> a new area of nanotechnology has unlocked unprecedented additional potential for cancer. Specifically, nanotexturing of theranostic

nanoparticles (or those which can both detect and treat cancer), using nanoparticles to kill cancer cells, adopting implants to regenerate healthy tissue after tumours are removed, and more are new areas of nanotechnology taking the field by storm.<sup>(5)</sup>

To understand the importance of nanotexturing, one must realise that specific proteins in your body are known to be cancer cell resistant. And these proteins, like all proteins, possess a specific surface tension or energy. Thus, for nanoparticles or implants alike, nanotextures have been shown to significantly alter surface energy, even when composed of the same chemistry (Figure 1).<sup>(6)</sup>

Close to half a century of research in biomaterials has indicated that changing implant or nanoparticle chemistry (e.g. from polymers to metals to ceramics or even within these material categories) changes surface energy, which alters which proteins adsorb and which do not. It has also been established over this time frame that the proteins that adsorb to nanoparticles (the so-called protein corona) or medical devices immediately after implantation within a time frame we cannot even measure will determine the fate of that implant. Will that medical device get infected? Will it induce chronic inflammation? Or will such nanoparticles reach a tumour to deliver a drug to kill it and keep that tumour from metastasising? Or if it is a medical device, will it grow healthy bone where a bone tumour once was?

And this is where nanotexturing comes in. Nanotexturing can change surface energy to control which proteins adsorb from those that don't, regardless of the chemistry. If designed correctly, it can promote the adsorption of proteins that keep cancer cells from growing (Table 1). It can promote the adsorption of proteins to inhibit angiogenesis or new blood vessel growth that keeps tumours alive. It can adsorb proteins that repel bacteria,<sup>(10, 11)</sup> promote or inhibit immune cells,<sup>(12)</sup> and adsorb proteins that promote healthy tissue growth in the place of continued cancer cell growth.<sup>(6)</sup>

Important Property for Fighting Cancer	Ability of Nanotextures
<p><b>Prevention/Diagnosis/Treatment:</b> Target a tumour or cancer cell</p>	<p>Limit the adsorption of proteins that stimulate immune system clearance, enhance the surface area to promote functional group availability and presentation to target cancer cells or tumours</p>
<p><b>Diagnosis/Treatment:</b> Amplify theranostic (the simultaneous diagnosis and therapy) properties</p>	<p>Limit the adsorption of proteins that stimulate immune system clearance and allow theranostic agents to reach a tumour or cancer cells. Enhance surface area to promote functional group availability and presentation to amplify cancer cell or tumour detection.</p>
<p><b>Treatment:</b> Limit or inhibit angiogenesis</p>	<p>Control the adsorption of proteins that inhibit endothelial cell function to inhibit new blood vessel growth, enhance surface area to promote functional group availability and presentation to inhibit endothelial cell function that inhibits new blood vessel growth</p>
<p><b>Treatment:</b> Limit or inhibit immune cell function</p>	<p>Control the adsorption of proteins that can stimulate the immune system to kill cancer cells, inhibit the immune system to allow a pharmaceutical agent to kill cancer cells, and enhance the surface area to promote functional group availability and presentation to inhibit or enhance immune cell functions for treating cancer</p>
<p><b>Treatment:</b> Promote healthy tissue growth in the place of a resected or current tumour</p>	<p>Control the adsorption of proteins that can promote healthy cell function (rather than cancer cell function) to replace cancerous tissue with healthy tissue – this can be useful for a tumour that was removed and where healthy tissue is needed to replace that tumour and inhibit the return of cancer cells, or for a tumour in which</p>

healthy tissue can outgrow cancerous tissue, enhance the surface area to promote functional group availability and presentation to grow healthy tissue in the place of cancerous tissue

Table 1: The enormous potential of nanotextures on anti-cancer nanoparticles or medical devices.

Importantly, the above concepts have been reduced to practice (Figure 2).<sup>(5)</sup>

Specifically, one of the most well-established polymers for drug delivery, poly-lactic-glycolic-acid (PLGA), was modified to possess nanoscale surface features and was demonstrated to have different surface energy, adsorb different proteins, and, most importantly, transition conventional PLGA from a material that promotes cancer cell growth over healthy cell growth, to one that supports healthy cell growth over cancer cell growth. This result cannot be understated as this reversal of cancer tissue growth over healthy tissue to healthy tissue growth over cancerous tissue growth was accomplished through nanotexturing alone; neither chemotherapeutics nor pharmaceutical agents nor different functionalisation strategies were used.<sup>(5)</sup>

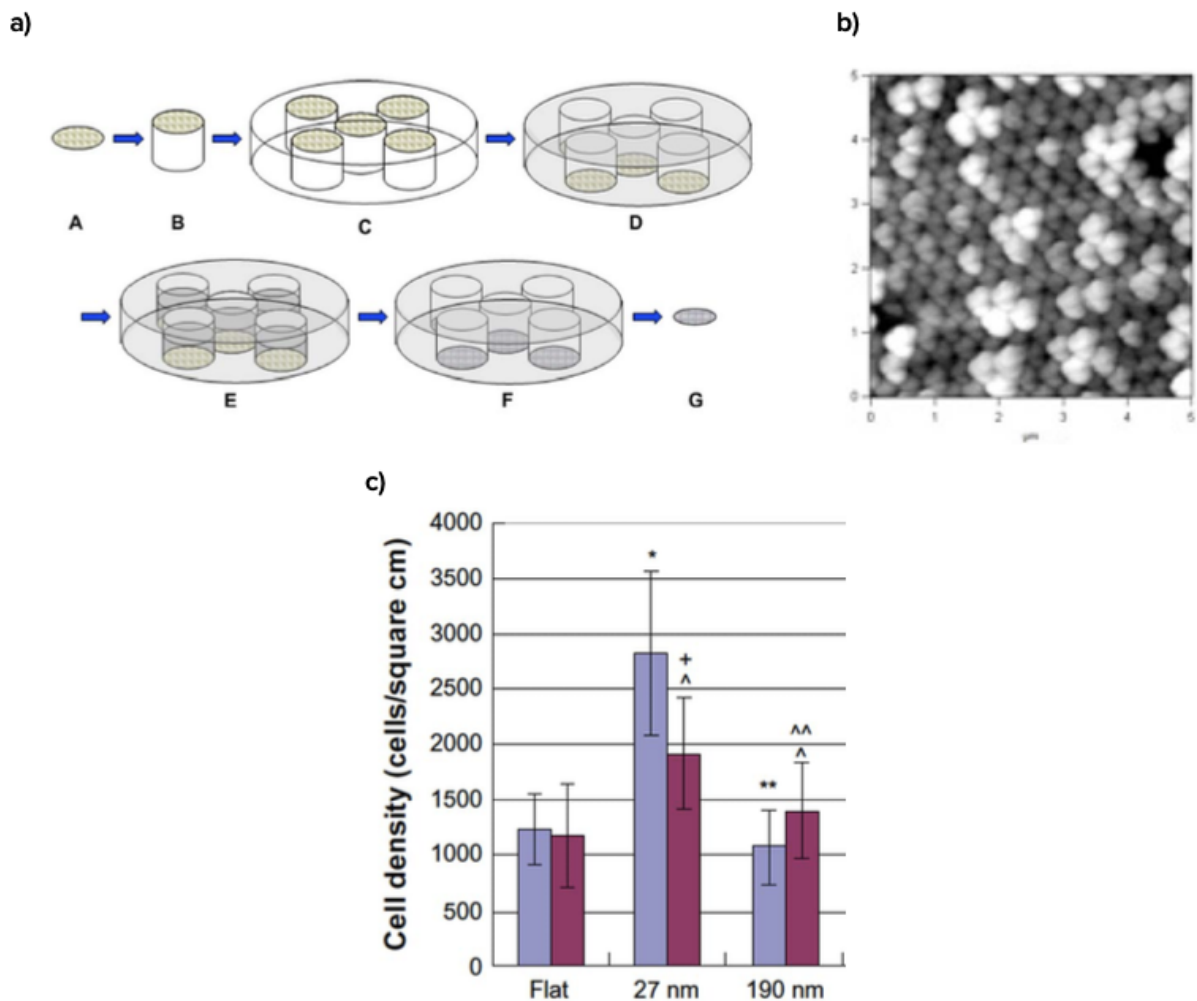


Table 1: The enormous potential of nanotextures on anti-cancer nanoparticles or medical devices.

So, in summary, as studies have shown, there is an enormous potential for using nanotexturing materials in medicine. Specifically, while numerous researchers have only focused on nanoparticles for improved diagnosis and treatment of various cancers, nanotexturing those nanoparticles will provide an extra advantage. Moreover, nanotextured medical devices have been proven to inhibit cancer cell return and stimulate healthy tissue regeneration for implants that are used to replace resected cancerous tissue. Most importantly, such results have been obtained through nanotexturing alone: no chemotherapeutics (to which cancer cells are developing a resistance) and no pharmaceutical drugs used; nothing but nanotextures. Furthermore, regulatory agencies (like the U.S. FDA) have shown accelerated approval of nanotextured chemistries (13), which starkly compares to introducing new chemistries into cancer treatment, which can take ten years or longer and billions of dollars.<sup>(14)</sup>

Nanotextures are an easy way to limit cancer cell function, and this issue needs to be urgently addressed by all research, industrial, and regulatory personnel.

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