ROSWELL PARK CANCER INSTITUTE

Tech Brief: Porphyrin-Based Compounds for PDT and Tumor Imaging

Above: Thomas J. Dougherty, PhD and Ravindra Pandey, PhD

Building on discoveries that made it possible to wipe out tumors without surgery, chemotherapy, or radiation, Roswell Park Cancer Institute researchers are finding new ways to minimize patient discomfort with multi-tasking drugs that can pinpoint hard-to-find cancers as well as destroy them.

More than two decades ago, scientists found that certain photosensitive chemicals make cancer cells vulnerable to red light. Since then, photodynamic therapy (PDT) has emerged as an increasingly effective, economical treatment for skin, lung, and esophageal cancers, and many other conditions.

PDT works like this: First, a specially formulated photosensitive compound is either applied directly (in skin cancer cases, for instance) or injected into the bloodstream. For reasons not yet fully understood, cancer cells take up high concentrations of the drug and retain it long after normal body tissues have flushed it away.

Pinpoint precision

While the photosensitizer lingers in the targeted cells, a therapist exposes them to predetermined intense doses of red light, triggering a "cytotoxic event" in which the drug interacts with naturally occurring oxygen molecules to kill abnormal cells with little or no effect on surrounding tissues.

In theory, PDT can be effective anywhere in the body, but red light penetrates only about a centimeter (approximately 1/3 of an inch) of human tissue. For that reason, PDT is most often used to treat tumors on or just beneath the skin's surface, or on the linings of internal organs and cavities. Endoscopes and fiber-optic catheters deliver the necessary wavelengths to sites deep inside the body.

The key ingredients in PDT are water-soluble, nitrogen-based organic pigments called porphyrins. PDT emerged from the lab and into clinical use worldwide when Roswell Park researchers discovered the first practical porphyrin-based photosensitizer, Photofrin®. While Photofrin is safe and effective, some patients have experienced inflammation and light-sensitive skin after treatment. To counter these side effects, Roswell Park's PDT team launched a search for even more effective photosensitizers. The result was a promising new drug — HPPH – which is now undergoing clinical trials. Studies show that HPPH exits the skin faster than first-generation photosensitizers, thus reducing the time of skin photosensitivity, common to Photofrin. Furthermore, HPPH absorbs PDT wavelengths more readily, making it possible to treat larger, more deep-seated tumors while using smaller, less intrusive instruments. And, finally, HPPH has little or no effect on normal skin's sensitivity to light.

Bringing tumors to light

But there's more to the PDT story than meets the endoscope's eye. Treating known tumors is essential, but most cancer deaths result from distant metastases — "satellite" tumors seeded by cells that, having escaped the original tumor site, take root and grow undetected elsewhere in the body.

It turns out that several diagnostic imaging agents can be combined with the photosensitizers to enhance the contrast between healthy tissues and photosensitizer-loaded cancer cells. PDT drugs injected into the bloodstream will concentrate in cancer cells no matter where they hide. So the Roswell Park team is exploring innovative "see and treat" approaches in which PDT drugs highlight tumors lurking anywhere in the body before helping to eradicate them.

So far, the Roswell Park team has developed photosensitizer spotting techniques compatible with positron emission tomography (PET), magnetic resonance imaging (MRI), and computed tomography (CT) technologies. Research continues, but the goal is in sight: clearer, more accurate pictures of tumors that will enable therapists or surgeons to target them precisely and treat them successfully with minimal impact on the patient.

For more information on porphyrin-based compounds under development at Roswell Park Cancer Institute, please contact Richard Matner, PhD, MBA, Tech Transfer Officer at ***Richard.Matner@roswellpark.com****.*

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