A plant immune receptor: It takes four to tango

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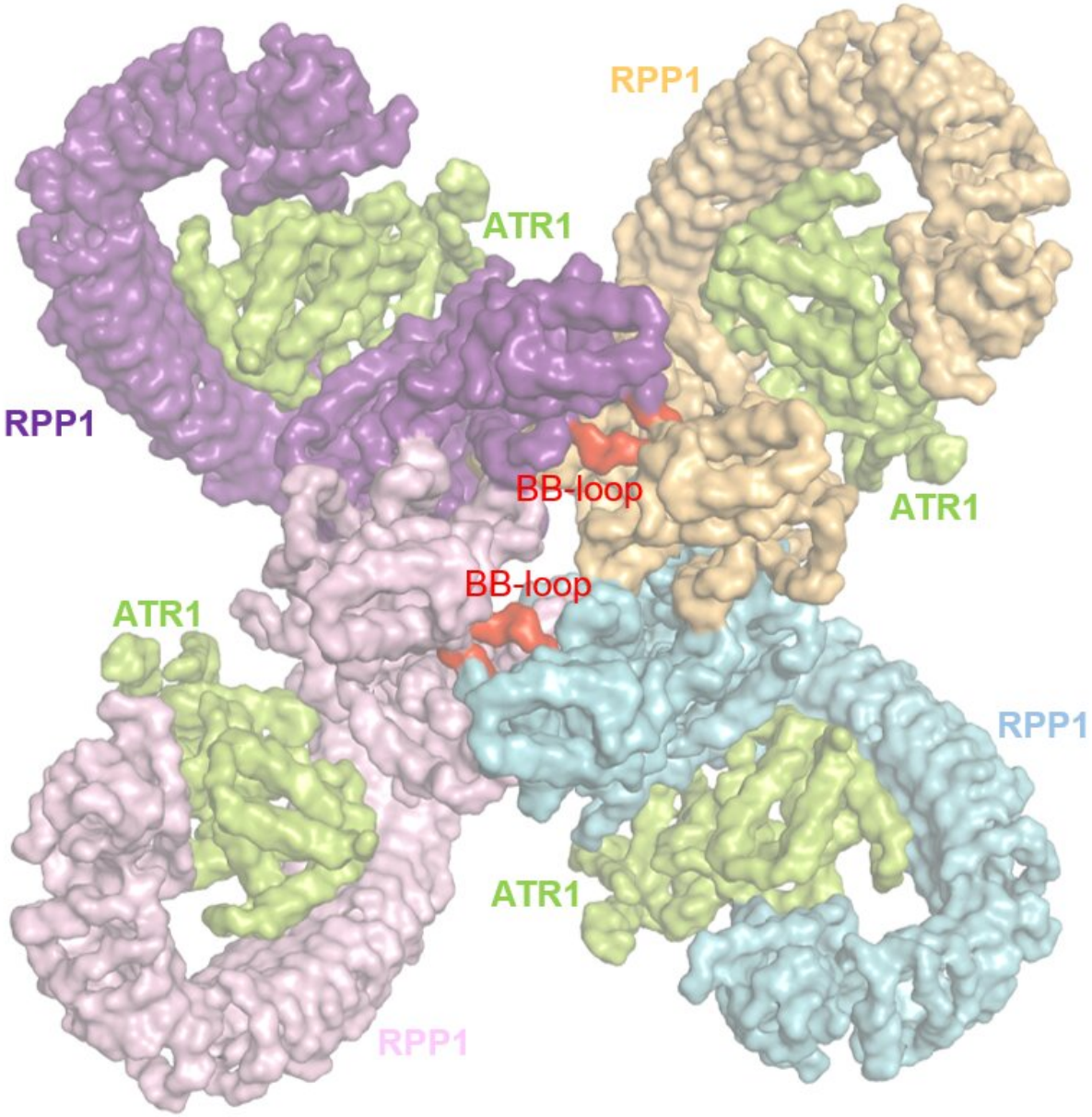

Tetrameric assembly of the RPP1 resistosome shown from the surface. The four RPP1 monomers are labeled and shown in different colors: ATR1 is shown in green; BB-loops that mediate formation of the asymmetric RPP1 TIR dimers are labeled and shown in red. Credit: Jijie Chai

A collaborative study on a plant intracellular immune receptor from researchers at the Max Planck Institute for Plant Breeding Research (MPIPZ) not only shows how an important resistance protein is activated during pathogen infection but also reveals some common operational principles with immunity proteins from humans.

Although separated by millions of years of evolution, plants and animals have independently alighted upon similar innate immune strategies to protect themselves against microbial infection. In both kingdoms of life, immune receptors called nucleotide-binding/leucine-rich-repeat (NLR) proteins form an important layer of defense inside cells against pathogen attack. NLRs are complex devices made up of several modules that recognize molecules from invading microbes termed effectors, and then locally activate resistance and cell death pathways to limit infection. Based on distinct structural and signaling features, plant NLRs are divided into two main classes: those that contain coiled-coiled (CC) modules (CNL proteins) and those that harbor Toll/interleukin-1 receptor/resistance (TIR) modules (TNL proteins). In a recent study, MPIPZ researchers and Humboldt Professor Jijie Chai and his team succeeded for the first time in piecing together the sequence of molecular events that convert an inactive TNL-type plant immune receptor into an active 'resistosome' complex that mediates host cell death.

Chai, who is also affiliated with the University of Cologne, joined forces with research group leader Jane Parker and MPIPZ director Paul

Schulze-Lefert to determine the structural and biochemical features underlying activation of the Recognition of Peronospora parasitica 1 (RPP1) TNL-type NLR receptor, which protects the model plant Arabidopsis thaliana from infection by the oomycete pathogen Hyaloperonospora arabidopsidis (Hpa). To understand at a molecular level how RPP1 shields plants from Hpa infection, Chai, Schulze-Lefert, Parker and colleagues expressed RPP1 together with a recognized Hpa effector ATR1 protein in insect cells, a system that allows high levels of protein expression. The ATR1-activated RPP1 receptor is an enzyme that breaks down nicotinamide adenine dinucleotide (NAD+), which is important for defense signaling.

By isolating RPP1-ATR1 oligomeric complexes and subjecting them to cryo-electron microscopy, the authors have answered two outstanding questions in NLR biology: how direct effector binding induces the conformational activation of an NLR receptor, and how organization of the TNL receptor oligomer (in this case a tetramer composed of four tightly-packed receptor molecules) creates a unique surface within a portion of the receptor, which is necessary for cleaving NAD+ to initiate defense signaling. Specifically, the tetramerization of RPP1 induced by ATR1 at one end of the receptor complex forces—at the opposite end—the four TIR modules to form two asymmetric TIR pairs, which are the sites of NAD+ breakdown. Thus, the RPP1 resistosome functions as a 'holoenzyme," the active form of an enzyme for NAD cleavage.

Strikingly, findings from the groups of Eva Nogales and Brian Staskawicz at the University of California, Berkeley, on another TNL-type NLR, Roq1 from the tobacco relative Nicotiana benthamiana, also show that TNL activation involves direct effector recognition and adoption of a similar tetrameric structure. The effector recognized by Roq1 is produced by a bacterial pathogen and the activated Roq1 receptor complex provides resistance to bacterial infection. Thus, the

discoveries of the MPIPZ researchers seem to have a broad relevance for understanding how these critical plant immune molecules protect their hosts from infection. More generally, the oligomeric configurations adopted by active RPP1 and Roq1 resemble induced oligomeric scaffolds of other plant and mammalian NLR receptor proteins, including human receptors of the innate immune system. This suggests that these receptors rely on a common structural principle to initiate intracellular immune signaling and cell death across different kingdoms of life.

The study is published in *Science*.

More information: Direct pathogen-induced assembly of an NLR immune receptor complex to form a holoenzyme *Science*, science.sciencemag.org/cgi/doi … 1126/science.abe3069

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