a larger proportion of scientists pursue the same anointed path.

These cautions, however, do not apply to all that more successful impact prediction portends. The ability to automatically extract scientific claims from research articles and reason across them should lead to the prediction or computational generation of promising new hypotheses. It likely will also expose common assumptions and practices of science to scrutiny and explicit evaluation (10). In this way, citation prediction represents one step on the path to creating algorithmic or robot “scientists” (11) that are more creative, risky, persistent, and wide-reading than ourselves (12). By enabling scientists to consider not only the most fruitful hypothesis but also the most fruitful algorithm for generating hypotheses, future prediction methods would augment scientific ability, increase productivity, and multiply returns from science for society.

References

Small RNA—the Secret of Noble Rot

David Baulcombe

Benjamin Franklin should have included infectious disease as a third certainty of life alongside death and taxes. We will always be plagued by pests and pathogens because they generally have shorter life cycles than their hosts, allowing them to evolve rapidly to avoid host defenses. The use of antibiotics, for example, may select for drug-resistant strains of bacteria and, in agriculture, the widespread cultivation of a disease-resistant crop is often followed by the appearance of resistance-breaking strains of the pathogen.

Whenever a host acquires a novel defense, the pest will, eventually, evolve a corresponding counter-defense system. On page 118 of this issue, Weiberg et al. (1) describe a strategy in which a fungal parasite uses RNA to block a host’s defense system.

In plants, the evolutionary arms race involves a set of host receptors that recognize components on the surface of the pathogen (2). These pathogen-associated molecular patterns (PAMPs) include, for example, flagellar proteins of Gram-negative bacteria and chitin in the cell wall of fungi. Triggering these receptors leads to intracellular signaling within and biochemical changes in and around the infected cell such that the invading pathogen is suppressed. Counter-defense then involves pathogen-derived effectors that either block the initial recognition on the surface of the host cell, or are transferred into the infected cell where they suppress the signaling pathways or biochemical changes. However, the arms race does not end there. The plant has a second set of receptors that recognize the effectors and trigger additional layers of defense. The pathogen, correspondingly, has additional counter-defense systems (2).

Most of the characterized pathogen effectors are proteins, but Weiberg et al. (1) demonstrate that we can add RNA to the list of effectors with trans-kingdom activity. The new research involves Botrytis cinerea—a necrotrophic fungal pathogen that infects many plant species, including tomato and strawberry, on which it causes gray mold.

Fungal sRNAs affect disease progression. In the absence of fungal sRNA (left) the pathogen-associated molecular pattern (PAMP) recognition system ensures that the fungus is suppressed and disease is weak. By contrast, in their presence (right), the host defense system is blocked, and the disease progresses rapidly.

Most notably, it is the noble rot that is so important for the production of exquisite dessert wines.

The new findings involve a class of small RNAs (sRNAs) that includes microRNAs and small interfering RNAs. These sRNAs are typically 20 to 24 nucleotides in length and they guide Argonaute (AGO) nucleases by Watson-Crick base pairing to coding or noncoding RNAs in either the nucleus or cytoplasm so that the targeted RNAs accumulate at a lower level than they would in the absence of the sRNA (3).

There are more than 800 fungal sRNAs that are induced when Botrytis is infecting plant cells and, of these, 73 were predicted from their sequence to silence host mRNAs, including some that have a role in immunity (1). This silencing potential could be due to
chance similarity of sequence motifs in the fungal and host-plant genomes and therefore have no functional importance. However, expression of the putative target genes was reduced in Botrytis-infected plants and, if their expression was blocked experimentally, the plants became hypersusceptible to the fungus (1). It is likely, therefore, that fungal sRNA silences the expression of host defense genes so that the plant cell is less able to resist the fungus attack.

Further support for this idea comes from the findings that fungal sRNAs bind to a plant AGO in the infected cells, and from the reduced fungal susceptibility of AGO mutant plants. The fungal sRNA is likely to be processed from a long RNA precursor into an sRNA before it is translocated into the plant cell (see the figure (1)) because knockout of the fungal Dicer enzyme responsible for sRNA biogenesis also led to reduced fungal susceptibility. Reduced amounts of the plant Dicer, by contrast, had no effect.

Of the 73 Botrytis sRNAs with the potential to silence plant genes in the infected plant cell, 52 were derived from mobile DNA elements of the fungal genome. This finding is not surprising—RNA silencing is well established as a defense system and many organisms use sRNAs to silence parasitic transposable elements and thereby protect their genomes (even parasites have parasites). However, the association of transposon sRNA with the suppression of host defenses may have important implications for the host pathogen arms race. Transposable elements are normally the most labile features in eukaryotic genomes (4). Perhaps a DNA transposition event triggers novel patterns of sRNA in the fungus of which, by chance, some can silence additional host defense genes and thereby increase the virulence or fitness of the pathogen. Such a system would further enhance the adaptation of a short-life cycle pathogen to the host defense systems.

The finding of Weiberg et al. with Botrytis is not the first report of RNA traffic between plants and their pathogenic fungi. Other recent work reveals how RNAs also move from plants into fungal cells, where they silence fungal genes (5). Until now, this “host-induced gene silencing” has been used to silence different fungal genes to determine whether they affect the disease-causing ability of the fungus. It remains to be tested whether endogenous plant sRNAs are also moved into the fungus. However, given the abundance of sRNAs in plant cells, it would be surprising if they did not both enter the fungus and silence complementary RNA.

There is clearly much more to be discovered about RNA-based communication between plants and pathogenic fungi. More information is needed about the transport mechanism and whether it applies to biotrophic pathogens (5) which form a long-term feeding relationship with their host, as well as necrotrophic pathogens. Another question is whether this transfer of RNA between plants and fungi is related to other “social RNA” in animals that may affect interactions between cells and organisms (6). In addition, the possibility should be explored that another layer exists in the arms race in which the plant blocks the effects of the transferred RNA, and whether the information can be exploited to develop management or control strategies for plant disease. It would be very pleasing if the answers to these questions lead to Chateau d’Yquem in the price range of a graduate student.

References

CHEMISTRY

Turn the Molecule This Way for a Faster Reaction

Michael C. Heaven

O bserved under normal conditions, chemical reaction rates and the relative ratios of products formed are highly averaged properties. These values sum over elementary events that sample wide ranges of collision energy, internal energies of the reactants, relative orientations, and collision strengths (e.g., glancing to head-on). It has been a long-standing challenge to look inside this statistical averaging to discern the intimate details of reaction dynamics (1). Many techniques have been developed that permit partial selection and control of the physical states of reactants before their encounters. As the averaging is stripped away, a deeper understanding of chemical reaction mechanisms begins to emerge. On page 98 of this issue, Chang et al. (2) describe a new approach to studies of bimolecular reactions using conformer-selected molecules and a target of ultracold atoms.

To demonstrate the capabilities of their method, Chang et al. have shown that two similar conformers of 3-aminophenol (cis- and trans-3AP, see the figure) have substantially different cross sections—the probability that they will react—with singly charged calcium ions (Ca+). Three levels of control were exercised in these experiments. First, a beam of 3AP molecules was formed by expanding the vapor (mixed with a high pressure of inert neon buffer gas) into a vacuum. This process cooled the vibrational and rotational motions of the molecules to a temperature near 1 K, which prevented interconversion between the conformers and compressed the velocity distribution to a narrow range. Hence, for this reagent, the translational and internal energies were sharply defined.

Spatial separation of the conformers, the second level of control, was accomplished by having the molecular beam traverse a region where a strong electric field bent the trajectories (3). The field exerted a force on the molecules through interaction with the molecular electric dipole moment. A key feature of this experiment is that the two conformers have markedly different dipole moments (4). The cis conformer, which has the larger dipole, deflected more.

Manipulation of molecules with molecular beams and field deflection is challenging, but the techniques are established. It is the third level of control applied in the experi-