have a role in adaptation," says plant ecologist Teresa Rego of the Universidade de Santiago de Compostela in Spain. Many mutations in wild plants have been limited to describing broad epigenetic differences across individuals, and it’s often unclear whether these changes have taken place within an organism’s lifetime or if they’ve been inherited across generations, she says. Another challenge with wild populations that aren’t genetically identical is that the observed patterns may not be purely epigenetic, if there are underlying mutations in the genes encoding the organism’s epigenetic machinery. Richards notes: “Every one change in DNA sequence can dramatically change the methylation pattern in the genome.”

In humans, the evidence is even harder to interpret, with correlational studies so far failing to yield definitive answers about transgenerational epigenetic inheritance, Bassa says. “I’m not a total skeptic,” she says. Given the often short-lived nature of epigenetic inheritance, one proof for this is quite high. And it hasn’t been achieved in many of the studies, especially when you’re talking about humans.”

**Effects of epigenetics on the genome**

Given the often short-lived nature of epigenetic inheritance, one way that inherited extra-genomic factors could influence evolutionary processes overall is by changing the DNA itself—a phenomenon for which there is some evidence now surfacing. (See illustration on this page.) Rechavi’s group has shown this directly in C. elegans, indirectly, by promoting somatic reproduction in the worms and thereby turburbing their genetic evolution. In that case, the mutations that make their way into young worms are neutral or negative. “There is selective neutrality, but there is strong mobilization of somatic recombination and randomization across the genome; the effect of the epigenetically inherited trait is simply that their genetic diversity is increased—although Rechavi adds that the team didn’t respond the epigenetically to explore how this effect ultimately affects genetic evolution.

Another hypothesis that some scientists have floated in the literature is that inherited epigenetic regulation of particular genes can influence genetic adaptation at those specific genes. If an environmental pressures maintain long-term gene silencing, for example, the gene could naturally accumulate random mutations over time, changing its function, or, more likely, rendering it defunct. At some point, “that epigenetic silencing of that gene would no longer be required because the gene has mutated anyway,” Ashe says.

That idea hasn’t yet been tested in animals. Ashe continues. But a 2020 study by Stajic and colleagues provides some proof of concept in yeast cells that had been engineered to have URA3 purely silenced. When the researchers placed the strains in a potentially toxic growth medium, “We actually see that first step in adaptation is through epigenetics,” Stajic says. Specifically, the cells strengthened silencing of URA3, and some generations later, knock-out mutations emerging that rendered the gene defunct. “In this way, epigenetic inheritance could form kind of bridging mechanism to long-term changes. Stajic says—in essence, a ‘soft’ adaptation to probe the waters, followed by a hard evolutionary change that will stick in the genome indefinitely. “It seems that epigenetics, in this case, acts as a buffering system that allows the population to survive this initial step… until the beneficial mutation appears and spreads.”

More directly still, some epigenetic marks have long been known to induce mutations and shape mutational patterns across the genome. Methylation marks, for instance, are known to trigger a chemical reaction that mutates cytosines into a different base, thymine. Methylation patterns also influence genomic stability by repressing highly mutagenic DNA sequences called transposable elements. “These stability changes can influence the DNA sequence directly, which subsequently can lead to genetic adaptation,” Woychik says. A recent paper by the Aukbiological challenge suggests that mutations aren’t truly random but are shaped by epigenetic marks, including not just methylated but also histone modulations and the general accessibility of chromatin. When such mutations occur in germ cells and become inherited across generations, they have the potential to influence a species’ evolution, Giedroc says.

Through mechanisms like these, says evolutionary biologist and philosopher of biology Eva Jablonka of Tel Aviv University, epigenetic inheritance roles can lead to the diversification of species. “The first thing that happens in an environment is an