Quick guide

Micromalthus debilis

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What is* Micromalthus*? *Micromalthus debilis* is a small beetle, the only species in the family Micromalthidae. Larvae of *M. debilis* live in rotting wood, and are an occasional pest in wooden structures, hence their colloquial name 'telephone pole beetles'. They are native to eastern North America but have been moved around the world by humans.

There are over 360,000 described species of beetles. Why does this one deserve its own Quick Guide? For two reasons. The first is its bizarre life cycle (Figure 1). Most of the year, a population of *M. debilis* consists entirely of larvae, which reproduce by giving live birth to more larvae. This is a form of parthenogenetic reproduction — all the individuals are females, and no mating occurs. But in late summer or if the habitat starts to dry out, some of the female larvae develop into pupae, which then molt into winged adult females. Other female larvae, however, do something odd: each of these females produces a single unfertilized egg, and then becomes torpid. The egg hatches into a male larva, who inserts his head into his mother's genital opening and begins to feed upon her. It takes a male about a week to devour his entire mother, after which he pupates and molts into a winged adult male.

Males eat their own mothers? Yes, it's in fact all they ever eat. Females just eat fungus-infested rotting wood.

What's up with that? No one knows. But insects that feed on nutrient-poor food like rotting wood often have endosymbiotic bacteria that synthesize nutrients that are missing from the insects' diet. These bacteria thus benefit the insects and are usually transmitted by females to their eggs. Males, however, don't transmit bacteria. Thus, as far as the bacteria are concerned, males are a 'dead-end'. That's why other maternally transmitted endosymbiotic bacteria, such as the well-studied *Wolbachia*, sometimes evolve to kill their male hosts. *Micromalthus* has maternally transmitted endosymbiotic bacteria, though little is known about them. Possibly these bacteria evolved to be non-functional in males, which may initially have had the effect of starving the male hosts and leaving more food for their sisters, helping the bacteria get into more eggs. It is conceivable that, in response to this, *Micromalthus* males evolved to be cannibalistic, and the *Micromalthus* life cycle evolved to minimize the role of males.

But the males must still be good for something, right? We're not so sure, actually. Researchers who reared *Micromalthus* in the laboratory in the 1930s reported that males were sterile. This is very surprising given how costly for mothers they are to produce — your son eats you! It's also surprising because often species that seem to be purely asexual turn out to actually be sexual. Some insects need to fly before they become fully mature and capable of mating; and males surrounded by clones of genetically identical sisters may be especially likely to evolve adaptations that ensure dispersal prior to mating. Thus, we should be cautious and say perhaps that researchers have so far failed to create laboratory conditions conducive to complete male maturation and mating, rather than say that *Micromalthus* males are sterile.

And what was the second interesting thing about* Micromalthus*? All this crazy innovation in the life cycle seems to be the only evolution *Micromalthus* ever does. The anatomy of the adults doesn't change much: morphologically, adult *Micromalthus* are pretty similar to the oldest known beetle fossils. And there doesn't seem to be much in the way of origins or extinctions of species: there is only one species in this family of beetles and there seems to have been only one species for tens of millions of years. There are many fossil *Micromalthus* in amber and all are *M. debilis* (Figure 1). This species has been evolving — or at least existing — independently of other beetles for so long that its evolutionary relationship to other beetle species remains obscure despite intensive research.

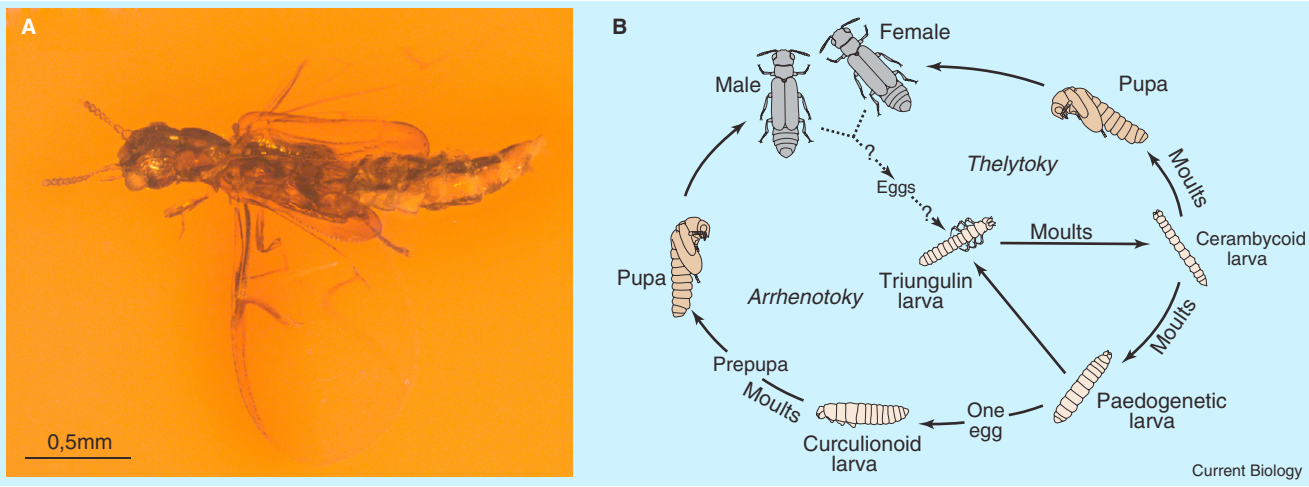

Figure 1. *Micromalthus debilis* and its life cycle.
(A) Adult *Micromalthus debilis* in Dominican amber, approx. 20 million years old. From Hörnschemeyer *et al*. (2010), photo courtesy of Karin Wolf-Schwenninger, Staatliches Museum für Naturkunde, Stuttgart, Germany. (B) The life cycle of *Micromalthus debilis*. Most reproduction consists of paedogenetic larvae giving birth to triungulin larvae. After Hörnschemeyer *et al*. (2010).

Is it fair to say that* Micromalthus *is an ancient, primitive beetle? Many of *Micromalthus'* anatomical characters are indeed primitive, in the sense of resembling the most recent ancestor it shares with other beetles, but of course its life cycle is anything but. No one thinks the ancestral beetle — or the ancestors of any other living beetles — had *Micromalthus'* bizarre genetic and developmental system. *Micromalthus* can be seen as a particularly extreme example of 'mosaic evolution' — the evolution of different characters at different rates — and of why it's probably not a good idea to call any species 'primitive' even if it looks that way superficially.

Is* Micromalthus *unique? Some species of fungus gnats and gall midges resemble *Micromalthus* in many ways: they live in rotting wood feeding on fungi and have a complex life cycle in which most reproduction consists of paedogenetic larvae giving birth to more larvae. But larvae of these species don't eat their own mothers. Some species in the recently-discovered marine phylum Loricifera turn out to have complex life cycles with paedogenic larvae and mother-eating, but it is the females that eat their mothers, males are still unknown. Male-specific maternal cannibalism seems to have been found only in *Micromalthus*. So far.

Where can I find out more?

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Primer

Covalent lipid modifications of proteins

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Attachment of lipophilic groups is a widespread modification that occurs on nearly 1,000 proteins of diverse structure and function. At least five different types of lipids can be covalently attached to proteins: fatty acids, isoprenoids, sterols, phospholipids, and glycosylphosphatidyl inositol (GPI) anchors. Proteins can contain more than one type of lipid, e.g. myristate + palmitate, palmitate + cholesterol, or farnesyl + palmitate. An important principle derived from studies of lipid-modified proteins is that not all fat is the same. Each type of lipid moiety is attached by a different lipid transferase and each modification confers distinct properties to the modified protein. The most common outcome of lipid modification is an increased affinity for membranes. However, attachment of myristoyl or prenyl groups can also promote intramolecular and intermolecular protein–protein interactions. Another key concept is reversibility. The covalent linkage between a protein and either thioester-linked palmitate or a GPI anchor can be broken by the actions of thioesterases and phospholipases, respectively. By contrast, neither myristate nor the isoprenoids farnesyl or geranylgeranyl are physically removed from a modified protein. Instead, Mother Nature has devised a clever means for some proteins to sequester these lipophilic groups within a hydrophobic cleft, effectively shielding them from the aqueous milieu. Here, I provide an overview of the structural and functional consequences for proteins containing each type of lipid modification (depicted in Figure 1).

N-myristoylation of proteins

Proteins that are destined to be covalently modified with the 14-carbon saturated fatty acid myristate generally contain the sequence Met–Gly–X–X–X–Ser/Thr at the amino terminus. In eukaryotes, 0.5–0.8% of all proteins are predicted to be N-myristoylated. Web-based algorithms are available to analyze whether a particular amino-terminal sequence is likely to be modified, e.g. http://mendel.imp.ac.at/myristate/SUPLpredictor.htm; http://web.expasy.org/myristoylator/. After removal of the initiating Met by methionine aminopeptidase, myristate is attached to the amino-terminal Gly. No other residue can substitute for Gly at the amino terminus, and mutants with a Gly-to-Ala substitution are often used as non-myristoylated, negative controls for determining the effect of N-myristoylation on a particular protein.

N-myristoylation is catalyzed by N-myristoyl transferase (NMT), a 50 kDa cytosolic enzyme that is expressed in most organisms as one or two gene products (e.g. NMT1 and NMT2 in humans). The reaction typically occurs co-translationally, and is facilitated by binding of NMT to ribosomes. However, post-translational myristoylation of proteins can occur during apoptosis, when caspase cleavage exposes a cryptic myristoylation site. In addition to the target protein, the other substrate for NMT is myristoyl-CoA. Catalysis proceeds via an ordered reaction mechanism: myristoyl CoA binds to the enzyme first, followed by the target protein to form a ternary complex. Myristate is transferred to the protein, CoA is released, and finally the myristoylated protein is released. The linkage between myristate and the protein is an amide bond, which is extremely stable. Myristate therefore remains attached to the modified protein throughout its lifetime and a pool of endogenous, non-myristoylated protein does not generally exist in cells. Detection methods for N-myristoylated proteins include mass spectrometric analysis of the purified protein, or analysis of proteins in cells labeled with radiolabeled fatty acids or with alkyne- or azide-linked fatty acids in combination with Cu(I)-catalyzed click chemistry.

One of the major functions of myristate is to assist in directing the modified protein to membranes. A central tenet, originally established by Peitzsch and McLaughlin, is that myristate alone is not sufficiently