Research team discovers epigenetic pathway that controls social behavior in carpenter ants

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Minor (left) and Major (right) *C. floridanus* workers. Typically, Minor workers perform the vast majority of foraging, while Major workers defend the nest from intruders and rarely forage for food. Credit: Riley Graham

Through early adulthood, exposure to new experiences—like learning to drive a car or memorizing information for an exam—triggers change in the human brain, re-wiring neural pathways to imprint memories and modify behavior. Similar to humans, the behavior of Florida carpenter ants is not set in stone—their roles, whether it is protecting the colony or foraging for food, are determined by signals from the physical and social environment early in their life. But questions remain about how long they are vulnerable to epigenetic changes and what pathways govern social behavior in ants.

Now, a team led by researchers in the Perelman School of Medicine at the University of Pennsylvania discovered that a protein called CoRest, a neural repressor that is also found in humans, plays a central role in determining the social behavior of ants. The results, published today in *Molecular Cell*, also revealed that worker ants called Majors, known as "brawny" soldiers that protect colonies, can be reprogrammed to perform the foraging role—generally reserved for their sisters, the Minor ants—up to five days after they emerge as an adult ant. However, the reprogramming is ineffective at the 10-day mark, revealing how narrow the window of epigenetic plasticity is in ants.

"How behavior becomes established in humans is deeply fascinating—we know it's quite plastic especially during childhood and early adolescence—however, of course, we cannot study or manipulate this experimentally," said the study's senior author Shelley Berger, Ph.D., the Daniel S. Och University Professor in the departments of Cell and Developmental Biology and Biology, and director of the Penn Epigenetics Institute. "Ants, with their complex societies and behavior, and similar plasticity, provide a wonderful laboratory model to understand the underlying mechanisms and pathways.

The findings add to an extensive body of work, led by Berger and colleagues over the last 12 years, examining the social behavior of ants and the role epigenetics plays in determining that behavior. Ants provide ideal models to study social behavior because each colony is comprised of thousands of individuals—the queen, who carries out all the egglaying, and all of her highly-related offspring workers—with nearly identical genetic makeup, much like human twins. However, the sister workers possess distinct physical traits and behaviors based on caste. For example, Major workers have large heads and powerful mandibles that help protect their colonies, while Minor workers are much smaller and assume the responsibility of searching for food and caring for the brood (developing "baby" ants).

In a previous revelatory study, published in Science in 2015, researchers in Berger's lab showed it's possible to reprogram, or directly alter, the caste-specific behavior in Major workers by injecting them with a single dose of a histone-altering chemical. Although the size of the ants didn't change, their identities did—the Major workers wandered away from the colony and began to forage for food. While the results suggested epigenetically-encoded behavioral malleability in ants, it was unclear how long the "epigenetic window of vulnerability" remained open, and what pathways actually determined the behavioral differences between ant castes.

In this study, researchers injected the same histone-altering chemical, a histone deacetylase inhibitor called trichostatin A (TSA), in ant brains at specific points in early adulthood: zero, five and 10 days after they emerged. They found that many genes that are normally only turned on in the Minor workers were also turned on in the reprogrammed Major workers, and these changes persisted well after the short half-life of the drug. Surprisingly, neither the behavioral reprogramming nor the gene expression similarities occurred in Major workers injected after 5 days of age.

More importantly, researchers saw that the protein CoRest, which is found widely throughout animals and mammals, was upregulated in the reprogrammed Major workers. They conducted epigenomic profiling, and found that when Major workers are reprogrammed, CoRest repressed enzymes that degrade Juvenile Hormone (JH), a hormone which is naturally elevated in the Minor workers but normally degraded in Major workers. Additionally, researchers found that CoRest represses these genes in natural Minor workers—but not natural Major workers—and that this epigenetic control of JH levels was responsible for the natural behavioral differences between Major and Minor workers. Taken together, the results reveal mirrored patterns in natural Minor foragers and reprogrammed Major workers: high CoRest, high JH levels, and low JH degradation.

"Given how highly related workers of different castes are to one another, we've always suspected that the epigenome plays a big role in their huge behavioral differences," said the study's lead author Karl M. Glastad, Ph.D., a postdoctoral researcher in the Berger lab. "However, this is the first study where the actual mechanism has been identified, from epigenome, through hormonal signaling, and finally to behavior."

More information: *Molecular Cell*, Glastad et al. "Epigenetic regulator CoRest controls social behavior in ants." www.cell.com/molecular-cell/fu … 1097-2765(19)30790-7 , DOI: 10.1016/j.molcel.2019.10.012

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