

THE AUTHOR FILE

Nathan Shaner

Engineering a protein from a little-known marine invertebrate brings labs a bright, neon green sheen

Jellyfish such as *Aequorea victoria* use the fluorescent protein GFP to shift their bioluminescence from



Nathan Shaner with Goliath (left) and Bowie (right)

blue to green, probably for better visibility in algae-filled waters, says biochemist Nathan Shaner, cofounder of the Scintillon Institute in San Diego. The lancelet *Branchiostoma lanceolatum*, a marine invertebrate that likes to burrow into the sand and that fluoresces for unknown reasons, sports a

protein brighter than any other Shaner has seen. Reinforcing this shine with stepwise protein engineering, he and his team have created mNeonGreen, a stable fluorescent protein that absorbs and emits light so well that he forecasts a bright future for it in the fast-growing field of super-resolution microscopy.

The Scintillon team found that mNeonGreen allowed them to map the locations of approximately four times more individual protein molecules than did GFP. “That’s a pretty substantial improvement, and it’s going to make a lot of experiments possible that weren’t before,” he says.

Shaner cofounded Scintillon a little over a year ago with Jiwu Wang, the CEO of Allele Biotechnology, a reagents company expanding into services such as antibody development and stem cell–line production.

What connects these men is a desire to perform “high-risk, high-impact basic research” in a climate of dismal federal science budgets, Shaner says. The company currently funds the institute, but the dream is to achieve self-sufficiency through grants, donations and technology license revenue.

Allele distributes mNeonGreen with different pricing for academic and commercial users and is building a construct repository to help foster collaboration and sharing of plasmids containing mNeonGreen, he says.

Although he occasionally advises the company, Shaner’s focus is on building tools for new bioluminescence applications, and he also explores sustainable food and energy production. He says that he gets his best ideas when outdoors, enjoying nature’s beauty.

In this new work, Shaner took the lancelet’s tetrameric protein LanYFP and engineered it into the monomer

mNeonGreen using methods pioneered in Nobel laureate Roger Tsien’s University of California, San Diego, lab, where Shaner did his PhD.

One challenge was that no structures of the lancelet fluorescent proteins were available. So the team had to computationally identify a starting point for the monomerization. “Monomeric fluorescent proteins give you the best chance that the fluorescent protein tag will not interfere with the function of whatever it’s attached to,” he says.

Reflecting on his time in the Tsien lab, Shaner says that what he liked best about it was the freedom to do research “combined with extremely focused and insightful feedback just when it was needed to keep things going in the right direction,” he says. As a postdoctoral fellow at the Monterey Bay Aquarium Research Institute (MBARI), Shaner continued working on bioluminescence, seeing “some of the world’s coolest glow-in-the-dark animals,” including a close encounter with a living vampire squid.

His advisor at MBARI, Steven Haddock, says he misses Shaner’s knack for drawing interesting connections between genes, proteins and biochemistry and for not shoe-horning data to fit a favored preconception. “It is always a good day that begins with Nathan saying, ‘Last night I had an idea about ...’” says Haddock. Although some “gifted thinkers” are not suited for a lab environment, Shaner is efficient and careful with a pipette. “He can accomplish more in a 6-hour stretch than most people will do in 2 days of struggling.”

Shaner’s high school career plan was to become an astronomer, and, as a teenager, he sold his Nintendo to buy a telescope. At Oberlin College, he studied physics and music composition. His then overfilled schedule forced him to drop music, but he made sure the piano stayed in his life. “Learning new music is very rewarding and keeps my brain in shape,” he says. “Bach’s *The Well-Tempered Clavier* is great for stress relief.”

After college, he was admitted into Princeton’s physics graduate program but left when he realized he did not want to continue in that field. As he made plans, he held various jobs—for example, as a minimum-wage bottle labeler for a company that packaged drugs for clinical trials. As an assistant in the University of Pennsylvania labs of cell biologists Joseph and Jean Sanger, he rekindled a childhood love of biology: he learned tissue culture and microscopy and had his first experiences with fluorescent proteins.

Vivien Marx

Shaner, N. *et al.* A bright monomeric green fluorescent protein derived from *Branchiostoma lanceolatum*. *Nat. Methods* **10**, 407–409 (2013).

“Learning new music is very rewarding and keeps my brain in shape.”