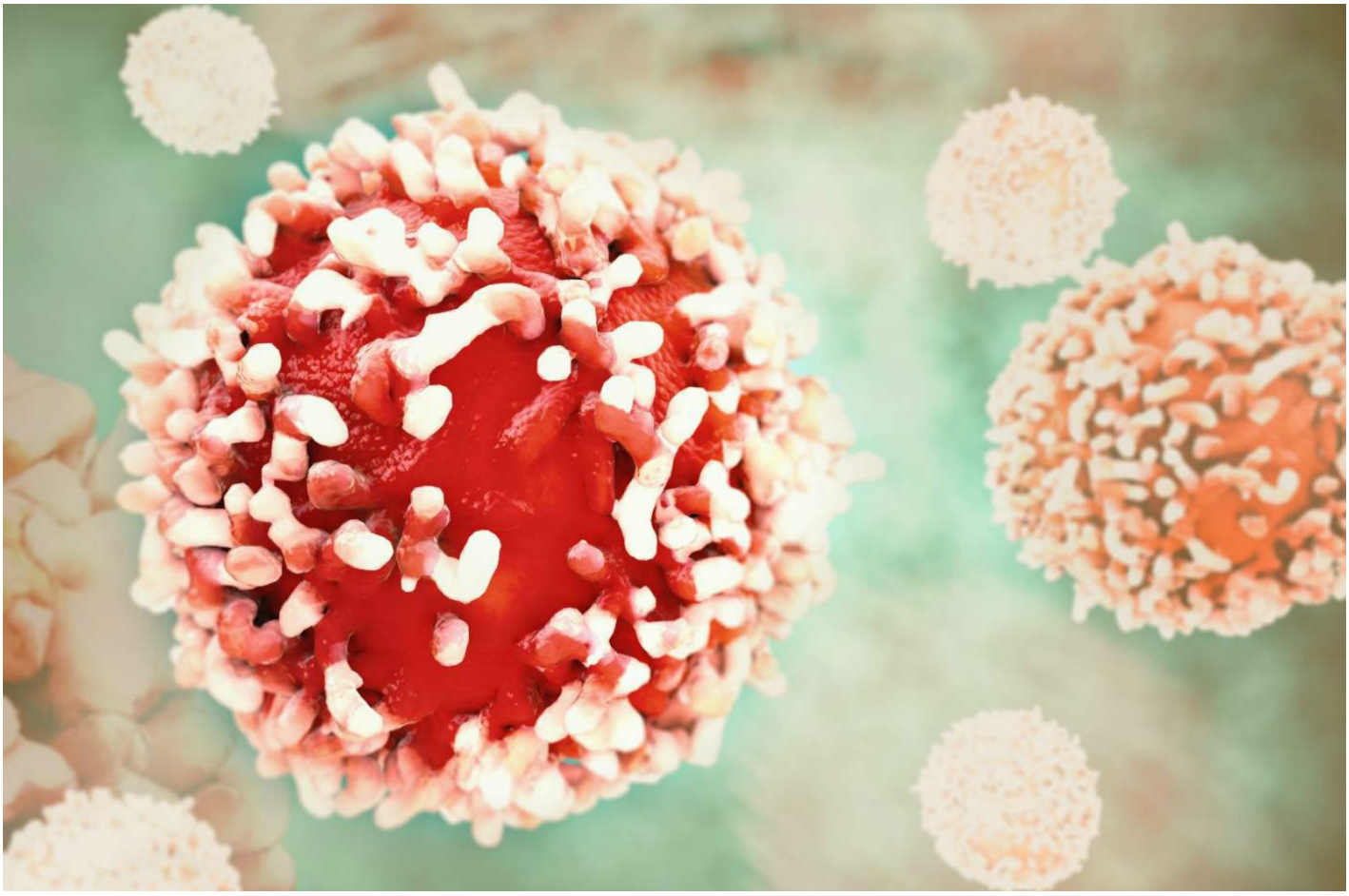
DUSA Pharmaceuticals Sheds Light On Cancer

Queen's University



With an initial grant of $8,000 and a long-held interest in light-based therapies, two researchers in Kingston, Ontario, develop a uniquely effective method to treat cancer, licensed by DUSA Pharmaceuticals.

On a shoestring budget and little else but a burning curiosity about light-based medicine, Jim Kennedy developed a simple and effective cure for actinic keratoses (AKs), the most common precursor of skin cancer. As researchers at Queen's University and the Royal Military College of Canada, both located in Kingston, Ontario, Kennedy and colleague Roy Pottier invented an unusually effective method for treating AKs and other skin cancers by combining two completely natural and harmless products: visible light and aminolevulinic acid (ALA), a small molecule synthesized by almost every nucleated cell in the human body.

Their research suggested the possibility that the administration of ALA to a cancer patient, when combined with an appropriate dose of visible light, might destroy at least certain types of cancerous and precancerous cells. Their hypothesis turned out to be correct. Subsequent studies showed that ALA could be effective when administered in an

appropriate vehicle by topical application, ingestion or through intradermal, subcutaneous or intravenous injection.

> *Kennedy has dedicated his professional life to the treatment of cancer. He began his academic career studying cancer immunology in the department of pathology at Queen's University. But he switched his research focus when he learned about photodynamic therapy, that is, the use of light, together with a photosensitizing agent, to treat disease.*

Also instrumental in his career change was meeting Dr. Tom Dougherty of Roswell Park Cancer Institute in Buffalo, N.Y. Dougherty was using photodynamic therapy as a way to destroy tumors in rats. Kennedy became fascinated by the potential of this new technique for treating cancer. His new focus required a change in grant-funding agencies and in professional affiliation, so he could have access to cancer patients.

"It was a risk," Kennedy says, "at that time, photodynamic therapy was almost completely unknown to the medical community, and grants for research in such an obscure field were difficult to obtain."

Kennedy's research in the area began with an $8,000 grant from the Ontario Cancer Treatment and Research Foundation to study photosensitizing compounds, also known as photosensitizers.

"These are compounds that absorb the energy of light and then transfer it to molecules of oxygen, which in turn become activated in such a way that they tend to react chemically with adjacent materials," Kennedy explains.

In the case of cancer treatment, photosensitizers can be combined with light to destroy cancerous cells. After many years of work, Kennedy and Pottier discovered that administering large amounts of ALA to patients could induce the accumulation of intracellular protoporphyrin IX (PpIX) in cells — especially in potentially cancerous cells.

PpIX can serve as a sort of marker in malignant or pre-cancerous cells. Administering ALA causes cells to accumulate higher levels of PpIX, thereby increasing the ability to detect malignant or pre-malignant cells, if the right equipment is used.

"It turns out that malignant, pre-malignant, and certain other abnormal cells accumulate significantly more PpIX than do normal cells," Kennedy explains. "This allows us to use ALA-photodynamic therapy to kill such cells preferentially — the normal cells experience only minor damage that is easily repaired, while the abnormal cells are severely damaged."

Because ALA is a small molecule, it passes easily through skin, unlike the other compounds they had tried, which had to be injected. Kennedy immediately tried ALA to treat tumors in mice, with mixed results. Then Kennedy, the quintessential scientist, tried it on himself — the skin of his arm, a patch of whiskers, a healing scratch on his skin.

"I wanted to see if it was like radiation therapy and I would lose my hair or cause depigmentation or a scar," he says, but there were no such side effects.

In 1987, Kennedy decided to try topical ALA on a patient he'd been treating who had cancerous tumors on her forehead, and he activated the process using a slide projector with a red filter. The experiment worked, and worked well. That success was followed by another: a man with a number of serious medical problems and large, painful ulcers of basal cell carcinomas at multiple sites on his skin. Because of his medical condition, his doctors did not want to operate to remove these cancers and asked Kennedy to see if his new therapy might get rid of the ulcers. Again, the treatment helped.

In 1991, Geoff Shulman, a dermatologist and businessman, heard a lecture by Kennedy about the use of photodynamic

therapy to treat skin cancer. He too became intrigued and just happened to be in the perfect spot to bring the idea to commercialization.

A few years earlier, Shulman had helped his father launch a pharmaceutical company in Canada. Suffering from Parkinson's disease, his father, who was also a doctor, found his most effective treatment was a drug called Deprenyl, which was not available at that time in Canada or the United States. The younger Shulman helped his father found a company called Deprenyl to bring that drug to Canada.

"The commercial potential of this light therapy for cancers and precancers appeared to be very large," says Shulman, "and the risks appeared to be relatively low, since Dr. Kennedy had already shown it worked in hundreds of patients."

Most drugs fail in clinical trials before ever getting to market, according to Shulman; this one was already curing people. With that kind of clinical success in place, Shulman knew the odds of getting the drug approved were good. He also knew that in order to ensure success, they had to get it approved in the United States.

"If it was approved only in Canada, it wouldn't be worth it," Shulman says.

So he set up DUSA Pharmaceuticals as a U.S. company. But the road to market for DUSA turned out to be a much longer journey than the one he'd been on with Deprenyl.

Kennedy and Pottier began treating patients with the experimental compound in 1987 and published their first paper in 1990. The first patent was issued one year later, held by Queen's University. When Shulman learned of it that year, he met with Kennedy and soon afterwards, Pottier. Deprenyl spun off Deprenyl USA, which later became DUSA Pharmaceuticals and licensed the invention. It wasn't until 1999 that the company won the first approval from the U.S. Food and Drug Administration, and in 2000, launched Levulan PDT for the treatment of AKs.

Today, DUSA has 90 employees, including its own 40-person dermatology sales force, and, after many years in the "development stage," it is growing. Sales have jumped from $1 million in 2003, to $11 million in 2005, to a projected $25 million in 2006. The company has used ALA-photodynamic therapy as a platform technology for applications such as aging skin and acne. In 2004, DUSA also entered into an agreement with the National Cancer Institute to test Levulan PDT in patients with oral and esophageal cancer.

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