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Eureka!: The molecular mousetrap inside us all

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Proteins, it turns out, can be a clever bunch.

New research by Lila Gierasch, a University of Massachusetts Amherst professor of biochemistry and molecular biology and chemistry, and Beena Krishnan, a senior postdoctoral fellow, has shown how a family of proteins called serpins makes a spring-loaded loop to snap up their prey - in this case, proteolytic (protein-digesting) enzymes - and catapult them back into the protein's slatted wall, ultimately to their death. It's a natural process necessary for enzyme regulation in the body.

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This "molecular mousetrap," as Gierasch calls it, is very effective, except when it misfires. Sometimes the protein hooks another serpin molecule, creating a large species of serpins that's extremely toxic.

When serpins misfire diseases such as emphysema, thrombosis (a blood clot within the blood vessels), some dementias and cirrhosis of the liver are born.

"The enzyme needs to be inhibited," she said. And in the case of emphysema "if it doesn't get inhibited it becomes overactive and chews up the surface of the alveoli (small sacs in the lungs) and you lose flexibility in the lung tissue."

Figuring out just how these proteins cut down on enzymes was no easy task. Because the process occurs quickly, Gierasch described observing it to "seeing a ghost." She credits Krishnan with figuring out a way to chemically mark the serpins and analyze their movements after the fact.

The discovery has implications for treating diseases.

"We hope describing the nature of the molecular slingshot gives (researchers) a better target for designing an inhibitor," Gierasch said.

Electric evolution

The goal wasn't necessarily to foster evolution in a test tube, but that's just what happened in Derek

Lovley's lab.

Lovley, a UMass distinguished professor of microbiology, and his research assistants were experimenting with Geobacter, a microbe Lovley found in river muck. The organism has an amazing ability to conduct electricity. Lovley says Geobacter may someday be used to create biological batteries.

For this recent experiment Lovley, Zarath Summers, a postdoctoral fellow, and their colleagues were trying to better understand a process called interspecies hydrogen transfer, which occurs indirectly when two species cooperate to use materials neither could use on their own. You can see interspecies hydrogen transfer at work in the biological production of methane, a greenhouse gas that can be converted into electricity. One bacteria will munch waste and expel hydrogen, then another will gobble up the hydrogen and produce methane.

"How did microorganisms evolve to exchange like that? That was the basis for our experiment," Lovley explained.

To figure this out he and Summers created a harsh environment for their Geobacter species. The microorganisms were given ethanol (which only one species could use) and an organic acid (which the other could use) on which to live. The scientists wanted to force the species to cooperate and document how they functioned.

"It was basically get along or die," Lovley said. "That's the strongest selective pressure you can apply."

Initially, the microorganisms weren't getting along. But then, about a month later, their relationship changed.

They began sharing hydrogen and became the "ultimate drinking buddies," Lovley joked, referring to the way they metabolized ethanol, an alcohol.

Then things got extraordinary.

The two species of Geobacter started clumping together in red blobs in the culture tubes: The microorganisms were evolving to make the exchange of hydrogen more efficient.

"We didn't expect this," Lovley said. "They just kept getting better and better. At first they were making small clumps, then it was this really large aggregate of cells, 1 to 2 millimeters in diameter."

Instead of indirectly exchanging hydrogen, the new organisms adapted to cut out the middle process and directly exchanged electrons - a more efficient process. Once the scientists mapped out the organisms' DNA, Lovley learned that the new species owed its conversion powers to a mutation in an iron-regulating protein.

The faster exchange of electrons is good news for Lovley and people interested in green energy. Geobacter has already been found to be covered in microbial nanowires capable of transferring electrons, or electricity, to power a battery. The quicker Lovley can ramp this process up, the better.

"It's a better electrical connection," he said.

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Editor's note: After a brief hiatus, Eureka! has moved from the Daily Hampshire Gazette and will now appear twice a month in Hampshire Life.

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