tidomimetic library was screened to find molecules that could compete with the binding of the SMAC peptide to the Bir domain of different forms of IAP. After further chemical modification of a candidate molecule, Li *et al.* generated compound 3 that, like SMAC, has a high avidity for different forms of IAP including X-chromosome encoded IAP (XIAP), cellular IAP-1, and cellular IAP-2. Compound 3 blocked the interaction of XIAP with active caspase 9. In previous work, SMAC was shown to act synergistically with a death receptor called TRAIL to induce tumor-selective apoptosis (*10*). Impressively, treatment of glioblastoma cells with a combination of the ligand for the TRAIL receptor and compound 3 resulted in apoptosis of the tumor cells, whereas normal cells were not harmed. Li *et al.* (*4*) also demonstrated that compound 3 could potentiate apoptosis in cells treated with TNF-α (tumor necrosis factor–α) without activation of the nuclear transcription factor NF-κB. Because TNF-α mediates host responses in acute and chronic inflammatory conditions, these results suggest that compound 3 may have potential for treating inflammatory diseases (*11*). Although the efficacy of compound 3 was not evaluated in vivo, the authors are using compound 3 as a lead structure for the refinement of future therapeutic compounds with better pharmacological properties.

Peptidomimetics are only now emerging as a powerful solution for overcoming the limitations imposed by the physical properties of native peptides. Walensky *et al.* (*3*) and Li *et al.* (*4*) demonstrate provocative proof-of-concept approaches to the design of peptidomimetics that may have a decided impact on future therapeutics that target disease by modulating specific protein-protein interactions.

References

1. C. A. Schmitt, *Nature Rev. Cancer* **3**, 286 (2003).
2. J. C. Reed, *Cancer Cell* **3**, 17 (2003).
3. L. D. Walensky *et al.*, *Science* **305**, 1466 (2004).
4. L. Li *et al.*, *Science* **305**, 1471 (2004).
5. J. A. Patch, A. E. Barron, *Curr. Opin. Chem. Biol.* **6**, 872 (2002).
6. N. N. Danial, S. J. Korsmeyer, *Cell* **116**, 205 (2004).
7. V. A. Levin, *J. Med. Chem.* **23**, 682 (1980).
8. J. S. Wadia, R. V. Stan, S. F. Dowdy, *Nature Med.* **10**, 310 (2004).
9. G. S. Salvesen, C. S. Duckett, *Nature Rev. Mol. Cell Biol.* **3**, 401 (2002).
10. S. Fulda *et al.*, *Nature Med.* **8**, 808 (2002).
11. R. M. Pope, *Nature Rev. Immunol.* **2**, 527 (2002).

ECOLOGY

Spite Among Siblings

Andy Gardner and Stuart A. West

> *"Sometimes I work my brother over…I make him squirm, I've made him cry. He doesn't know how I do it. I'm smarter than he is. I don't want to do it. It makes me sick."*
>
> —John Steinbeck, *East of Eden*

Although sibling conflict abounds in the literary world—from the Bible to Steinbeck—it also features prominently in the real world. Recent research from the laboratories of Strand and Hardy (*1–3*) on sibling conflict among parasitic wasps sheds light on that most puzzling of social behaviors—spite.

Social behaviors are those that affect the fitness of multiple individuals (*4*). The social behavior that has provoked the most interest is altruism, in which an action incurs a direct fitness cost for the actor and provides a benefit for the actor's social partners. Hamilton showed that altruism is favored when individuals are helping their close relatives, and hence still passing on their genes to the next generation, albeit indirectly. A pleasingly simple and elegant method for quantifying this idea of kin selection is Hamilton's rule, which states that an altruistic behavior will be favored if the cost to the actor (C) is outweighed by the product of the benefit (B) and the genetic relatedness (R) to the social partners, resulting in $RB > C$ (*5*). Hamilton, however, also pointed out that his rule has a more sinister interpretation (*6*). His rule can be twisted to predict that spiteful behavior—which hurts both the actor and the recipient—may be favored when there is sufficient negative relatedness between the social partners.

Negative relatedness may seem like a bizarre concept, but it simply means that the recipient of a particular behavior is less related than other competitors to the actor (*6–8*). It has generally been assumed that spite is unlikely to be an important evolutionary force because the conditions required to obtain significant negative relatedness are too restrictive. Nonetheless, theoretical interest in spiteful behavior rumbles on. It is clear that spite can evolve given the right conditions: (i) when there is strong competition for local resources among social partners and (ii) when individuals have the capacity to recognize (and refrain from being spiteful to) their close kin (*6*, *7*). In recent work, Strand, Hardy, and their colleagues (*1–3*) investigated a biological system that appears to satisfy both conditions—the sterile soldier caste of polyembryonic parasitic wasps.

These small wasps deposit their eggs into the eggs of moths, and the wasp larvae develop within the moth caterpillars (see the figure). A single wasp egg proliferates asexually (clonally) to produce multiple larvae such that, when the host contains larvae from several eggs, the limited food resources within the caterpillar will permit only a fraction of those larvae to complete development and emerge as adults. Thus, there is intense competition for resources among the larvae within the host, satisfying the first condition for spite.

The majority of the wasp larvae develop normally, whereas others develop precociously to form a soldier caste that differs morphologically and behaviorally from normal wasp siblings (see the figure). Donnell *et al.* (*1*) demonstrate that the mechanism underlying caste formation in the clonally developing wasp population involves asymmetric inheritance of germ cells. Embryos that develop into normal larvae inherit the germ line, whereas embryos that develop into soldiers do not, making them obligately sterile—the cost of developing as a soldier. Upon hatching, soldiers distribute themselves throughout the host and launch aggressive attacks on other larvae, murdering their unfortunate victims. This has the potential to be spite and not altruism because the benefits of reduced competition accrue to all larvae in the host and not preferentially to closer relatives (*7*).

This would be an adaptive spiteful behavior if soldiers preferentially attacked the larvae they are least related to in the caterpillar, which requires kin recognition, the second condition for spite (*7*). In a new study, Giron and colleagues (*2*, *3*) demonstrate that soldiers are indeed capable of recognizing their kin, and the investigators then elucidate the mechanism. First, they varied kinship by introducing either full (but not genetically identical) sisters and brothers or unrelated larvae into a host caterpillar containing a developing female brood of wasp larvae (*2*). The introduced larvae were labeled with a fluorescent tracer, and attack rates were assessed by measuring how many of the resident soldiers ingested labeled larval tissue (see the figure). As predicted, the researchers found a strong negative correlation between attack rates and kinship.

The authors are in the School of Biological Sciences, University of Edinburgh, Edinburgh EH9 3JT, UK. E-mail: andy.gardner@ed.ac.uk

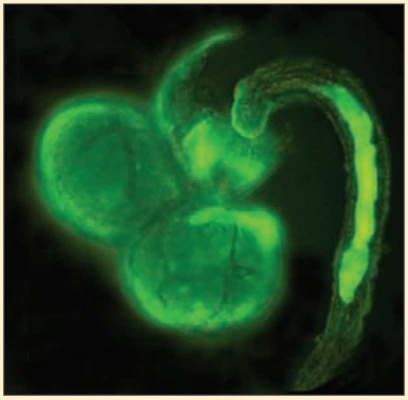
A **Life cycle of a polyembryonic wasp**

A female wasp deposits her eggs into a caterpillar host egg.

The wasp larvae undergo clonal proliferation within the caterpillar host.

Larvae develop either precociously into soldiers (left) or normally (right).

B **Caught in the spiteful act**



A soldier wasp larva ingests its fluorescently labeled victim.

In a companion study (*3*), the investigators shed light on the mechanism of this kin recognition faculty. They reveal that the key element is the extraembryonic membrane surrounding each larva during its development in the caterpillar host. They show that attack rates correlated negatively with kinship when the membrane was present, but not when the membrane was removed. In addition, by transplanting membranes between larvae they were able to fool the soldiers, whose attack rates correlated negatively with the kinship of the membrane donor but not with the larva encased inside. Mechanisms of kin recognition are unstable because deceptive variants arise that signal strong kinship to everyone; such variants can become common. However, the importance of the membrane in protecting larvae from host immune attack means that rare variants are intrinsically favored and that common variants are disadvantageous, providing a robust, honest signal of kinship. This may be true for many endoparasites, rendering such species masters of kin recognition.

One potentially puzzling result is that manipulation of resource availability by starving the host caterpillars did not influence the level of aggression exhibited by the wasp soldier caste (*2*). Possibly because competition is always local, resource availability does not influence how soldiers vary their relatedness-dependent behavior. Alternatively, soldier larvae may not be able to assess the intensity of competition for resources, either because doing so is difficult or because natural variation in competition is negligible and there has been no need for this faculty to evolve. Future work on how local competition for resources relates to soldier aggression could benefit from explicit theoretical modeling, as well as alternative methods for varying the scale of competition such as selection experiments (*9*) or comparative studies across species and populations. Nonetheless, the existence of an aggressive soldier caste among parasitic wasps provides evidence that spite does exist in the real world, as Hamilton predicted it would.

References

1. D. Donnell, L. S. Corley, G. Chen, M. R. Strand. *Proc. Natl. Acad. Sci. U.S.A.* **101**, 10095 (2004).
2. D. Giron, D. W. Dunn, I. C. W. Hardy, M. R. Strand, *Nature* **430**, 676 (2004).
3. D. Giron, M. R. Strand, *Proc. R. Soc. B (Suppl.) Biol. Lett.*, 17 June 2004 (10.1098/rsb1.2004.0205).
4. S. A. Frank, *Foundations of Social Evolution* (Princeton Univ. Press, Princeton, NJ, 1998).
5. W. D. Hamilton, *Am. Nat.* **97**, 354 (1963).
6. W. D. Hamilton, *Nature* **228**, 1218 (1970).
7. A. Gardner, S. A. West, *J. Evol. Biol.*, 22 July 2004 (10.1111/j.1420-9101.2004.00775).
8. A. Grafen, *Oxford Surv. Evol. Biol.* **2**, 28 (1985).
9. A. S. Griffin, S. A. West, A. Buckling, *Nature* **430**, 1024 (2004).

PLANETARY SCIENCE

Looking into the Giant Planets

Jonathan J. Fortney

Enhanced online at www.sciencemag.org/cgi/content/full/305/5689/1414

Images of Jupiter and Saturn from telescopes and space probes only show the outermost layers of these giant planets. Learning about their interiors, which consist mostly of hydrogen (H) and helium (He) and make up over 90% of the planetary mass in the solar system, is more challenging. Recent model studies (*1*–*3*) show how new measurements from the Cassini spacecraft—now in orbit around Saturn—could lead to a better understanding of the interior of Saturn and, by extension, all giant planets.

The most important input into giant planet models is the equation of state—that is, the relation between pressure and density—of hydrogen. Uncertainties in the equation of state translate directly into uncertainties in the estimated size of the "heavy element" (elements more massive than He) cores of the giant planets and the abundances of elements in their hydrogen-rich envelopes (*1*). Two groups have measured the shock-induced compressibility of deuterium, a heavy isotope of H, but there is a 50% discrepancy between their data sets (*4*, *5*). As Saumon and Guillot (*1*) show in a recent paper in *The Astrophysical Journal*, this uncertainty profoundly affects inferences about the composition of the planets and the sizes of their cores. These quantities must be known before we can understand the process of giant planet formation and properties of the early solar system.

The authors created static models of Jupiter and Saturn that match all available constraints, including mass, radius, oblateness, rotation period, atmospheric temperature, and gravitational moments for each planet. They also used a wide range of possible equations of state for H to allow for the disparate experimental data sets. According to their model, Jupiter's core is 0 to 11 Earth masses. Saturn's core is likely larger, between 9 and 22 Earth masses. (For comparison, Jupiter is 317.8 Earth masses and Saturn 95.2 Earth masses.) Overall, Jupiter is enriched in heavy elements by a factor of 1.5 to 6 relative to the Sun, and Saturn by a factor of 6 to 14. The most striking of these results is that we cannot be sure whether Jupiter has a core.

The greatest uncertainty in the structure of Jupiter comes from unsatisfactory understanding of liquid metallic H at Mbar pressures. In contrast, for Saturn, poor knowledge of its gravitational moments, which describe how the planet's mass responds to its rotation, is the main obstacle. Gravitational moments are determined by measuring small accelerations of a spacecraft as it passes near a planet. During Cassini's 4-year mission, error bars on the low-degree gravitational mo-

---

The author is with the Planetary Systems Branch, NASA Ames Research Center, Moffett Field, CA 94035, USA. E-mail: jfortney@arc.nasa.gov

PHOTOS: M. STRAND, D. GIRON, J. JOHNSON