

Scientists discover new DNA modification system in animals, captured from bacteria more than 60 MYA

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Bdelloid rotifer (*Adineta vaga*) under polychromatic polarization microscope.
Credit: M. Shribak and I. Yushenova

Your DNA holds the blueprint to build your body, but it's a living

document: Adjustments to the design can be made by epigenetic marks.

Epigenetic marks are modifications to DNA bases that don't change the underlying genetic code, but "write" extra information on top of it that can be inherited along with your genome. Epigenetic marks usually regulate [gene expression](#)—turn [genes](#) on or off—particularly during [early development](#) or when your body is under stress. They can also suppress "jumping genes"—transposable elements that threaten the integrity of your genome.

In humans and other eukaryotes, two principal epigenetic marks are known. A team from the Marine Biological Laboratory (MBL) has discovered a third, novel epigenetic mark—one formerly known only in bacteria—in bdelloid rotifers, small freshwater animals. This fundamental and surprising discovery is reported this week in *Nature Communications*.

"We discovered back in 2008 that bdelloid rotifers are very good at capturing foreign genes," said senior author Irina Arkhipova, senior scientist in the MBL's Josephine Bay Paul Center. "What we've found here is that rotifers, about 60 million years ago, accidentally captured a [bacterial gene](#) that allowed them to introduce a new epigenetic mark that was not there before." This is the first time that a horizontally transferred gene has been shown to reshape the gene [regulatory system](#) in a eukaryote.

"This is very unusual and has not been previously reported," Arkhipova said. "Horizontally transferred genes are thought to preferentially be operational genes, not regulatory genes. It is hard to imagine how a single, horizontally transferred gene would form a new regulatory system, because the existing regulatory systems are already very complicated."

"It's almost unbelievable," said co-first author Irina Yushenova, a research scientist in Arkhipova's lab. "Just try to picture, somewhere back in time, a piece of bacterial DNA happened to be fused to a piece of eukaryotic DNA. Both of them became joined in the [rotifer](#)'s genome and they formed a functional enzyme. That's not so easy to do, even in the lab, and it happened naturally. And then this composite enzyme created this amazing regulatory system, and bdelloid rotifers were able to start using it to control all these jumping transposons. It's like magic."

"You don't want transposons jumping around in your genome," said first author Fernando Rodriguez, also a research scientist in Arkhipova's lab. "They will mess things up, so you want to keep them in check. And the epigenetic system to accomplish that is different in different animals. In this case, a [horizontal gene transfer](#) from bacteria into [bdelloid rotifers](#) created a new epigenetic system in animals that hasn't been described before."

"Bdelloid rotifers, especially, have to keep their transposons in check because they primarily reproduce asexually," Arkhipova said. "Asexual lineages have fewer means for suppressing proliferation of deleterious transposons, so adding an extra layer of protection could prevent a mutational meltdown. Indeed, transposon content is much lower in bdelloids than it is in sexual eukaryotes that don't have this extra epigenetic layer in their genome defense system."

In the two previously known epigenetic marks in eukaryotes, a [methyl group](#) is added to a DNA base, either cytosine or adenine. The team's newly discovered mark is also a cytosine modification, but with a distinct bacterial-like positioning of the methyl group—essentially recapitulating evolutionary events of over two billion years ago, when the conventional [epigenetic marks](#) in early eukaryotes emerged.

Bdelloid rotifers are extremely resilient animals, as the Arkhipova and

David Mark Welch labs at MBL have discovered over the years. They can completely dry up (desiccate) for weeks or months at a time, and then spring back to life when water becomes available. During their desiccation phases, their DNA breaks up into many pieces. "When they rehydrate or otherwise render their DNA ends accessible, this might be an opportunity for foreign DNA fragments from ingested bacteria, fungi, or microalgae to transfer into the rotifer genome," Arkhipova said. About 10 percent of the rotifer genome comes from non-metazoan sources, they have found.

Still, the Arkhipova lab was surprised to find a gene in the rotifer genome that resembled a bacterial methyltransferase (a methyltransferase catalyzes the transfer of a methyl group to DNA). "We hypothesized that this gene conferred this new function of suppressing transposons, and we spent the last six years proving that, indeed, it does," Arkhipova said.

It's too early to know what the implications may be of discovering this new epigenetic system in rotifers. "A good comparison is the CRISPR-Cas system in bacteria, which started out as a basic research discovery. Now CRISPR-Cas9 is used everywhere as a tool for gene editing in other organisms," Rodriguez said. "This is a new system. Will it have applications, implications for future research? It's hard to tell."

These discoveries open the door to new tools and research directions to investigate [genome](#) function and resilience in this rotifer system. In the future, such knowledge may be applied in creative ways to impact society during this time of rapid environmental change.

More information: Bacterial N4-methylcytosine as an epigenetic mark in eukaryotic DNA, *Nature Communications* (2022).

Provided by Marine Biological Laboratory

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