

## Introduction

# Pathogens and hosts: The dance is the same, the couples are different

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History was made December 9–11, 1999, at the Beckman Center in Irvine, CA with the National Academy of Sciences colloquium “Virulence and Defense in Host–Pathogen Interactions: Common Features Between Plants and Animals.” This was the first colloquium dedicated to the discussion of virulence mechanisms shared by plant and animal pathogens and defense mechanisms shared by plants and animals. It has become clear from the commonality in microbial virulence mechanisms and the occurrence of similar innate resistance systems in animals and plants that all of these mechanisms have an ancient and intertwined history. It also is becoming increasingly evident that susceptibility or resistance to disease involves subtle and highly specific exchanges of molecular signals between pathogens and their hosts and that understanding them can provide new approaches to controlling diseases.

The colloquium provided a remarkable closure to a century that began with only a primitive understanding of the microorganisms that cause disease in plants and animals. Indeed, it was only because of breakthroughs of the past decade in understanding the molecular biology of microbial virulence and eukaryote defense that the need to bring the plant and animal fields together became apparent. In a meeting highlight, David Baltimore emphasized in his closing keynote lecture that lessons from the study of microbiology and microbial pathogens continue to greatly influence science. The animal systems discussed during the colloquium ranged from humans to insects and an array of microbial pathogens. Several plant–pathogen systems were considered, including those involving the genetic model plant, *Arabidopsis thaliana*. The genetic tractability of this plant, particularly its amenability for efficient mutant screens, offers experimental advantages not present in many other eukaryote model systems.

A feature of pathogenic microorganisms that attracted considerable attention was the frequent use of conserved type III secretion systems by both plant and animal bacterial pathogens to introduce virulence determinants into host cells. Indeed, some of the delivered effector molecules are also functionally similar in plant and animal cells. For example, some pathogen effector molecules block animal and plant defense reactions or alter host cell structure and function to accommodate pathogen development. Pathogen effector molecules also often have interesting and unique structures, leading to the suspicion that they have resulted from long and intense evolution. There is currently great interest in determining the precise localization and functions of these molecules in animal and plant cells because such information opens the door for therapy. The acquisition and evolution of these molecules by microbial pathogens is also a topic receiving considerable attention.

Although pathogen effector molecules generally are considered to increase virulence or otherwise abet development of a pathogen in its host, plants and animals have evolved surveillance systems to co-opt microbial effectors and use them as cues

for initiation of defense mechanisms. This long-standing evolutionary cat and mouse game is being rapidly elucidated, particularly in plant–pathogen systems. Pathogens appear to have evolved functionally overlapping and redundant effector virulence molecules to confound host surveillance, and plants have responded by directing surveillance mechanisms to the particular subcellular sites of effector molecule virulence activity.

The common features of inducible defense used by plants and animals are, in some ways, even more surprising than the pathogen side. For example, active oxygen species and nitric oxide are shared signaling mechanisms, as are lipid systems involving phospholipase activations. Furthermore, it recently has also become clear that leucine-rich repeat (LRR) proteins (such as Toll in *Drosophila* and so-called “disease resistance gene” proteins in plants) are conserved in active defense of vertebrates, insects, and plants, and these systems all show features of the well-studied vertebrate NF- $\kappa$ B pathway. For animal systems, attention was focused on innate immunity, which is a rapid defense response independent from the well-known acquired immunity involving circulating antibodies. In insects, the corresponding pathogen defense system is called humoral immunity and involves the ultimate production of antimicrobial peptides. For plant systems, the equivalent mechanism of defense is the hypersensitive response, again culminating with the release of pathogen-antagonistic molecules. Structural studies on the conserved LRR proteins discussed at the colloquium promise to greatly influence our view of disease control, including the eventual design of custom LRR proteins to target new pathogen effector ligands.

Plant resistance phenotypes expressed as a hypersensitive response typically follow a “gene-for-gene” model first described genetically by H. H. Flor in the late 1940s. According to this model, that probably occurs in most eukaryotes, plant genes coding for resistance surveillance proteins are matched by complementary genes in the pathogen that lead to production of the recognized effector ligands. As noted earlier, these pathogen effectors are generally, if not always, virulence determinants—the plant strategy is to impose a penalty on the pathogen if it mutates to lose the effector ligand.

At the Irvine colloquium, there was considerable discussion of pathogen genes that biochemically interact with genes in vertebrates, insects, and plants. In many cases, pathogen effectors (often introduced by a type III secretion system) are thought to interact either at the host cell surface or at specific subcellular locations within host cells. In vertebrates and insects, as well as plants, these initial recognition events trigger

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This paper is the introduction to the following papers, which were presented at the National Academy of Sciences colloquium “Virulence and Defense in Host–Pathogen Interactions: Common Features Between Plants and Animals,” held December 9–11, 1999, at the Arnold and Mabel Beckman Center in Irvine, CA.

cascades of signal transduction events, eventually leading to the activation of genes whose products antagonize pathogen development. It was clear at the colloquium that the advent of microarray gene expression technologies will greatly assist in inventorying these genes and those encoding microbial effec-

tor functions. Such technical advances and the conceptual realization of evolutionary commonalities have put scientists interested in diseases of plants and animals on a solid footing for future manipulation of the respective defense responses to minimize the threat of diseases.