A Light in the Darkness

Osamu Shimomura dims the lights in his home laboratory. Cupped in his hand are silvery brown, dried out sea fireflies that he has carefully shaken out of a jar marked "*Cipridina* 1944." He runs his other hand under a water faucet and then begins gently crushing the tiny crustaceans, rubbing them into a grainy paste. Soon a soft blue luminescence lights the hollow of his hand, which deepens in intensity when he presses harder. "Ah, this one is pretty good," he murmurs.

The dim glow of this marine creature led Shimomura from the darkest days of his life, in post-war Japan, to his receipt this year of one of science's great honors, the Nobel Prize in Chemistry. Soon after the award was announced, a clearly astonished Shimomura offered these words to young scientists: "Never give up. If you find an interesting subject, study it through to the finish. If you confront difficulties, overcome them. Don't be discouraged."

Shimomura's dedication to pure science, his perseverance even in the most difficult times, has rewarded him far beyond earning the esteem of his peers. The Nobel Prize recognized Shimomura's discovery of green fluorescent protein (GFP) in the jellyfish *Aequorea*, which in its application has launched a technical renaissance in the imaging of cells. (See story on Page 15). But when Shimomura found GFP, he was searching for something else entirely: the molecule that gives *Aequorea* its natural ability to generate light, called bioluminescence. (Fluorescence is not the generation of light, but its conversion from one wavelength to another.) Shimomura did also discover that luminescing protein in *Aequorea*, and he named it aequorin.

"GFP was a just a by-product in my work," says Shimomura, who is now 80. "My target was aequorin. I wanted to understand, chemically, how light is emitted from animals."

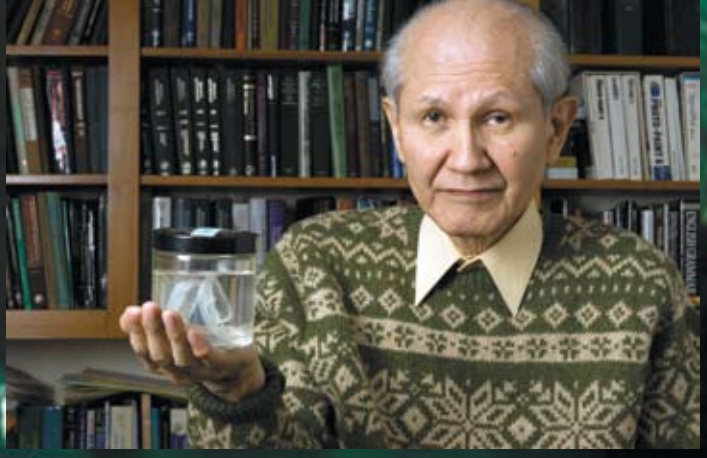
Over three decades of heroic effort, Shimomura and his wife, Akemi, collected some 850,000 jellyfish from the waters off Friday Harbor Laboratories in Washington State, and extracted minute amounts of aequorin from each animal's luminescent rim. He spent countless hours analyzing the photoprotein at Princeton University, where he was a researcher, and later at the MBL. But Shimomura did achieve his goal. "I am very proud of my work to show how aequorin emits light," he says. "It took a long, long time and it was very difficult."

It's a classic example of how basic research can have unexpected, yet enormously important applications in other fields. "Even if GFP was a by-product in my work, I'm very glad it's made huge contributions to science," Shimomura says.

None of this would have happened if Shimomura hadn't first purified the bioluminescent molecule from *Cipridina* at Nagoya University in Japan in 1956. This extremely difficult feat had eluded chemists at Princeton for 40 years, and Shimomura accomplished it largely through independent study and experimentation. It was the turning point of his life.

"When I succeeded with that crystallization, I was so happy I couldn't sleep for three days," Shimomura says. "I was ten times happier than when I won the Nobel Prize. That success gave me self-confidence. Then, I knew, I can do anything!" He is silent for a while. "Before that time, my life was very dark. Since the atomic bomb, nothing was good. That success gave me some light, somewhere."

The study of bioluminescence lights the path of 2008 Nobel Laureate Osamu Shimomura's life



Shimomura had found his way to Nagoya University against all odds in 1955, when Japan was struggling to emerge from the devastating bombings of World War II. Ten years earlier, on August 9, 1945, the 16-year-old Shimomura had been working in a military plane factory about 10 miles outside of Nagasaki. Like many of Japan's youth, he had been taken out of school to work for the war effort. Shortly before 11 AM, he heard the sound of enemy planes flying over Nagasaki, and he and a friend ran outside and climbed a hill to watch them. A few minutes later, thinking the danger had passed, Shimomura went back into the factory and sat down on his chair.

"At that moment, a big flash came. It blinded me for about 30 seconds. I couldn't see anything because of the brightness. Then about 40 seconds later was a very strong, not a sound, but a pressure wave. I had pain in my ears, I couldn't hear for a couple of minutes. We wondered, what has happened? We knew it was an explosion. We didn't know it was an atomic bomb."

At 5 PM, Shimomura left the factory to walk home, three miles away. "On the way home, then started the black rain," he says of the nuclear fallout. "I was soaked. I was wearing a white shirt, and I became completely gray. When I got home, my grandmother saw me and quickly made a bath and washed everything off." Shimomura thinks this reduced the amount of radiation damage he received.

In the following days, Shimomura was shocked by the sight of Nagasaki and victims of the bomb. The next years were bleak. "I tried to get into a school, but I couldn't get in because I had no school record. I had no teachers to ask for a recommendation." Three years later, "the pharmacy school at Nagasaki University, which had been completely destroyed by the atomic bomb, made a temporary campus within a 10 minute walk from my home. Somehow, I was able to enter that school."

Shimomura had no interest in pharmacy, he says, but he had "no choice. I had no other place to go." He graduated in 1951, but stayed on as a supervisor of student experiments. In 1955, one of the professors, Shungo Yasanuga, recognizing Shimomura's potential, took him to Nagoya University to meet a well-known molecular biologist, Fujio Egami. But Egami wasn't there. Before leaving, they briefly visited Professor Yoshimasa Hirata, an organic chemist. Hirata might have misunderstood the visit because after chatting for a few minutes, he told Shimomura, "Please come to my lab. You may start at any time."

"That was puzzling," Shimomura says. "We had just met." But he thought the offer might be "a direction given by heaven." A month later, he accepted.

On Shimomura's first day, Hirata crushed *Cipridina* in his palm, added water, and demonstrated its bioluminescence. He asked Shimomura to determine the structure of *Cypridina's* light-emitting luciferin molecule, which was known to be extremely unstable. Shimomura's unlikely success one year later would be the beginning of a new life, as Frank H. Johnson of the Princeton bioluminescence group invited Shimomura to join them. And it was Johnson who gave Shimomura the challenge of isolating the bioluminescent molecule from *Aequorea*, during which Shimomura also discovered GFP.

Osamu Shimomura exemplifies patient devotion to scientific inquiry, no matter how hard the problem, in a world too often focused on quick results. "Osamu is very steady, very hardworking, very interested in the basic aspects of a problem," says J. Woodland Hastings of Harvard University, a good friend and collaborator of Shimomura's who was instrumental in bringing him to the MBL in 1982. In science, Hastings says, "Osamu sets his own directions."