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New quartet of ant genomes advanced by experts



Ant genome research at ASU has the potential to accelerate discoveries and genomics-based approaches in the understanding of social behavior and development of pest management. Photo by Adrian Smith

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“Look to the ant thou sluggard and consider her ways and be wise.” This proverbial wisdom was taken to heart recently by an international group of ant experts who have published the genome sequences of four ants in a series of coordinated releases in the online early edition of the journal *Proceedings of the National Academy of Sciences (PNAS)*.

The quartet includes the genomes of the red harvester ant *Pogonomyrmex barbatus*; the Argentine ant *Linepithema humile*; the fire ant *Solenopsis invicta*, and the leaf-cutter ant *Atta cephalotes*, whose genome will be published Feb. 10 in *Public Library of Science (PLoS) Genetics*.

Perhaps drawing insights from their study organisms, the scientists' distributed, coordinated effort sped the advancement of these genome projects from sequencing to assembly to annotation to interpretation in less than two years.

Ants are dominant members of almost all terrestrial ecosystems; they are master architects, voracious predators, farmers, ranchers, scavengers and come in a fantastic array of shapes, sizes and colors. Almost all humans have come into contact with ants in one fashion or another. There are fire ants in yards, Argentine ants in kitchens, harvester ants in ant farms, and trains of leaf-cutter ants dismantling forests in documentaries.

Ants originated more than 100 million years ago, their ecological dominance and evolutionary success, complex societies, variation in form and function, and the diverse roles they play in ecosystems, collectively contribute to the scientific rationale behind scientists' efforts to sequence their genomes. With more than 14,000 described ant species, and with many thousands yet to be described, it is the diversity of ants, matched with many genome sequences, that researchers believe can solve some fundamental questions in biology.

Much of the impetus behind these collaborative efforts grew out of a workshop on ant genomics that took place at the Center for Social Dynamics and Complexity at ASU in 2009.

“Our goal was to sequence 10 ant genomes across the ant family tree and we are well on our way,” said Chris R. Smith, an assistant professor at Earlham College in Indiana. “The pace of our progress was also advanced by employment of the same annotation pipeline, MAKER, developed by Mark Yandell's group at the University of Utah.”

Smith co-organized the ASU workshop with his *P. barbatus* co-author,

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ASU scientists among first to sequence ant genomes

Two ASU scientists are among those taking an audacious approach to studying the role of epigenetics in aging and behavior – using the genome of ants.

Jürgen Gadau, a professor with ASU's School of Life Sciences. These publications bring the total number of sequenced ant genomes to six, all released since 2010.

Lead authors of the four studies, in addition to CR Smith and Gadau for *P. barbatus*, were Christopher D. Smith (San Francisco State University) and Neil Tsutsui (University of California, Berkeley) for *L. humile*; Yannick Wurm and Laurent Keller (University of Lausanne), Ioannis Xenarios (Swiss Institute of Bioinformatics) and Dewayne Shoemaker (USDA ARS) for *S. invicta*; and Garret Suen and Cameron Currie (University of Wisconsin-Madison) for *A. cephalotes*.

Gadau's team at ASU included School of Life Sciences doctoral students Joshua Gibson, Rick Overson, Elizabeth Cash, and postdoctoral fellows Martin Helmkampf and Florian Wolschin. Their studies, and those of co-author CR Smith, were supported by a grant from the National Science Foundation.

"These publications open the gates to entirely new and highly significant research ventures," said Bert Hoelldobler, Pulitzer Prize-winning co-author of "The Ants," with Edward O. Wilson, and a professor in ASU's College of Liberal Arts and Sciences.

Among these four newly sequenced ant species are two of the world's most damaging invasive species, the Argentine ant, *L. humile*, and fire ant, *S. invicta*. Control of these two pest species is a multi-billion dollar per year industry. Both are native to South America, but now can be found worldwide. The ant research community hopes that having the fully sequenced genomes of these ants will help researchers decode both the secrets of their success as invasive species and open avenues for new means for their control.

"Controlling invasive ant populations has long involved pesticides that also hurt native competitors including ants and other insects," said Wurm, lead author on the *S. invicta* genome. "The genome sequence represents a crucial milestone towards understanding how the members of an ant colony communicate. Ultimately, reverse engineering their communication system might facilitate the development of pesticides that specifically induce workers of a given species to kill their nestmates, while minimizing impact on other species and the environment."

"Argentine ants may seem like only a nuisance to many since they don't sting humans like their compatriot fire ant invaders, but studies have shown that they decimate native arthropods wherever they invade," added CD Smith, lead author of the *L. humile* genome. "They also protect crop pests, leading to pesticide use that contaminates waterways and probably human health. With luck, the genome will shed light on how to short circuit the destructive behaviors of both invasive ants."

The other two ant species in this quartet, the harvester ant, *P. barbatus*, and leafcutter ant *A. cephalotes*, were sequenced largely because of their unique biology. These two species have queens and workers that differ greatly in size, morphology, physiology, behavior and longevity. Researchers hope to illuminate how ant colonies manage to produce such genetically similar, but vastly different individuals. For example, harvester ant queens may live several decades, but workers only six months. Similarly, the range of sizes of leaf-cutter ant workers varies from smaller than a grain of rice, to as large as a peanut.

Scientific studies of these ants already have offered insights into molecular pathways that enable the ants to produce individuals with such differences and allow researchers, such as Gadau and CR Smith, to find those genes that ultimately distinguish queens from workers. CR Smith notes that, "these are the quintessential genes for advanced sociality, the genes that fate an individual to a life of royalty or drudgery."

Access to the leaf-cutter genome also offers opportunities to study the molecular underpinnings of a highly complex mutualism. Leaf-cutter ants evolved agriculture more than 10 million years ago. They not only cut leaves as a substrate to grow fungal gardens, but they also use bacteria to increase the intake of nitrogen and fight off harmful (parasitic) fungi.

"The intricate and obligate relationships between the ants and their symbionts are reflected in gene losses in the leaf-cutter ant genome, especially in pathways related to nutrient acquisition and storage, as would be expected when other organisms obligately supply nutrients," said Suen, one of the lead authors of the *A. cephalotes* genome. "As one of the most ancient forms of non-human agriculture, having access to the leaf-cutter ant genome will also help us understand how this complex behavior evolved. This ant-fungus association led to the development of the immense colony size in these ants, which can contain hundreds of fungus gardens and millions of workers."

Colleague and co-author Currie also noted that "having a genome for a leaf-cutter ant will greatly facilitate our ability to understand the molecular underpinnings of this complex agricultural symbiosis."

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Ultimately, however, the insights to be gained from the combination of these social insect genomes outweighs the individual contribution of each study, CR Smith said, in keeping with the ant genome researchers' collective, ant-like approach to "the greater good."

Smith's co-author, Gadau, agreed, noting that "large scale genomics analysis within a group of related organisms will also allow the identification of new functional non-coding DNA sequences that play a critical role in the organization of insect societies and phenotypic plasticity in general. This allows social insects to contribute to our understanding of how the environment and genome interact to generate an intricately intertwined society. At the same time, such studies also help us to understand how genomes in general interact with the environment to generate adaptive phenotypes or complex diseases like diabetes which are the result of an interaction between the environment, individual behavior and genes."

For example, these four genomes, taken together, have revealed that the brand of sociality that evolved among ants is different from, but similar to, that which has evolved among bees. By comparisons to the previously published honey bee genome, researchers have independently found that ants have much expanded odorant receptor genes, whereas honey bees have a contracted set, relative to other insects. Ants have the most odorant receptor genes of any insect described to date and this difference likely reflects an increased dependence on and sophistication of chemical communication. On the other hand, both the bees and ants have a relatively depauperate set of innate immunity genes, as compared to other insects, which seems to reflect an increased reliance on social immunity – the processes whereby individuals of a society rely on others to clean and 'de-bug' each other and the nest. All of the ant genomes also contain a complete DNA methylation toolkit. DNA methylation is known to modify the expression of genes, independent of changes in DNA sequence, and is involved in differentiating the developmental pathways of queens and workers in honey bees. Analyses in some of the ant genomes suggest that DNA methylation is also involved in making ant queens and workers different.

The studies' authors noted, "We know bees use DNA methylation to execute caste programs and now have the first hints that ants may too. But even while they appear to have the same genes as bees, it is already clear that they use methylation differently, and that both species use it differently than humans."

The researchers believe that epigenetic processes such as methylation likely also contribute to the astonishing life-span differences between queens (that live more than 20 years) and workers that typically die after several months.

Myrmecology, or the study of ants, has entered the genomic era, according to these four studies' authors. Such advances in genomics will, they believe, allow scientists to ask questions related to pest management, phenotypic plasticity, evolutionary novelty, the interaction of environment and genotype in the production of adaptive phenotypes, kinship and the evolution of sociality, reproductive conflict, disease management in social environments, and other fundamental questions in development, ecology and evolutionary biology. However, the scale of integrating genome knowledge across so many species will also require "databases, new software tools, data-sharing policies and the continuation of the kind of unprecedented cooperation offered by the authors and institutions in these four studies," said Gadau and CR Smith. Perhaps scientists, by following the principles of their social study organisms, by sharing information and resources to tackle complex problems, can hope to fully resolve how ants reign as some of the most successful organisms on Earth.

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