

Core Technology Overview:

The core technology underlying Vitanova Biomedical's proprietary light-activated intracellular acidosis (LAIA) is based upon the delivery of an actively targeted yttriumbased upconverting nanoparticle (UCNP) targeted to specific cancer cells. The nanoparticle may be targeted to specific cancer cell types by the conjugation of an antibody to the nanoparticle surface.

It has been documented that disruptions of cancer cell acidity can lead to cancer cell death, however, achieving cancer specific intracellular acidosis has eluded researchers for decades. LAIA technology kills cancer cells through the induction of intracellular acidosis within cancer cells upon activation of the nanoparticle by deep penetrating near infrared laser light. VNB's nanoparticles are fabricated to:

- Contain rare earth elements that will absorb deep penetrating light and upconvert this light to the necessary ultraviolet (UV) light.
- Include the molecule nitrobenzaldehyde (NBA), the hydrogen ion carrier that will release hydrogen ions and facilitate acidosis in response to UV light.
- Include an antibody, such as prostate specific membrane antibody, which is attached to the surface of the nanoparticle. This antibody is intended to bind to PSMA (prostate specific membrane antigen) which is highly expressed on prostate cancer cells.
- Be less than 90 nm in diameter, thereby allowing it to be brought inside the cancer cell via endocytosis.



Diagram illustrating the key steps in product development. 1) fabrication of the yttrium-based nanoparticle with a shell coating to enhance absorbance and upconversion; 2) the attachment of polyethylene glycol linkers for the conjugation of 3) nitrobenzaldehyde, and 4) prostate specific membrane antibody.

Upconversion by Deep Penetrating Light:

The nanoparticle triggers the intracellular acidosis when UV light activates the molecule NBA, an integral component of the nanoparticle. Because UV light does not penetrate deep into human tissue, we have created a novel way to deliver a deep penetrating light which ultimately triggers the acidosis and offers more advantages for the treatment of cancers in humans. The way we accomplish the delivery of a deep penetrating wavelength of light and the translation to ultraviolet light is through a process called "upconversion." Upconversion means that deep penetrating laser light (976 nm) can travel into the tumor and is absorbed by the nanoparticle. The nanoparticle is "tuned" to convert this light energy to UV light (350 nm) at the surface of the nanoparticle, thereby emitting UV light, activating the NBA and causing acidosis. This upconversion process is commonly used in research. We have optimized our nanoparticle to absorb deep penetrating light and convert it to the UV light that is needed to activate NBA, produce intracellular acidosis, and cause cancer cell death.

