THE AUTHOR FILE

Luke D. Lavis

Why it's fun to be a 'dye Santa,' how to fine-tune *in vivo* probes, what to name your firstborn.

As a chemist "through and through," Luke Lavis, a group leader at Janelia Research Campus, lives chemistry; he draws chemical structures on the shower door and has named his firstborn Linus, after his fellow Oregon State University alum and scientific hero, chemist and Nobel laureate Linus Pauling.

T.C. Binns

Luke D. Lavis

Lavis runs Janelia's lone chemistry group because, he says, "I want to hang out with biologists, protein gurus, and microscope builders." He and colleagues have made four new members of the Janelia Fluor (JF) rhodamine dye family that excite in blue to far-red. Lavis and Jonathan Grimm, a medicinal chemist in the lab, previously tinkered with rhodamine synthesis. They brightened the dye by using cross-coupling reactions to add four-membered azetidine rings. They have now further tuned the dyes with the addition of a few more atoms to the ring, and devised rules for dye fine-tuning and for predicting spectral properties of dyes with nanometer precision. By putting these tuning rules to work, "we knew what to make from the start," says Lavis. They avoided the need to make dozens of molecules to find the ones that worked with commonly used lasers. They tuned the dyes' biological qualities, too, making them more permeable to cells and able to cross the blood–brain barrier in mice while maintaining the dyes' brightness and photostability. As Lavis explains, this approach opens up many possibilities including single-particle tracking *in vivo* or the use of hybrid small-molecule protein-based sensors with the genetic specificity of fluorescent-protein-based tools and the spectral qualities of JF dyes.

The new dyes are brighter than the older ones, which to a chemist is mere incrementalism, but Lavis knows his microscopy colleagues find it transformative to have four times the photons to play with. "I have been surprised by how many people want to try out the dyes," he says. He enjoys being a "dye Santa" who disseminates dyes freely to Janelia colleagues and labs around the world.

Chemist Markus Sauer of the University of Würzburg, who collaborates with Lavis, says that improvements in super-resolution microscopy depend on new and improved fluorescent probes and labels but that proven experts in fluorescent dye design and synthesis are rare. "Luke is the exception; he is a calm contemporary with brilliant ideas and also technical capabilities to put new ideas into practice," says Sauer. He has ideas to "roll up the entire super-resolution microscopy field from behind by developing intelligent new dyes: Lucky Luke!"

As a chemistry history buff, Lavis reads old papers, wading through descriptions of ballpoint pen ink chemistry to develop sensors that work in the brain. "Fun stuff," he says. The first synthetic dye was made in 1856. Dyes and their many applications—the first antibiotic was a dye—shaped the chemical industry. Rhodamine synthesis dates to 1887 and involved acid-catalyzed condensation in strong acid with heating. Performing chemistry in boiling sulfuric acid is not the mildest of conditions, he says; the Mafia's '*lupara bianca*' method of disposing bodies is rumored to follow this protocol. Many 21st century papers on fluorophores have involved 19th century chemistry and rhodamine synthesis did not change much, he says, which limited the functionality that could be put on the rhodamine structure, he says. He is motivated to change that.

Lavis grew up in southwest Oregon, a child of hippies who moved there from California. The family's first college student, he studied chemistry at Oregon State University. He joined Molecular Probes, now owned by Thermo Fisher Scientific, where he made small-molecule dyes for use in biology. He worked on high-throughput screening reagents when he followed his boss to Molecular Devices. He next completed his PhD in organic chemistry with Ronald Raines at the University of Wisconsin-Madison. As Lavis hunted for a postdoctoral fellowship, he landed a principal investigator position at Janelia in 2008. He enjoys its collaborative culture and advises scientists more generally that "the surest way to kill a collaboration is to try and take all the credit," he says. "Be generous and expect to have that reciprocated. If it is not, then move on."

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Beyond the lab, Lavis and his wife stay busy with their two children, ages three and six. "Kids are the 'great do-over,' " he says, letting adults "redo all the cool stuff for the first time again through their eyes." Together they check out Washington DC's museums, enjoy a sunset on the Oregon coast, a kayak float or bike ride in the Virginia wilds.

Vivien Marx

Grimm, J. *et al.* A general method to fine-tune fluorophores for live-cell and *in vivo* imaging. *Nat. Methods* **14**, 987–994 (2017).