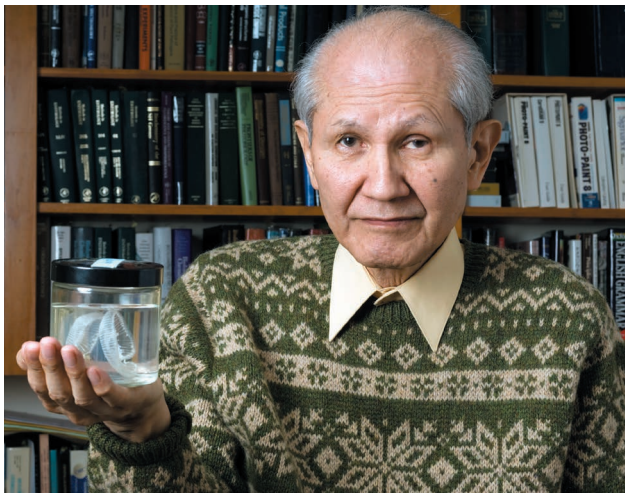
Osamu Shimomura

(1928–2018)

Chemist who illuminated bioluminescence.



MARINE BIOLOGICAL LABORATORY/TOM KLEINDINST

Growing up during one of the darkest times in history, Osamu Shimomura devoted his long and fruitful career to understanding how creatures emit light. He discovered green fluorescent protein (GFP), with which — decades later — biomedical researchers began to monitor the workings of proteins in living tissue, and to confirm the insertion of genes. For that discovery, he shared the Nobel Prize in Chemistry in 2008 with neurobiologist Martin Chalfie and the late Roger Tsien, a chemist.

Shimomura, who died in Nagasaki, Japan, on 19 October, was the first to show that a protein could contain the light-emitting apparatus within its own peptide chain, rather than interacting with a separate light-emitting compound. The significance of this discovery was that the gene encoding GFP could, in principle, be copied (or 'cloned') and used as a tool in other organisms. Others eventually took that step, but it would have been impossible without the exemplary patience of Shimomura, who spent years gathering enough material to extract, purify and determine the chemical structure of GFP.

Born on 27 August 1928 in the town of Fukuchiyama, at the height of Japanese expansionism, Shimomura was the son of an army captain whose frequent postings abroad disrupted his child's school education. Shimomura's grandmother instilled in him the samurai principles of honour and fortitude. In 1944, with the Pacific War turning against Japan, he and his fellow school students were mobilized to work in a munitions factory in Isahaya, about 25 kilometres from Nagasaki. On 9 August 1945, he was at work when a blinding flash, followed by a huge pressure wave, signalled the dropping of the atomic bomb on the nearby city. He walked home under a shower of black rain. He later wrote that his grandmother's quick action in putting him straight in the bath might have saved him from the effects of the radiation.

Without a high-school diploma, he despaired of finding a college place. Eventually, Nagasaki Pharmacy College admitted him in 1948. On graduation, he worked for four years as an assistant in practical classes. He devised research projects in his own time, and his professor obtained permission for him to do a year of advanced study. He joined the laboratory of organic chemist Yoshimasa Hirata at Nagoya University, and his lifelong fascination with bioluminescence began.

Hirata asked him to extract and purify a compound, luciferin, which enables the tiny marine crustacean *Cypridina* to glow in the dark. Hirata thought the results too uncertain for a PhD student, but because Shimomura was not registered for a degree, he allowed him to try. In just ten months, Shimomura made pure crystals of luciferin (O. Shimomura *et al. Bull. Chem. Soc. Japan* **30**, 929–933; 1957). "I learned that any difficult problem can be solved by great effort," he wrote in his Nobel biography.

The luciferin paper brought an invitation for Shimomura to join the bioluminescence lab of biologist Frank Johnson at Princeton University in New Jersey. Three weeks after marrying Akemi Okubo in August 1960, Shimomura sailed to the United States, his travel paid for by a Fulbright scholarship. Johnson asked him to work on the jellyfish *Aequorea*, which has a ring of organs around the edge of its umbrella that emit blue light. In July 1961, Johnson, Shimomura and his wife, and several assistants and students made a road trip across the United States to collect hundreds of jellyfish, scooping them out of Friday Harbor in Washington state, cutting off the rings and transporting them to Princeton for analysis.

In the face of scepticism from Johnson and others, Shimomura determined that the luminescent substance was a protein; he named it aequorin. He discovered almost at once that it was activated by calcium (later, aequorin became an essential reagent as a glowing marker of calcium release). Shimomura, his family and his research colleagues spent 19 summers at Friday Harbor, collecting hundreds of thousands of jellyfish to obtain enough of the elusive material for a full structural analysis. Until a way of making genetically engineered aequorin became available in the 1990s, Shimomura freely shared his carefully harvested stocks with laboratories the world over.

It was in the process of purifying aequorin that Shimomura discovered small amounts of GFP, which fluoresces green when aequorin emits its blue light. It took him and his team until 1979 to accumulate enough to explore how the protein works. Shimomura described GFP's unprecedented incorporation of the light-emitting function within the protein chain (O. Shimomura *FEBS Lett.* **104**, 220–222; 1979), and then put GFP aside to work on wide-ranging studies of bioluminescence in other organisms.

In 1994, Chalfie's group reported the successful creation of bacteria and roundworms that could express GFP (M. Chalfie *et al. Science* **263**, 802–805; 1994). Soon afterwards, Tsien and his colleagues created GFPs of different colours (R. Heim *et al. Nature* **373**, 663–664; 1995). Others have extended the technique to vertebrates, with headlines about 'glow-in-the-dark monkeys' obscuring the method's great value in confirming the successful incorporation of genes from other organisms.

From 1982 until his retirement in 2001, Shimomura moved to the Woods Hole Marine Biological Laboratory in Massachusetts with Akemi, who had continued to work as his research assistant. After their retirement — a concept that was clearly difficult for them — they moved their laboratory into their home and continued to work. Shimomura's textbook *Bioluminescence: Chemical Principles and Methods* was released in 2006, and in 2017 he published an autobiography, *Luminous Pursuit: Jellyfish, GFP, and the Unforeseen Path to the Nobel Prize*. ■

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