

Statement of Research

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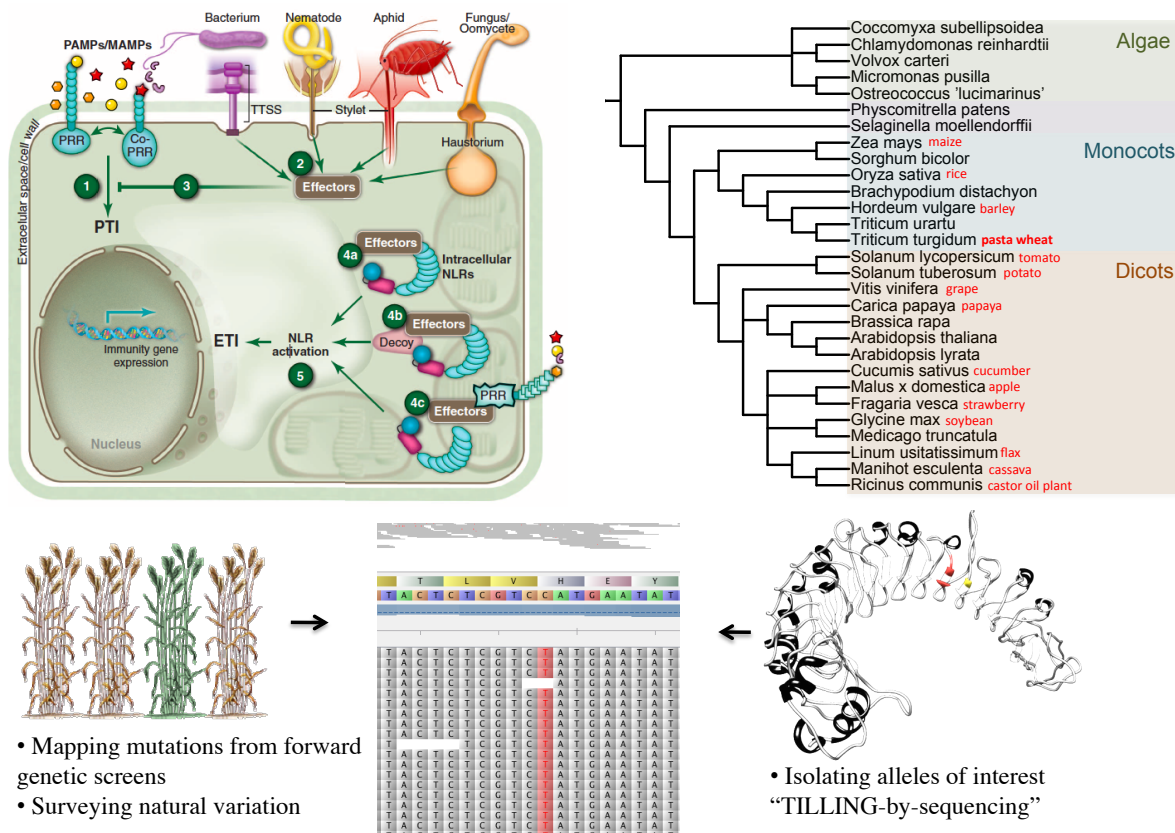
My research interests include comparative genomics, plant cell biology and plant-microbe interactions. Specifically, I want to study fundamental principles of plant innate immunity and provide new approaches for engineering robust disease resistance. In my PhD work, I demonstrated the biochemical basis for pathogen recognition by an *Arabidopsis* immune receptor. During my post-doc, I adapted exome-capture technology to sequence 1,000 mutant wheat lines, making this important crop species highly accessible to basic research. I will combine my expertise in *Arabidopsis* immunity and wheat genomics to establish an independent research program in plant comparative genomics and innate immunity of cereals.

Mechanisms of pathogen recognition are common to organisms from different kingdoms. In both plants and animals, the first level of immune system relies on recognition of conserved pathogen-derived molecules, while the second tier of immunity consists of more flexible immune receptors: antibody-based adaptive immunity in animals and disease resistance gene (*R-gene*)-mediated immunity in plants. Plant *R-genes* share structural similarity with mammalian NOD-like receptors; both classes are intracellular receptors capable of pathogen recognition and initiation of immune responses.

In the coming years it will be very important to address several key questions about plant immunity. What is the full recognition potential of any given *R-gene*: is it possible to find or create an *R-gene* that would recognize any chosen protein associated with a pathogen? How does the recognition of pathogen effectors leads to R-protein activation? Finally, what are the molecular functions of all downstream signaling components and are they conserved across plant species? The program outlined below is aimed to address these topics.

I. Selecting for novel recognition specificities in plant immune receptors: An immune system relies on maintaining a repertoire of genetically diverse receptors and on selecting beneficial recognition specificities under the disease pressure. There are two methods to explore such genetic diversity in the lab: i) by examining the natural variation in different species and varieties ii) by screening against the induced genetic diversity created with known mutagens. I will use the exome capture platform that I developed as a postdoc to discover *R-gene* diversity in natural wheat cultivars and mutant collections. I will perform comparative genomic analyses in plant pathogens and identify conserved effectors in the recently sequenced genomes of emerging wheat rust strains. These core effectors will be screened against the library of *R-gene* variants to identify new specificities that can be deployed to control the emerging threats. The long-term goal of this part of the program is establishing directed-evolution approaches for engineering novel recognition specificities in plant immune receptors. In my PhD work, I demonstrated that it is possible to apply rational design to alter recognition specificity of a plant immune receptor using structural modeling and information from natural diversity. I want to develop this strategy further and apply this approach to wheat.

II. Discovering new networks in plant innate immunity: Most of the disease resistance studies have been done in *Arabidopsis* and little is known about immune networks in grasses. In 2012-2013, I conducted a forward genetic screen on mutant wheat population and identified lines with increased disease resistance or increased disease susceptibility against stripe rust, one of the



most devastating wheat pathogens. I already applied exome-capture and next-generation sequencing technologies to identify mutations present in these lines and assembled a short list of candidate genes. I predict that some lines will provide new recognition specificities, while others will be a result of auto-activated immune responses and will provide insights to plant immunity in wheat and other grasses. In the long term, I will focus on molecular characterization of these mutants and the mechanisms underlying defense responses in wheat.

III. Understanding evolution of plant disease resistance: Currently, there are 28 plant genomes available for comparative analyses. I scanned these genomes for plant-immunity networks. In wheat, I discovered several novel fusions between domains previously associated with immune responses. These protein fusions are also present in several other grass species, but not in other plant clades. My comparative genomic analyses revealed that wheat contains many but not all of the plant innate immunity genes previously described in *Arabidopsis*. Working with wheat and *Arabidopsis*, I will address a broader topic of evolution of disease resistance mechanisms, specifically looking at the differences between dicots and monocots. Currently, very little is known about plant immunity in monocots and it is not clear how much of our understanding of the *Arabidopsis* immunity will be applicable to grasses. I will continue to use comparative genomic approaches to elucidate evolution of disease resistance in plants.

In summary, I propose to study plant innate immunity focusing on wheat, a grass easily grown in the laboratory and with immediate potential for translational research. My laboratory will build upon my expertise in *Arabidopsis* and wheat and explore directed evolution, rational design and comparative genomics approaches to study evolution and mechanisms of plant innate immunity.