# Project Violet

BY JIM OLSON, MD, PHD

Every animal, every plant in nature has a way of protecting itself so it can survive.

Sunflowers are able to keep their bright yellow petals from being completely devoured by bugs by manufacturing a trypsin inhibitor, a peptide that neutralizes the enzyme insects spit on their food to break it down so they can eat it. Spiders and scorpions, over millions of years, have developed powerful toxins that enable them to paralyze their prey, ensuring a leisurely, trouble-free meal—and the survival of their species. Even that ball of starch we know as a potato is able to protect itself from being completely consumed by insects and grubs and whatever else lives underground because of a substance—a protective drug—produced in the potato skin.

Nature's medicine chest is both imaginative and boundless. Luckily for us, it's also malleable.

For the past 10 years, our lab at Fred Hutchinson Cancer Research Center in Seattle has been working with the mini proteins or peptides produced by various organisms—drugs that are encoded into the DNA of plants and animals and passed from generation to generation—with a mind toward using these amazing molecules to obliterate cancer cells without harming healthy tissue.

Our first candidate for investigation was a chlorotoxin peptide produced by the Israeli deathstalker scorpion. This peptide is useful to the scorpion because it's able to travel through the bloodstream of prey to hit its target. It's useful to us because that same tough little peptide also happens to bind to cancer cells but not to normal tissue.

When we first started working with scorpion chlorotoxin, we didn't know why it bound itself exclusively to cancer cells. Now we do—it has to do with a protein target that is usually inside cells but gets flipped to the outside of cancer cells, making it available to chlorotoxin. But that's not the amazing part of the story. The amazing part is that we were able to think creatively and optimize the scorpion venom peptide by binding it to a safe fluorescent dye to create a sort of molecular flashlight that illuminates cancer cells under near-infrared light.

In 2004, a colleague and I injected this optimized peptide—optide, for short—into the tail of a mouse that was growing a human brain tumor under its skin. That optide traveled through the mouse's bloodstream and an hour later, its brain tumor was glowing brightly while the rest of the mouse was not. My colleague and I were dancing around in our white lab coats because we'd just come up with a drug that could clearly—brilliantly, even—differentiate healthy tissue from tumor.

This drug, which we call a Tumor Paint imaging agent, is currently in clinical trials in Australia. It got there in a very reasonable amount of time—10 years—thanks to research that was funded in an unconventional way. I'd written grants to the National Institutes of Health—six of them, in fact—but each was rejected because the idea seemed "too speculative" or "overly ambitious."

My colleagues and I believed in the incredible potential of Tumor Paint molecules, however, as did the families of the pediatric brain cancer patients in our practice. These are families who've seen their children die or suffer debilitating consequences because it is so difficult for surgeons to distinguish brain cancer from normal tissue. These families—along with their friends and neighbors and colleagues—began fundraising and eventually brought in more than $8 million to fund the research at Fred Hutch. Subsequently, we created Blaze Bioscience, a new biotech company spun out of Fred Hutch, specifically designed to efficiently and expediently advance our discoveries to human clinical trials and eventual FDA approval.

Along with thinking creatively in the lab, we're also trying to think creatively about how to fund and develop our cutting-edge research.

That's where ProjectViolet.org comes in. Inspired by my patients, the crowdfunding success of Tumor Paint and the idea of a new class of anti-cancer compounds derived from nature, Project Violet allows everyday individuals—bus drivers, beauticians, database managers—to adopt new drug candidates for as little as $100. These candidates, derived from the DNA of everything from spiders and scorpions to potatoes and cone snails to sunflowers and violets, will become part of a larger library that we plan to share with other scientists around the world, to collaborate on diseases long considered incurable.

We created Tumor Paint with pediatric brain cancer patients in mind. As a pediatric neuro-oncologist, I've seen far too many children lose healthy tissue during brain surgery. I've seen far too many children come out of surgery only to have MRIs reveal

Clockwise from above:
Dr. Jim Olson with Carver Faull, a former patient.

Dr. Jim Olson hugs Carver Faull, a former patient, as Carver's family looks on.

Blitz (the official mascot of the Seattle Seahawks) comes to cheer on brain cancer patients and Dr. Jim Olson and team.

that their brains still house remnants of a tumor. I've seen far too many children die. We desperately need a way to make cancer cells light up so surgeons can see them while operating. We hope that Tumor Paint will do just that.

Tumor Paint also has potential well beyond brain cancer. In pre-clinical studies, it's been found to light up prostate, colon, breast, skin, and other cancers. We believe that if it's as successful in humans as it is in animals, this powerful little peptide—borrowed from nature and bettered through science—has the potential to help over a half million cancer patients a year.

And Tumor Paint is just the beginning. Over the past few years, we've been able to boost the number of optides we can develop from about 12 a year to 10,000 a month. Each of those optides is a potential key to turn the lock of a particular disease. Our team is working to uncover better treatments for a variety of cancers, along with autism, Alzheimer's, and other rare diseases unlikely to receive attention from pharmaceutical companies. We intend to share libraries of optide therapeutic candidates with other scientists around the world provided that Project Violet is successful.

Every animal, every plant in nature has a way of protecting itself so it can survive. Human beings are no different except we protect ourselves through science, through innovation, through creativity and, in this case, the generosity and vision of "citizen scientists" who've lost friends, neighbors and loved ones to cancer and other debilitating diseases. We protect ourselves with hope and heart and inspiration and, yes, a few amazing tricks borrowed from nature. OI

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