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Plant immunity research in China

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Background

Throughout history, humans have battled with plant diseases since the beginning of agricultural civilization. In ancient cultures, people appealed to gods for bountiful harvests. It wasn't until the late blight epidemic in Ireland in 1845 that had led significant discoveries pertaining to the famine and gave rise to plant pathology. Miles J. Berkeley and Anton de Bary's experiments, which transferred pathogen spores to healthy plants, demonstrated that plants became sick due to pathogen infection, establishing that pathogen infection causes disease. These findings underpinned the foundation for modern plant pathology. A crucial breakthrough was Harold Flor's famous 'gene-for-gene' hypothesis in the 1970s (Flor 1971). The concept of 'plant innate immunity' emerged, advancing the field substantially over the last three decades. Along with the fast development of plant immunity research worldwide, the Chinese community has also made significant contributions in the last two decades. In China, the exact time for the concept of 'plant pathology' established is difficult to verify textually, but the teaching of plant pathology can be traced back to the year 1910, and the first Department of Plant Pathology and Pests was established in 1921, the time that Southeast University offered plant pathology classes for students. The history of plant pathology in China is relatively short, spanning just over a century, but the Chinese community has become a significant player in the field. In this special issue, we provide a brief overview of the Chinese community's contributions to plant pathology/immunity from a century-long perspective.

Early concept of plant immunity

The term 'plant immunity' first appeared in a Chinese journal in 1954, where МеННиКОВ, a Soviet Union plant pathologist, proposed the concept of 'active immunity', in which he described that plants could actively suppress pathogen infection by invoking their immunity. In 1958, Qiyi Shen and the Soviet Union scientists began teaching plant immunity at China Agricultural University (formerly Beijing Agricultural University), marking the first time this concept was conveyed to students in China. The concept of 'plant immunity' was largely adopted from vertebrate adaptive immunity. It was known that some less virulent pathogen pretreatment can enhance the plant disease resistance to virulent pathogens. Later, it was known as 'induced immunity'. As an example, the immunized plant was achieved by Zatlin's laboratory in Connell biotechnology institute, who expressed a tobacco mosaic virus (TMV) 54kD protein in tobacco, and demonstrated that the transgenic plants were not only resistant to TMV but also to the closely related viruses (Golemboski et al. 1990). Similar publications were translated and commented on by many Chinese scientists in domestic journals in the early 1990s. Heretofore, the concept of 'plant immunity' has become well-established in the Chinese plant pathology research community.

The booming of 'plant immunity' starts from 1990. Although 'gene-for-gene' hypothesis was proposed in 1970s, the concept could only be accessed around 1991 in domestic journals. The earliest article was a direct translation from Pierre J G M de Wit's review or book in 1994 by Shuping Zhang and Xun Pan, where the concepts of the 'avirulence gene' and 'hypersensitive response (HR)'

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were likely introduced for the first time. Following the fast development of gene cloning techniques, many avirulence genes and cognate plant resistance genes were cloned. These achievements significantly increased our knowledge regarding plant immunity. Notably, some pioneer Chinese researchers started exploring plant immunity in the late 1990s.

However, although many research groups found and cloned the genes with typical NB-LRR (NLR) structures in the late 1990s, known as the cytosolic resistance proteins nowadays, how the genes acted in plant immune responses was not deeply investigated. The turning point was around the year 2000, when many excellent scientists from overseas set up their laboratories in China and employed the 'plant innate immunity' concept to investigate plant and pathogen interactions. Since then, more and more scientists have established their laboratories in China. These scientists help the Chinese research community earn a reputation in the plant immunity field.

Advancements since 2010

Plant immunity-related publications have incredibly increased in China since 2010 in both quantity and quality. Since 2015, the number of publications from China has gradually ranked first place among all the countries. Here, we briefly summarize the major achievements of the domestic groups.

The key contribution: immune complex structures and resistosome

One of the key contributions of domestic groups is the achievements in the structure biology of plant immune complexes. Pattern recognition receptors (PRRs) are primarily responsible for the recognition of conserved microbial patterns. Three well-characterized PRRs, the FLS2, EFR, and CERK1, recognize bacterial flagellin, elongation factor-Tu, and fungal chitin, respectively. However, the recognition mechanisms were unknown due to a lack of structure biology evidence. Jian-Min Zhou's laboratory at the Institute of Genetics and Developmental Biology, Chinese Academy of Sciences (CAS) in collaboration with Jijie Chai at TsingHua University, resolved the Arabidopsis CERK1 structure and revealed that chitin-induced dimerization of CERK1 ectodomain is required for the immune activation (Liu et al. 2012b). A year later, the two laboratories further uncovered the FLS2 activation mechanism based on the structures of FLS2 and co-receptor BAK1's ectodomains, where they formed an immune complex with reciprocal activation (Sun et al. 2013). These works offer valuable insights into the activation of PRR-mediated immunity.

Phytopathogens secrete diverse effectors to interfere with plant immune responses. In resistant plants, there is a set of NLR (nucleotide-binding site, leucine-rich repeat) proteins (R proteins) to directly or indirectly perceive these effectors and to initiate immune responses. Based on the 'gene-for-gene' hypothesis, dozens of key effectors from various pathogens have been cloned over the years. Correspondingly, many NLR proteins have been identified, and majority of them have been discovered to perceive the cognate effectors. Following these discoveries, several hypotheses have been proposed to explain how NLR-mediated immunity is initiated in plants, for example, the 'guard hypothesis' and 'decoy hypothesis' (Jones and Dangl 2006; Khan et al. 2016). However, due to a lack of resolved protein structures, none of the hypotheses has been experimentally proved, and the NLR-mediated immune activation remained elusive. Until 2019, Jian-Min Zhou's laboratory and Jijie Chai's laboratory collaborated again and resolved the cryo-EM structure of a CC-NLR ZAR1 immune complex for the first time. Based on the complex structure, they resolved the mystery of NLR-mediated hypersensitive response, where the NLR protein ZAR1 forms a wheel-like pentameric ZAR1 resistosome during immune activation. The resistosome associates with the plasma membrane to initiate cell death and disease resistance (Wang et al. 2019a; b; Bi et al. 2021). This is a landmark event in plant science, which answers the question that has remained in the last 30 years since the NLR proteins were discovered. Following this discovery, similar structures and activation mechanisms of NLR-mediated immunity were discovered and confirmed by many other laboratories, and notably, Jijie Chai's group was heavily involved (Ma et al. 2020; Huang et al. 2022; Jia et al. 2022). These groundbreaking discoveries have substantially pushed the movement towards fully elucidating plant disease resistance.

Exploration of plant immune recognition

In addition to the outstanding achievements in structural biology, the knowledge of plant and microbe interactions has been incredibly advanced in both the PRR-mediated immune recognition as well as the NLR-mediated immune recognition. Notably, as in many other research groups in the world, the majority of these studies used *Arabidopsis thaliana* and rice as research materials. Arabidopsis is a model plant in plant sciences. Many important scientific phenomena were discovered using Arabidopsis plants as the material. Rice is a staple food in China. Understanding of rice immunity is crucial for breeding disease-resistant varieties. It's exciting to note that significant breakthroughs have been made in recent years using these two plant species as research materials.

PRR-mediated defense

PTI and plant development PRRs perceive PAMPs (pathogen-associated molecular patterns) or DAMPs (damage-associated molecular patterns) to initiate immune responses. While, the regulation can be temporal, as it has been known for a long time that plants at different developmental stages display distinct disease resistance. Dongping Lu's group at CAS revealed that the miR172b regulates immune receptor FLS2 to control the ontogeny of plant immunity (Zou et al. 2018). By identifying additional PRR interactors, Dingzhong Tang's group at Fujian Agriculture and Forestry University found an important plant development-regulated protein, the LORELEI-LIKE GPI-ANCHORED PROTEIN1 (LLG1), that is associated with FLS2, ERF, and BAK1 to regulate PAMP recognition and disease responses (Shen et al. 2017), which connects plant immunity with growth and development in Arabidopsis plants.

PTI activation For a long time, we used to think that ETI and PTI are two separate events. However, Xiufang Xin's group at CAS recently revealed that these two pathways are interconnected, and NLR signaling rapidly augments the transcripts and protein levels of key PTI components, and PTI components are required for full resistance during ETI (Yuan et al. 2021). PTI activation is always a focus in plant immunity. In addition to the impressive crystal structure of PRRs from Jian-Min Zhou and Jijie Chai's groups, Jianfeng Li and Hongbin Wang's groups at Sun Yat-sen University have made impressive contributions to understanding how PRR activation/deactivation occurs in plants. They discovered that the phosphorylation/dephosphorylation cycle of a CERK1-specific residue coordinately regulates immune signal transduction (Liu et al. 2018). The juxtamembrane phosphorylation induced by a bacterial pathogen can prime disease resistance to a fungal pathogen, revealing that the cross-talk defense to bacterial and fungal pathogens can be executed by a single PRR (Gong et al. 2019).

Downstream of PTI The downstream signals after PRR activation have also been uncovered by multiple laboratories recently. Jian-Min Zhou's group demonstrated that PRRs transmit signals to downstream receptor-like cytoplasmic kinases (RLCK), specifically the RLCK VII subfamily; the latter further directly phosphorylate the MAPKs to initiate disease resistance (Bi et al. 2018; Rao et al. 2018). Similarly, Jun Liu's group at CAS discovered that the PRR LIPOOLIGOSACCHARIDE-SPECIFIC REDUCED ELICITATION (LORE) perceives the medium-chain 3-hydroxyl-fatty acids and transduces the signal to downstream RLCKs for immune activation (Luo et al. 2020). In addition, Zhou's group discovered that the FLS2-associated kinase BIK1 directly phosphorylates the NADPH oxidase RbohD to control immunity (Li et al. 2014b). RbohD produces ROS upon pathogen recognition, which serves as the alert signal and primes the immune activation. H_2O_2, the major form of ROS, is recognized by the plasma membrane-located leucine-rich-repeat receptor kinase HPCA1 (Wu et al. 2020), while the intracellular sensor has been discovered as a cytosolic thiol peroxidase by Jian-Min Zhou's group recently (Bi et al. 2022). Multiple kinases are involved in the MAPK activation in addition to the RLCKs in Arabidopsis. Dingzhong Tang's group showed that BRASSINOSTEROID-SIGNALING KINASE 1, RLK902, and the immune protein EDR1 are also involved in the PTI activation, which is largely by activating the MAPK cascade (Zhao et al. 2014; Shen et al. 2017; Chen et al. 2022; Shi et al. 2022). In this case, 14-3-3 proteins are found to be required for the subsequent activation of MAPK cascades (Dong et al. 2023).

PTI in rice In rice, pattern recognition is always a focus of plant and microbe interaction, as PRRs-mediated immune activation often displays broad-spectrum resistance. The first identified rice PRR is OsCEBiP that was cloned and characterized in 2006 (Kaku et al. 2006). Later, the co-receptor OsCERK1 was characterized (Shimizu et al. 2010). OsCERK1-OsCEBiP forms an immune complex to perceive chitin (Shinya et al. 2012). Interestingly, Jun Liu's group at China Agricultural University (CAU) found that OsCERK1 not only recognizes chitin but also recognizes the β-1,3-1,4-linked glucan (Yang et al. 2021). In addition, Liu's group also found that a chitinase MoChia1 significantly induced immune response in rice cells, although the cognate PRR hasn't been identified yet (Yang et al. 2019). By a genetic screening, Hongbin Wang's group at Sun Yat-sen University revealed that the plasma membrane located LYP4/6 are LysM receptor-like proteins that recognize chitin and peptide glycine (PGN) (Liu et al. 2012a). Unlike OsCERK1, rice OsFLS2 does not mediate a strong immune response to *Xoo*/*Xoc*. This enigma was resolved by Wenxian Sun's group at CAU, where they revealed that the *Xoo*/*Xoc* changes the conserved flagellin amino acids to evade the recognition of rice OsFLS2 (Wang et al. 2015).

Effector targets and NLR-mediated immunity

PTI interfering Pathogens deliver many virulence effectors to interfere with PTI. The key targets of effectors are the PRRs. As early as 2007, Jijie Chai's group demonstrated that *P. syringae*-secreted effector AvrPto inhibits R protein Prf-associated Pto kinase based on the structure of AvrPto-Pto complex (Xing et al. 2007). Likewise, Jian-Min Zhou's group found that AvrPto suppresses Arabidopsis

PRR FLS2 and EFR and the tomato FLS2-mediated immunity (Xiang et al. 2008). By further exploring the mechanisms of PTI suppression, Jian-Min Zhou's group demonstrated that the effector AvrPphB and HopB1 inhibited PTI by cleaving multiple PBS1-like (PBL) kinases and PRR co-receptor BAK1, respectively (Zhang et al. 2010; Li et al. 2016). In collaboration with Chaozu He's group at CAS, they demonstrated that the *Xanthomonas campestris* effector AvrAC enhances the pathogen virulence by targeting and inhibiting BIK1 and RIPK, two RLCKs known for immune activation (Feng et al. 2012). Similarly, Xiaoyan Tang's group at Shenzhen Molecular Crop Design Center found that the effector HopF2 inhibits MAPK-mediated PTI by HopF2-mediated ADP-ribosylation of these kinases (Wang et al. 2010). In addition to the well-studied effector targets of FLS2 and EFR, several other PRRs are also reported to be targeted by pathogen effectors. LORE, the receptor for bacterial Lipopolysaccharide bound medium-chain 3-hydroxyl-fatty acid, is targeted by *P. syringae* effector HopAO1, where HopAO1 dephosphorylates the activated LORE after perceiving the 3-hydroxyl-fatty acid, thereby blocking the immune signal transduction (Luo et al. 2020).

Nutritional targets Although the concept that effectors target PRRs for immune suppression is well accepted, many effectors appear to target non-PRR proteins. Jun Liu's group showed that *P. syringae* effector AvrRps4 interferes with plant iron metabolism pathways to acquire iron (Xing et al. 2021). Alberto Macho's group at CAS found that *Ralstonia solanacearum*, a bacterial pathogen that causes wilt disease, secretes an effector protein RipI to target gamma-aminobutyric acid as nutrition (Xian et al. 2020). These works unravel the novel functions of pathogen effectors. In addition, Macho's group spent years elucidating the roles of effectors in *R. solanacearum*. They found RipAC, another effector, that targets E3 ligase-associated BIK1 degradation to suppress host immunity (Yu et al. 2022). They also found that the effector RipAY and RipAC inhibit redox signaling and SGT1-dependent NLR activation, respectively (Sang et al. 2018; Yu et al. 2020).

In addition, recent work by Yongli Qiao's laboratory at Shanghai Normal University showed that *P. sojae* boosts trehalose biosynthesis in soybean through the virulence activity of an effector PsAvh413. PsAvh413 interacts with soybean trehalose-6-phosphate synthase 6 (GmTPS6) and increases its enzymatic activity to promote trehalose accumulation. *P. sojae* acquires trehalose from the host and exploits it as a carbon source (Zhu et al. 2023). Effectors are always attractive, and undoubtedly that there will be more exciting discoveries of novel effector targets on the way.

Rice NLR Plants carry hundreds of NLR resistance proteins to recognize pathogen-secreted effectors and to activate downstream immune responses. Typical immune output following NLR activation is the hypersensitive response, a robust immune response that often causes cell death at the infection site. Although many NLRs have been discovered in rice, their activation mechanisms are barely known. It should be pointed out that Zuhua He's group at CAS made a great contribution in deciphering the rice NLR-mediated immunity. In rice, it has been known for a long time that there is a resistant locus Pigm which contains a cluster of NLRs to resist blast infection, but how these NLRs act in plants is elusive. Zuhua He's group resolved the mystery, where they found that NLR PigmR is a broad-spectrum resistance gene. However, its expression caused a yield penalty. Interestingly, they found that the paired NLR PigmS in the locus counteracts the yield loss caused by PigmR (Deng et al. 2017). They further discovered that PigmR interacted with an RRM (RNA-recognition motif) protein to mount defense (Zhai et al. 2019). Therefore, they revealed an interesting mechanism that how paired NLRs balance plant defense and growth. On the other hand, pathogen effectors and their interactions with rice plants are also a focus. In line with the discovery of PigmR-mediated disease resistance to *M. oryzae*, Zuhua He's group also found that PigmR protects a deubiquitinase from degradation by the effector protein AvrPi9 from *M. oryzae*. However, the effector AvrPiz-t can structurally mimic a calcium sensor to suppress immunity in rice, unraveling an interesting mechanism of effector-triggered immunity in rice (Gao et al. 2021).

With the knowledge of the activation mechanism for NLR-mediated immunity, it has been proved that NLR can be modified to recognize conserved effectors from pathogens. In fact, rice host target protein-binding is rather conserved. Junfeng Liu and Youliang Peng's groups at CAU collaborated with Tomas Kroj at the University of Montpellier and resolved the structure of a decoyed and integrated heavy metal-associated (HMA) domain from a rice NLR, where they demonstrated the importance of this domain in effector recognition (Guo et al. 2018). The rice NLR RGA5 carries HMA that recognizes the conserved *M. oryzae* Avrs and ToxB-like (MAX) effectors. By reconstructing the NLR containing the HMA domain, Liu and Peng were able to show that the engineered $RGA5^{HMA}$ recognizes structurally similar MAX effectors in *M. oryzae*. These works provide a promising approach for developing broad-spectrum resistance rice plants (Liu et al. 2021).

Oomycete effectors and Arabidopsis In addition, Weixing Shan's group at Northwest A&F University spent years unraveling the pathogenicity of the oomycete pathogen

Phytophthora parasitica on Arabidopsis plants. *P. parasitica* has a host range of over 60 plant families, especially the *Solanaceae* and many other economically important crops. Shan's group established the Arabidopsis-*P. parasitica* as a model pathosystem for the first time (Wang et al. 2011), slightly later than Attard et al., who reported the root infection of this pathogen on Arabidopsis plants (Attard et al. 2010). With this pathosystem, Shan's group has characterized the roles of many *P. parasitica* RXLR and non-RXLR effectors and virulence factors. By screening the T-DNA insertion lines of Arabidopsis, they discovered a set of *RESISTANCE TO PHYTOPHTHORA PARASITICA* (*AtRTPs*) genes that either direct respond to effectors or function in the basal defenses against *P. parasitica* (Pan et al. 2016; Qiang et al. 2021). In addition, Shan's group also explored several other *Phytophthora* pathogens, the potato late blight pathogen *P. infestans* and, *Phytophthora capsici* that causes foliar blight and wilting on many vegetables by elucidating the roles of the effectors in these pathogens (Fan et al. 2018; Du et al. 2021).

Basal disease resistance

Phytoalexin Camalexin and many other phytoalexins are produced to prevent pathogen infection either by direct killing or suppressing pathogen proliferation following PTI activation. In this regards, Xiangzong Meng's group at Shanghai Normal University found almost all the missing pieces of the puzzles that connect the phytohormone-activated signaling to camalexin biosynthesis. Their work revealed that ethylene and JA pathways act synergistically with MPK3/MPK6, two well-known downstream PTI components, and CPK5/CPK6, which cooperatively regulate WRKY33 and further induce the camalexin biosynthesis gene expression. Additionally, CPK5/CPK6 and MPK3/MPK6 cooperatively regulate the expression of PENETRATION 3 (PEN3) and the PDR transporter PDR12 to mediate the secretion of camalexin in Arabidopsis upon pathogen infection (He et al. 2019; Zhou et al. 2020, 2022).

Rice broad spectrum resistance There are several groups that have done particularly well in the rice basal defense. Xuewei Chen's laboratory in Sichuan Agricultural University found that a natural allele of a transcription factor BSR-D1 has been selected as a durable resistance gene through breeding in rice (Li et al. 2017). In addition, they also found that the Ideal Plant Architecture 1 (IPA1), which is a key gene in rice tillering that can switch to a disease-resistance gene during pathogen infection (Wang et al. 2018). Rice false smut caused by *Ustilaginoidea virens* is emerging as a devastating disease recently. *U. virens* infects rice florescence and eventually forms black smut, leaving the rice seed under development and inedible. Wenxian Sun and Youliang Peng's groups at CAU sequenced the genome (Zhang et al. 2014). Later, Sun's group spent years exploring the virulence roles of the secreted proteins in *U. virens*, where they found that the secreted proteins primarily interfere with host basal defenses by targeting the ATPase, MPK cascades, and auxin response pathways (Zhang et al. 2020; Zheng et al. 2022; Yang et al. 2022a).

Rice viral diseases Virial diseases also seriously threaten rice production. The epidemics of several rice viral diseases, such as Rice stripe virus (RSV) and Rice black-streaked dwarf virus (RBSDV), attract more and more attention in the plant immunity field. RSV is one of the most devastating diseases affecting rice production in East Asia, which is first reported in China in 1963 (Wei et al. 2009). Rice plants have developed multiple strategies to counteract viral infection, such as miRNA and hormone-mediated defense. Yi Li's group at Peking University found that rice plants activate JA signaling, which is triggered by RSV coat protein (CP), to initiate a defense network. In this case, JA signaling activates AGO18-mediated small RNA silencing to mount antiviral defense (Yang et al. 2020b). Interestingly, they also found that copper homeostasis is beneficial for miRNA-mediated antiviral pathways (Yao et al. 2022). Xueping Zhou's group at Chinese Agricultural Academy of Sciences (CAAS) found that RSV-caused disease symptom is largely due to the alteration of chloroplast and function in rice cells during infection, and the virus movement is inhibited by the remorin proteins (Kong et al. 2014; Fu et al. 2018). These works significantly help us understand the infection mechanisms of viruses in rice.

Other crop and pathogen interactions

Soybean and oomycete interactions

Oomycete pathogens infect many economically important crops. The most devastating oomycete pathogen *P. infestans* causes the potato late blight and is the culprit that led to the great famine of Ireland in 1860–1890. *Phytophthora sojae*, another serious pathogen that causes soybean root and stem rot, is a longstanding problem for soybean plants. Yuanchao Wang's group and their collaborators at Nanjing Agricultural University (NAU) have done impressive work in elucidating the interactions between *P. sojae* effectors and the soybean immune system. By screening the proteins that can trigger immunity in *Nicotiana benthamiana*, they identified a glycoside hydrolase family 12 (GH12) protein PsXEG1, produced by *P. sojae*, which exhibits xyloglucanase and β-glucanase activity, and is required for full virulence of *P. sojae*. After years of hard work, they not only revealed it being a PAMP, but also discovered the cognate receptor

RXEG1 in *N. benthamiana* plants (Ma et al. 2015, 2017; Sun et al. 2022b). Similar to Arabidopsis FLS2, the receptor recruits BAK1 as a co-receptor to be functional. It is interesting that they discovered a decoy mechanism where *P. sojae* secretes a paralogous PsXEG1-like protein that loses the enzyme activity but shields XEG1 from the inhibition by the apoplastic glucanase inhibitor proteins (Ma et al. 2017). In addition, by collaborating with Jijie Chai's group, they resolved the RXEG1 crystal structure and deciphered the recognition mechanism (Sun et al. 2022b). This impressive work further demonstrates the intensive arms race between plant and pathogen interactions. Importantly, their work extended this arms race to plant apoplastic niche and may apply to many other interactions when the causal agents carry XEG1-like proteins.

In addition to PsXEG1, Wang's group has investigated many other *P. sojae* effectors that are able to interfere with the host immune system to promote infection. For instance, they discovered an effector PsAvh23 that can manipulate host histone acetylation and reprograms defense gene expression (Kong et al. 2017). In the other case, they revealed an effector target GmTAP1 that can acetylate histone H2A and H3 to promote infection (Li et al. 2018). It appears that manipulating of host epigenetic pathway is one of the key strategies for *P. sojae* infection. In close collaboration with Suomeng Dong's group at NAU, they proved that 6 mA methylation of *P. sojae* genome is associated with the adaptive evolution of this important pathogen (Chen et al. 2018). To support this notion, they reported that the pathogen evades the resistance gene *Rps1b* through transcriptional polymorphisms in the effector gene *Avr1b*, which encodes a key effector of immune suppression in soybean. In addition, Dong's group identified many splicing regulatory effectors (SREs) that can modulate genome-wide alternative splicing of host mRNAs to subvert immunity (Huang et al. 2017). Similarly, Yongli Qiao's group at Shanghai Normal University identified multiple effectors as the *Phytophthora* suppressors of RNA silencing (PSRs), and these PSRs are required for the pathogenicity of *P. sojae* (Gui et al. 2022b). These PSRs are considered presumably to suppress small RNA (sRNA)-mediated immunity in plants.

Crop-virus interactions

Although viral diseases also cause huge economic losses every year to agriculture production, virus and plant interactions are still not well explored in general. Notably, viral disease-related researches are relatively fruitful in China. In addition to the impressive work of rice RSV by Yi Li, Xueping Zhou and many other laboratories, the interactions of viruses with other plants are also well explored. Xiaorong Tao's group at NAU demonstrated that ER network is required for viral movement in *N. benthamiana* and Arabidopsis, highlighting the role of plant ER employed by viruses for infection (Feng et al. 2016). While, Yule Liu's group at Tsinghua University discovered that calcium influx induced multiple RNAi genes to prime the combats against virus invasion through calmodulin-binding transcription factors, filling up the gap between early viral infection signal to the RNAi-mediated defense (Wang et al. 2021b).

In addition, Xueping Zhou and Yule Liu's groups have done tremendous work on elucidating the virulent targets of the geminivirus *Cotton leaf curl Multan virus* (CLCuMuV) and Tomato yellow leaf curl virus-encoded C4 proteins and its satellite-encoded βC1 proteins. Their work showed that βC1 proteins are viral suppressors of RNA silencing, which targets diverse defense pathways, including RNA silencing, ubiquitination, DNA-methylation, MAPK cascade, and hormone-mediated defense pathways (Li et al. 2014a; Jia et al. 2016; Hu et al. 2019; Gui et al. 2022a); however, resistant plants deploy ubiquitination and proteasomal degradation of βC1 proteins to subvert infection (Shen et al. 2016; Zhou et al. 2021). One of the roles of C4-assisted viral infection is to induce host cell division. Later, Liu and Zhou's groups further unraveled them as gene silencing suppressors by suppressing both transcriptional gene silencing (TGS) and post-transcriptional gene silencing (PTGS) and hijacking brassinosteroid pathways to enhance host susceptibility and to activate cell division, respectively (Ismayil et al. 2018; Mei et al. 2018a, b, 2020). Autophagy is another strategy that is deployed by plants to counteract virus infection. The CLCuMuV satellite βC1 protein is targeted by plant autophagic machinery for degradation, reported by Liu's group (Haxim et al. 2017). Interestingly, Dawei Li's group at CAU collaborated with Liu's group and discovered that *Barley strip mosaic virus*-encoded proteins γa and γb suppress host autophagy by blocking vacuolar lumen acidification and disrupting ATGs interaction (Yang et al. 2018, 2022b).

In addition to the above-mentioned plant-deployed well-known defense strategies, NB-LRR protein-mediated antiviral defenses are also worth mentioning. Yule Liu's group found that the plasma membrane-located tomato mosaic virus NLR protein Tm-22 recognizes viral movement protein (MP) for immune activation by coiled-coil domain self-association (Wang et al. 2020), which is similar to the activation of NLRs in recognizing bacterial and fungal effectors. A recent work reported by Xiaorong Tao's group at NAU showed that the pepper NLR protein Tsw recognizes the effector nonstructural protein NSs of tomato spotted wilt orthotospovirus, which targets hormone receptors to disable phytohormone-mediated defense; Tsw structurally resembles hormone receptors

to counteract the interference of hormone pathways by NSs (Chen et al. 2023), uncovering an interesting NLR-mediated defense strategy.

Wheat and Pst interactions

Wheat is the second most important staple food in China. Wheat disease control is always the most important task for local governments. One of the major diseases of wheat is strip rust caused by the causal agent *Puccinia striiformis f.* sp. *tritici* (*Pst*). Understanding the epidemics of *Pst* is very important to manage this disease. Zhensheng Kang's group at Northwest A&F University (NAFU) spent over 30 years on the investigation of the epidemics of *Pst* in Northwest of China, one of the key wheat producing areas. He discovered the overwinter and oversummer epidemics and the outbreak pattern of this pathogen (Zhao and Kang 2023; also in this issue). In addition to the contributions to the epidemiology of *Pst*, Kang also collaborated with Xiaojie Wang and Jun Guo's groups at NAFU and extensively explored the *Pst* effector functions. Specifically, they found *Pst* exploited host targets to suppress immune activation by disrupting chloroplast function to reduce ROS accumulation (Qi et al. 2019; Xu et al. 2019; Wang et al. 2021a; Liu et al. 2022), by stabilizing or activating the negative kinase regulators in immunity (Wan et al. 2022; Wang et al. 2022), by regulating host pre-mRNA splicing (Tang et al. 2022) or by targeting other enzymes for immune suppression (Yang et al. 2020a). Nevertheless, the interaction mechanisms between *Pst* and wheat are still at the infancy stage due to the complex pathogenicity of *Pst*, the large genome of wheat plants, and the difficulties of their genetic manipulations.

Cotton and verticillium dahliae interactions

Cotton is another important crop, which is widely planted nationwide. Huishan Guo's group at CAS has done impressive work in elucidating the infection mechanisms of the serious cotton wilt disease. *V. dahalie* causes severe economic losses in China. In fact, *V. dahliae* infects many economically important crops. Using T-DNA insertion-caused gene knockouts of the fungi, Guo's group found several key genes of *V. dahlia* involved in initial penetration and the following infection (Zhou et al. 2017), and the secreted proteins that modify fungal cell wall to evade host immunity and to promote immune suppression (Gao et al. 2019). In collaboration with Jie Zhang's group at CAS, they discovered that one of the cotton immune targets of the secreted proteins is the salicylic acid pathway (Qin et al. 2018). Calcium-activated immune signaling is essential for many defense pathways. Zhang's laboratory found that calcium-mediated SA activation also contributes to fungal resistance in plants (Sun et al. 2022a).

Cross-kingdom RNAi was discovered in plant and pathogen interactions in 2013, where the fungal pathogen *B. cinerea* small RNAs could enter host cells and suppress host immune gene expression (Weiberg et al. 2013). Notably, plants can also deploy small RNAs to inhibit virulence gene expression in pathogens. Huishan Guo's group discovered that cotton plants export mRNA to *V. dahliae* and inhibit its virulence gene expression (Zhang et al. 2016). These shreds of evidence imply that the cross-kingdom RNAi strategy is likely employed by both plants and pathogens for defense/infection.

Future perspective

It is a great time to celebrate the centurial history of plant pathology in China. As one of the major achievements in plant pathology, Chinese plant immunity researchers have earned the reputation and respect worldwide. However, what are the future directions of plant pathology, and how can we improve the ability to genetically tailor crops? It is worth mentioning that several groups, especially the domestic groups, have some exciting discoveries and strategies which have shed light on the future studies of plant pathology in China.

Gene editing techniques have become a very attractive and powerful tool to tailor crop for favorable agronomy traits. In this regard, Caixia Gao's group at CAS has emerged as a leading laboratory in the genome editing field, especially in rice and wheat plants, which makes China one of the few leading countries in crop gene editing. Jinlong Qiu's group at CAS has a close collaboration with Gao's laboratory, where they use CRISPR-CAS9 simultaneously knocked out three homoeoalleles of a susceptible powdery mildew genes in wheat (Wang et al. 2014). As a result, it significantly enhanced the disease resistance and dramatically shortened the wheat disease resistance breeding cycle. Recently, they created a powdery mildew resistance elite wheat without penalties by genome editing (Li et al. 2022), demonstrating the robustness of this technique and promising application for crop disease resistance. This technique was also developed to tailor the crop for herbicide-resistant recently in several Chinese laboratories, such as Huanbin Zhou at CAAS, Kabin Xie at Huazhong Agricultural University, and Linjian Jiang at CAU. As a fast-moving field, the gene-editing technique is benefitting mankind and will largely secure our food supply in the future.

In addition to the known immunity strategy, plants and pathogens have co-evolved for hundreds of million years, where the horizontal gene transfer between pathogens significantly increased the diversity of pathogens and facilitated their evolution. In fact, horizontal gene

transfer events seem extensively occurring in nature. Youjun Zhang's group at CAAS found that the cosmopolitan agricultural pest *Bemisia tabaci* has acquired a plant-derived gene through a plant-to-insect horizontal gene transfer event, enabling the whiteflies to detoxify plant defense compounds and continuing to feed on their plant hosts (Xia et al. 2021). These cases shed light on gene shifting research, which may help us better understand the co-evolution of pathogens and their hosts. On the other hand, we could use this knowledge to engineer gene modules to help plants defend against pathogen/pest invasion by synthetic biology. There is an excellent case done by Dapeng Li at CAS, who collaborated with Ian Baldwin at Max Planck Institute, and engineered a defense hormone JA-JAZi module to induce a volatile compound to resist leafhopper feeding (Bai et al. 2022). These works revealed the widely existing horizontal gene transfer phenomena in nature, and the synthetic biology strategy will improve crop disease resistance by integrating the exogenous genes from either pathogens or the feeding herbivores.

Engineering the immune receptors for broad-spectrum disease resistance is also very attractive. For example, Junfeng Liu and Youliang Peng's group resurfaced the NLRs to recognize the core effectors of *M. oryzae*, which leads to broad resistance to the pathogens (Liu et al. 2021). It is also experimentally proved that the pyramiding of multiple resistance genes in wheat could acquire a broad disease resistance to several devastating pathogens (Luo et al. 2021). In addition, cross-species resistance is also worth noting. By introducing Arabidopsis EFR to *N. benthamiana* and tomato plants, Lacombe and the colleagues were able to enhance the disease resistance to agro-bacteria in the transgenic plants (Lacombe et al. 2010).

Although Arabidopsis and rice are the important and widely studied plants in China, many other economically important diseases should be noted and investigated because these plant diseases threaten our food security. For example, the Citrus Huanglongbing and cotton wilt disease caused huge economical losses in China. Unfortunately, there is no good disease resistance germplasm for these plants. Similarly, fusarium head blight is emerging to be one of the major diseases in wheat, but there are no effective measures to constrain the disease outbreak and spread. In fact, there are also many diseases occurring on the vegetables and fruits in the protected facilities, such as *Botrytis cinerea*-caused grey mold on grape and strawberry, and the soft rot of cabbages. However, disease controls are largely dependent on pesticides, which is seriously threatening our health. How to reduce pesticide use has become a major topic in agriculture. Green and sustainable agriculture will be one of the key directions for the Chinese groups.

Abbreviations

DAMPs	Damage-associated molecular patterns
HR	Hypersensitive response
PAMPs	Pathogen-associated molecular patterns
PRRs	Pattern recognition receptors
RBSDV	Rice black-streaked dwarf virus
RLCK	Receptor-like cytoplasmic kinases
RSV	Rice stripe virus

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JL wrote the paper; DT reviewed the manuscript. Both authors read and approved the final manuscript.

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Declarations

Ethical approval and consent to participate

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Competing interests

The authors declare that they have no competing interests.

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