Foundational and translational research opportunities to improve plant health.

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[3] A full list of all workshop participants and their affiliations is provided at the end of the supplementary e-Xtra document.

This workshop was sponsored by the UK Biotechnology and Biological Sciences Research Council (BBSRC), the US National Science Foundation, Directorate for Biological Sciences (NSF BIO), and the US Department of Agriculture, National Institute of Food and Agriculture (USDA NIFA), the UK Science Innovation Network, and the Research Councils UK in the US in partnership with the University of California, Davis and the British Consulate-General, San Francisco.

All authors contributed ideas to many of the sections through participation in breakout sessions focused on the molecular basis of plant-pathogen/pest interactions, variation in and the evolution of plant-pathogen/pest interactions, and translational strategies for more durable disease or pest control. Major contributors in addition to the first two authors to the writing of each section are shown.

In recognition that a small group of researchers cannot adequately cover all aspects of this large field, additional domain experts were invited to provide input and contributors were added to the list of authors. Furthermore, at the end of the on-line version of this article there is the opportunity for the international community at large to provide feedback within four weeks of publication. These comments will be collated and published as an addendum.

Summary

This whitepaper reports the deliberations of a workshop focused on biotic challenges to plant health held in Washington, D.C. in September 2016. Ensuring health of food plants is critical to maintaining the quality and productivity of crops and for sustenance of the rapidly growing human population. There is a close linkage between food security and societal stability; however, global food security is threatened by the vulnerability of our agricultural systems to numerous pests, pathogens, weeds, and environmental stresses. These threats are aggravated by climate change, the globalization of agriculture, and an over-reliance on non-sustainable inputs. New analytical and computational technologies are providing unprecedented resolution at a variety of molecular, cellular, organismal, and population scales for crop plants as well as pathogens, pests, beneficial microbes, and weeds. It is now possible to both characterize useful or deleterious variation as well as precisely manipulate it. Data-driven, informed decisions based on knowledge of the variation of biotic challenges and of natural and synthetic variation in crop plants will enable deployment of durable interventions throughout the world. These should be integral, dynamic components of agricultural strategies for sustainable agriculture.

Specific findings:

- Genetic improvement of crops is the most reliable, least expensive management strategy when suitable genetic variation is available. Nonetheless, some interventions have not proved durable due to the evolution and global dispersal of virulent pathogens and pests as well as herbicide-resistant weeds.
- Additional strategies are becoming essential as multiple fungicides, nematicides, and herbicides become ineffective due to the evolution of resistance and/or are phased out due to registration withdrawals.
- Strategies are needed that maximize the evolutionary hurdles for pathogens, pests, and weeds to overcome control measures. Interventions need to evolve as fast as the biotic challenges. Moreover, deployments of interventions must be driven by knowledge of the evolutionary capacity of the biotic challenge.
- Considerable knowledge exists but more research into the mechanisms of plant immunity and other forms of resistance is needed as the foundation for translational applications.
- Several new technologies are increasing foundational knowledge and providing numerous opportunities for generating crops with durable resistance to pests and diseases as well as control of weeds and reduction of the environmental impact of agriculture.
- There are multiple strategies for counteracting biotic challenges involving canonical and non-canonical disease resistance genes, genes encoding susceptibility factors, small RNAs, or immunomodulators. Simultaneous deployment of disease resistance strategies with different modes of action, as well as the judicious use of fungicides, will enhance durability of control measures.
- Pathogen effectors provide tools for discovering resistance genes and susceptibility factors as well as for dissecting/manipulating plant biology and breeding plants for durable disease resistance.
- There are several, as yet little exploited, opportunities for leveraging beneficial interactions among plants, microbes, insects and other organisms in the phytobiome to enhance plant health and productivity as well as breeding plants to promote beneficial phytobiome communities.
- Global monitoring of plant health is feasible and desirable in order to anticipate and counter threats.
- Climate change increases the need for continual global monitoring of pathogens, pests, and weeds and adjusting of control strategies.
- There are numerous current and future opportunities for knowledge exchange and partnerships between developed and developing countries to foster improved local and global food security.
- Both genetically modified (GM) and non-GM strategies are needed to maximize plant health and food security.
- Significant, sustained financial support is required if the beneficial impacts of foundational and translational research on global food security are to be realized.

The needs, opportunities, approaches, and deliverables for addressing biotic challenges to plant health are detailed in the accompanying e-Xtra table. These can be broadly classified as assessing variation, characterizing it in detail at a variety of scales, and deploying beneficial interventions. Immediate investments in global monitoring of pathogens/pests and *in situ* and *ex-situ* determination of what natural

variation exists in crop plants for countering challenges and threats should be a high priority. Detailed investigations of the molecular basis of the various types of plant resistance and of the basis of pathogen/pest virulence are critical for providing the foundation for novel intervention strategies; these will be facilitated by development of high resolution structural and functional analytical techniques. Optimization of protocols for delivery of reagents for allele replacement and gene insertions into diverse major and minor crop plants should be a high priority. Monitoring and deployment should be a global endeavor involving multinational partnerships and knowledge exchanges in order to ensure that interventions are locally relevant and globally durable.

The full whitepaper is provided as a supplementary e-Xtra document.

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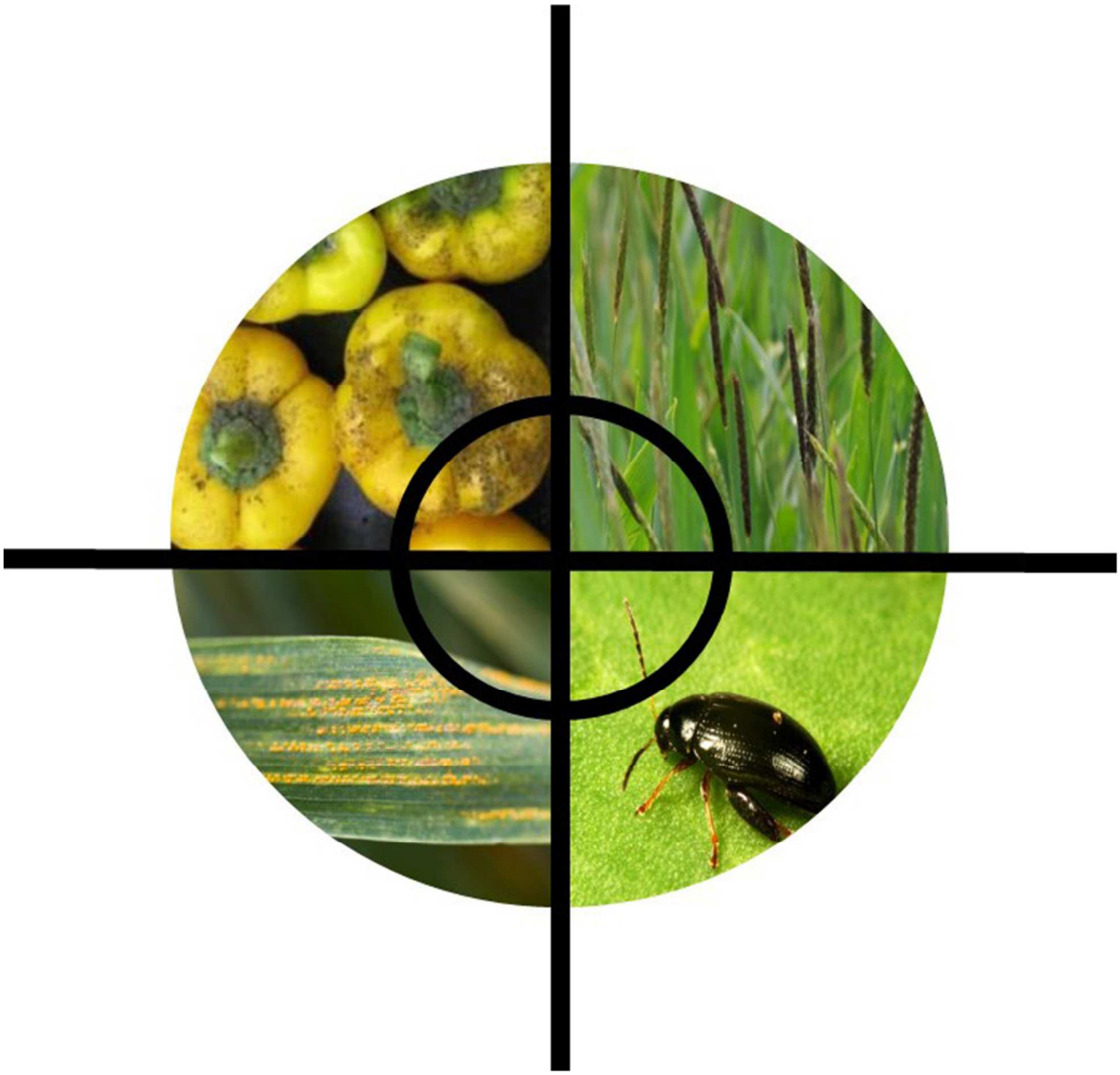

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The figure shows some of the highest ranking targets as rated by farmers and agronomists in the UK (www.croprotect.com). Clockwise: the black grass weed, *Alopecurus myosuroides*, which has evolved herbicide resistance; the cabbage stem flea beetle, *Psylliodes chrysocephalus* on canola that has high levels of pyrethroid resistance; yellow rust, *Puccinia striiformis* f. sp. *tritici*, for which new biotypes have overcome previously resistant cultivars; sweet peppers contaminated with honeydew from the aphid, *Myzus persicae*, and sooty mold which has grown on the honeydew. Created by Toby Bruce using images from Rothamsted Research and Rob Jacobson Consultancy.

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Abbreviations and Glossary

AMF: Arbuscular mycorrhizal fungi. Symbionts which improve uptake of mineral nutrients from the soil.

CRISPR/Cas9: Clustered regularly interspaced short palindromic repeat/CRISPR-associated protein 9. An RNA-guided endonuclease increasingly used for genome editing applications.

DAMPs: Damage-associated molecular patterns. Host components released by wounding and other pathogen/pest activities that elicit a defense response mediated by PPRs.

Effectors: Virulence proteins secreted from diverse microbial pathogens and pests that manipulate plant immunity or physiology to the microorganism's/pest's advantage. Some effectors can be detected by NLRs.

ETI: Effector-triggered immunity. Resistance to pests or pathogens mediated by recognition of pathogen effectors; often mediated by plant NLR proteins.

GM: Genetically modified. **GMOs:** Genetically modified organisms.

HIGS: Host induced gene silencing. Production of RNAs targeting pathogens in the host plant.

NLRs: Nucleotide-binding, leucine-rich repeat receptors. Plant intracellular receptors that recognize effectors.

PAMPs: Pathogen-associated molecular patterns. Conserved microbial components that can be recognized by PRRs.

PGPR: Plant growth-promoting rhizobacteria. Bacterial symbionts that improve plant growth.

PRRs: Pattern-recognition receptors. Surface-localized plant receptor proteins that recognize PAMPs or DAMPs. Often RLKs or RLPs.

PTI: Pattern-triggered immunity. Resistance to pathogens mediated by recognition of PAMPs.

PTM: Post-translational modification of proteins.

QDR: Quantitative disease resistance. Incomplete host resistance conferred by one or multiple genes.

QTL: Quantitative trait locus. A chromosomal region determining a quantitative phenotype.

R gene: Plant gene conferring resistance to a pest or pathogen, often via ETI. May be have a narrow spectrum of resistance and only be effective a subset of the pathogen population.

RLK: Receptor-like kinase. A type of surface localized receptor capable of pathogen recognition.

RLP: Receptor-like protein. A type of surface localized receptor capable of pathogen recognition but lacking an intracellular kinase domain.

S gene: Susceptibility gene. A gene required for susceptibility to a pathogen or pest.

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Introduction

Numerous reviews and reports have documented the global challenges to feeding the growing human population (Battilani et al. 2016; Chakraborty and Newton 2011; Davis et al. 2016; Garrett 2016; Kurrey et al. 2016). More people living longer, healthier, more affluent lives will put increased pressure on food production systems. Climate change is predicted to further exacerbate challenges to food production. Furthermore, insufficient food is a major causal factor inciting civil strife. The large investments being made in human health will be of little benefit if people are undernourished.

Sustainable increased food production requires both technical and organizational advances. Major, sustained investments in foundational and translational agricultural research are needed. Pathogens, pests, and weeds cause large pre- and post-harvest losses, while beneficial symbionts provide the opportunity to improve yield stability, quantity, and quality (Biber-Freudenberger et al. 2016; Palmgren et al. 2015; Rodriguez and Sanders 2015). Support for this area of agricultural research is therefore both justified and urgent.

Forty researchers from the USA and UK gathered at the British Embassy in Washington, D.C. for two days in September, 2016, to explore research opportunities focused on the understanding of interactions of plants with pathogens, pests, and weeds as well as with symbionts and other beneficial organisms in the phytobiome. Participants discussed the potential of foundational knowledge generated by such research to enhance the health of plants economically important for agriculture, horticulture or forestry in the UK, USA, and globally. Research to understand and ameliorate the emergence and spread of resistance of pathogens, pests or weeds to control measures was discussed. In addition, the workshop considered the potential transformative impacts of new technologies, such as high throughput sequencing, synthetic biology, genome editing, and cryo-electron microscopy (cryo-EM), on plant health research. This whitepaper describes the product of these deliberations.

Breeding crops for resistance to pests and diseases has tended to be a lower priority than breeding for yield and quality when control chemicals have been available. However, the availability such chemical interventions as well as their efficacies are now becoming limited due to changes in legislation and the evolution of pathogen/pest resistance to control chemicals. Consequently, established cropping systems are highly vulnerable to disruption by adapted pests, weeds, and diseases and there is a pressing need for new interventions (Bruce 2016; Tamiru, Khan, and Bruce 2015). For example, management of insect pests has become much more challenging after recent restrictions on neonicotinoid and organophosphate insecticides in the UK. There are significant problems with herbicide resistant weeds such as black grass and fungicide resistant pathogens such as *Septoria* leaf blotch. Roundup resistant weeds have emerged in the USA, challenging soil-conservation measures dependent on minimum tillage. Similarly, new strategies for nematode control become essential as soil-acting nematicides are phased out.

Research on plant-microbe/pest interactions is at an inflection point. Durable disease resistance to pests or pathogens can be defined as “resistance that has remained effective over long periods of widespread agricultural use” (Johnson 1984). This has been a continual and often elusive goal in many disease control programs for decades; however, we now have opportunities to provide more durable resistance based on foundational knowledge and recent technological advances. Long-standing questions as to the molecular and genetic basis of specificity between hosts and pathogens/pests are being answered in increasing detail (Couto and Zipfel 2016; French, Kim, and Iyer-Pascuzzi 2016; Toruño, Stergiopoulos, and Coaker 2016). There is still much more to be discovered as to how the plant immune system functions and how it can be predictably deployed with minimal side effects on yield and other important agronomic traits. Nevertheless, there is now sufficient foundational knowledge to develop and implement strategies that are likely to provide durable control of pathogens, pests, and weeds as well as to improve yields and yield stability (Dangl, Horvath, and Staskawicz 2013; Michelmore, Christopoulou, and Caldwell 2013). Although less is known, advances are also being made in the understanding of beneficial biotic interactions, with concomitant opportunities for improving plant health (Bulgarelli et al. 2013; Hacquard et al. 2015; Vorholt 2012).

Many of the recent advances have been enabled by technological innovations and further high-impact developments are imminent. In particular, the ever-decreasing cost and increasing output of DNA sequencing technologies now enables the genome sequencing of multiple genotypes of many model and

non-model plants as well as microbes, pests, weeds and whole communities associated with plants or in soils. Combined with increasing computational resources, these sequences are allowing the characterization of genomic variation, gene expression patterns, the identification of candidate genes for resistance, and pathogen population genetics. Proteomics, functional screens, ultra-high resolution light microscopy, and cryo-EM are revealing the molecular events involved in resistance and susceptibility (Kuhlbrandt 2014). Synthetic biology provides multiple opportunities and approaches for redesigning plant responses, which may allow for more precise control of the plant's ability to sense and respond to pathogens (Feng et al. 2015; Medford and Prasad 2016). Genome editing technologies are greatly enhancing functional investigations and deployment of useful genes (Chandrasekaran et al. 2016; Zhang, Liang, et al. 2016). Both synthetic biology and genome editing also provide the opportunity for generating useful genetic variation in numerous crop plants (Soyk et al. 2017).

This workshop report considers the opportunities for advances in foundational research and then the issues involved in translating this knowledge to enhance plant health, particularly in less developed countries.

Foundational Research Needs, Opportunities, and Challenges

Improving Genetic Resistance

Durable resistance to pathogens and pests (Brett Tyler, Jean Greenberg, Jonathan Jones)

As defined above, durable resistance is an empirical, retrospective attribute that has no single inherent basis. Pathogen and pest populations are highly variable and are evolutionarily driven to overcome plant resistance. Consequently, predicting which new disease resistance genes may be durable is challenging. While some resistance genes are rapidly rendered ineffective by changes in the pathogen, others have proved to be durable. for example, *Rps1k* in soybean (40 years and still widely effective; (Schmitthenner 1999), *Xa21* in rice (Song et al. 1995), and H1 in potato for resistance to cyst nematode (first deployed in 1960s and still controls almost all European *G. rostochiensis*; (Bakker et al. 2004). Knowledge is needed to implement strategies that maximize evolutionary hurdles for the pathogen to become virulent. Therefore, identification of resistance genes that may prove to be durable requires a comprehensive understanding of pathogen biology, population structure, epidemiology, mechanisms of genetic and epigenetic variation as well as knowledge of plant immune system recognition and signaling to provide predictive outcomes upon manipulation.

While it is difficult to predict durability of disease resistance, it is easier to predict, and therefore avoid or minimize, a likely lack of durability based on analyses of pathogen populations. Breeding programs would benefit from avoiding or minimizing the use of narrow-spectrum R genes that are already ineffective against local pathogen races. It is therefore important to define the pathogen/pest component(s) recognized by any to-be-deployed R gene to avoid "pathogen-blind" resistance breeding (breeding that does not take pathogen variation into account; Vleeshouwers et al. 2011). Analyzing the durability of resistance (R) genes, including those incorporated into elite germplasm, at the center of pathogen diversity can help predict durability. For R genes (e.g. NLRs) that target effectors and for other classes of potential resistance genes (e.g. PRRs) that may target other aspects of pathogen biology, it is essential to determine the extent to which the pathogen population is able to evade the targeting of pathogen component(s) and to suppress the defense mechanisms associated with R genes. Even if an R gene is identified that the pathogen cannot be observed to evade or suppress, it is desirable to examine the ability of the pathogen to acquire new genetic or epigenetic variations that enable the pathogen to overcome resistance. R genes that recognize the most conserved and presumably indispensable effectors should be prioritized if it can be ascertained that recognition of such effectors is not masked by other effectors or abrogated by second site genetic variation in the pathogen.

Once effective disease R genes have been identified, they should not be deployed individually because widespread plantings will select for variants capable of overcoming single R genes. One approach is to pyramid different R genes; if possible representing different classes (e.g. NLRs, PRRs), should be pyramided together. This is beginning to occur e.g. soybean–*Phytophthora sojae* (Li et al. 2010), rice-bacterial blight (Singh et al. 2001), and potato-*P. infestans* (Tan et al. 2010) interactions. Challenges to implementing this obvious strategy include the efficient identification of sufficient numbers of R genes (see below) and ensuring preservation of gene pyramids during breeding that involves

crosses. Ideally, pyramids comprised of different combinations of R genes should be deployed in order to diversify selection on the pathogen population in space and time. Furthermore, it is necessary to monitor for any breakdown of individual R genes so that new stacks can be assembled for effective disease control. The use of genome editing (e.g. using CRISPR/Cas9) to generate stacks of R genes at single chromosomal locations will greatly facilitate the stable deployment of multiple R genes; however, while generating loss of function alleles is now facile, techniques for allele replacements and gene insertions using genome editing need improvement (Zhang, Liang, et al. 2016).

Additional layers of disease resistance can also be combined with stacks of PRR and NLR genes. For example, endogenous chemistries may be used to boost signaling, promote the association of beneficial microbes that confer induced systemic resistance, and restrict invading pathogens/pests (see section on chemical immunomodulators). There may also be opportunities to amplify responses to help create more durable resistance. Plants employ positive amplification loops mediated in part by membrane proteins that associate with PRRs and endogenous ligand/receptor complexes (e.g. DAMPs and receptors; (Hou et al. 2014; Yeh et al. 2015). The extent to which these associated proteins are limiting and could be manipulated to boost resistance signaling outputs is not known. However, lab experiments with model plants overexpressing some of these components have yielded promising results in priming for stronger immune responses (Yeh et al. 2015). Both mechanistic studies with tractable model pathosystems and translational trials with crops are needed to determine how well this approach will work. It will also be informative to test whether disease resistance responses mediated by PRR and NLR genes can be reprogramed or amplified using synthetic transcription factors based on engineered TAL effectors or CRISPR/Cas9-based transcriptional activators. Conversely, engineering suppressors of negative immune regulators could also be beneficial for tipping the balance towards plant resistance (Lin et al. 2015).

Identification and engineering of novel intracellular and extracellular receptors (Jonathan Jones, Jean Greenberg)

Plant defense against pathogens is activated upon pathogen/pest recognition, most commonly via cell-surface PRRs that recognize apoplastic pathogen-derived PAMPs or via intracellular NLR receptors that directly or indirectly recognize pathogen/pest effectors delivered into host cells (Couto and Zipfel 2016; Jones, Vance, and Dangl 2017). Plant breeders have long recruited diverse R genes, which typically encode NLRs, although some encode PRRs or other types of proteins. Elevating disease resistance of crops requires the identification and recruitment of large numbers of diverse resistance genes. This diversity can have multiple sources.

Wild relatives of crops are potentially abundant sources of R genes. Most plants carry 100s of NLR-encoding genes that exhibit extensive diversity (Jones, Vance, and Dangl 2017). Using sequence capture to enrich for NLR genes prior to genome sequencing enables cost-effective interrogation of sequence diversity (Andolfo et al. 2014). Combined with genetic analysis, this can greatly accelerate discovery and recruitment of new recognition specificities (Witek et al. 2016). Species outside the primary and secondary gene pools are also potential sources of NLR genes. The discovery of widespread NLR gene pairs, one member of which carries an integrated domain that mimics a host component targeted by pathogen/pest effectors, and the observation that such gene pairs often work when transformed into another plant family, suggests that many such pairs may provide resistance when transferred between distantly related taxa (Le Roux et al. 2015; Sarris et al. 2016). For example, rice is famously resistant to all rusts; perhaps some of its gene pairs with integrated domains would confer rust resistance if transferred into wheat. The presence of paired NLRs, one with an integrated effector decoy domain (Le Roux et al. 2015), has raised the prospect of replacing one integrated domain with another. For example, removing the Arabidopsis RRS1 WRKY domain and replacing it with another domain targeted by other effectors may be fruitful. However, since such domains are likely to have a role in maintaining the receptor complex in the inactive state prior to interaction with an effector, substitution may perturb intramolecular interactions and result in constitutive activation of defense. It is therefore necessary to better understand the functioning of a diverse set of such NLR pairs and to screen to find pairs that are amenable to substitution of integrated effector decoy domains while retaining function.

Engineered R genes have been a long-standing aspiration of researchers in the field and could be a useful source of additional variation. We have not currently reached the point where novel NLRs

can be designed to recognize any effector. To be able to design novel recognition capabilities, we need better understanding of the basic mechanisms of NLR protein function. This will be facilitated by structural insights gained by recent advances in biophysical techniques such as cryo-EM (Kuhlbrandt 2014; Maqbool et al. 2015). NLRs have two important functions: they must remain "off" and only turn "on" in the presence of a cognate effector. One challenge is that modifications often result in constitutive activity of an engineered NLR; so it is crucial to understand intra-protein domain interactions that inhibit NLR activation prior to effector recognition. It is often presumed that activation is associated with a change in oligomerization state that imposes or induces proximity or conformational changes on the N-terminal signaling domain (Jones, Vance, and Dangl 2017). However, knowledge of whether this occurs, and of ensuing steps in the process, is inadequate. There is a need for research on NLR mechanisms in multiple pathosystems. Although we cannot yet design new disease resistance genes, foundational knowledge has enabled some new recognition capacities to be created. For example, changing a protease recognition sequence in the PBS1 "guardee" protein enabled its guard, the RPS5 NLR protein, to recognize different protease effectors (Kim et al. 2016). Knowledge of which pathogen proteases are important players in plant-pathogen interactions will facilitate the development of multiple novel R genes. A major constraint on obtaining novel recognition abilities is the capacity to screen for R proteins that provide a useful phenotype without constitutive activation. If clones could be transiently delivered and tested for capacity to recognize specific effectors, for example with a defense promoter:luciferase reporter fusion, thousands of clones could be evaluated in a high-throughput manner. Synthetic biology and genome editing tools can also be used to develop rules for assembly and engineering of novel NLRs.

Signaling from cell surface PRRs is slightly better understood than signaling from NLRs (Couto and Zipfel 2016). We are, however, again not yet at the stage where PRRs can be designed with novel recognition capacities. As with NLRs, more detailed structural information is required before this will be possible. In the interim, identification of additional natural diversity in PRR recognition capacity would impact crop improvement. A promising approach is to screen diverse plants for novel PRR recognition capacities and to transfer useful corresponding receptors between taxa. For example, species in the *Brassicaceae* can detect the apoplastic bacterial translation factor EF-Tu via the RLK EFR, but Solanaceous species cannot; transfer of *EFR* to species in the *Solanaceae* elevates resistance to several bacterial diseases (Lacombe et al. 2010). There is an urgent need to discover novel PRR ligands from a broad spectrum of pathogens/pests, including nematodes and aphids (Manosalva et al. 2015). PRR ligands will be useful for direct identification of new PRRs, screening for natural variation in strongly responding PRRs, and engineering new PRRs. Prospecting for novel recognition capabilities should involve biochemical exploration of pathogen components that trigger defense responses, searching for natural or induced genetic variation in such recognition capacity, cloning the corresponding receptor, and inter-generic transfer. Sequence capture targeted to RLKs and RLPs ("PRR-seq") could enhance the efficiency of identification of novel PRR genes. Development of methods to engineer effector-insensitivity into PRR response pathways that are disrupted by pathogen effectors is an additional opportunity.

Identification and deployment of diverse resistance loci (Scot Hulbert, Richard Harrison, John Walsh, John McDowell)

In addition to canonical plant immune receptors such as NLRs and PRRs, genes encoding other types of resistance are important for adding diversity and potential durability to resistance. One source of useful genes will be quantitative disease resistance (QDR) loci. QDR determine host resistance that results in a reduction, but not complete absence of disease. QDR can be controlled by quantitative variation in NLR or PRR activation or by completely different mechanisms (French, Kim, and Iyer-Pascuzzi 2016). QDR is frequently controlled by multiple quantitative trait loci (QTL) that interact with each other and are influenced by the environment (French, Kim, and Iyer-Pascuzzi 2016). Some QTL may encode modifiers that enhance immunity; others may encode genes that are not components of the immune system. Emerging opportunities for engineering enhanced resistance includes a better understanding of the mechanisms underlying QDR, including the role of chloroplasts and other organelles in plant defense. Genes have been identified that confer partial resistance to multiple diseases, including several rust species, and even to broad ranges of pathogens (French, Kim, and Iyer-Pascuzzi 2016; Moore et al. 2015). Pyramiding multiple QDR loci, either through marker-assisted breeding or the application of genomic selection, can provide broad spectrum resistance; for example, four QDR loci, each controlling a different aspect of resistance to the blast fungus, have been pyramided in rice

(Fukuoka et al. 2015). Natural variability at QDR loci can be identified using classical genetic approaches, pathogen phenotyping, and analyzing molecular markers of defense. Characterization of QDR loci can determine at which step during infection resistance is acting and if weak activation of classical defense signaling is induced. Transfer of existing, evolutionarily unique resistance mechanisms to other plant species is likely to be feasible in many instances. Pyramiding multiple sources of QDR with canonical immune receptor loci is a desirable strategy to achieve durable resistance.

There is great interest in the identification of plant susceptibility (S) genes that facilitate pathogen development and their manipulation for durable disease control (Singh et al. 2001; van Schie and Takken 2014). S genes that act during different stages of infection and against different pathogens and insects have been identified (Liu et al. 2013; van Schie and Takken 2014). Recent advances in genome editing technologies greatly enhance our capacity to manipulate multiple S genes in crops. This approach is exemplified by S genes that control viral replication and translation in their hosts. Potyviruses require the host translation initiation complex including the cap-binding protein eIF4E (Kawaguchi and Bailey-Serres 2002). Natural variants in *eIF4E* and *eIF(iso)4E* have been identified in multiple plant species that abolish susceptibility to potyviruses (van Schie and Takken 2014). Importantly, plants possess more than one initiation factor complex isoform; isoforms seem to function redundantly and mutation of one isoform does not affect plant vigor (van Schie and Takken 2014). A natural knockout of *eIF(iso)4E* in *Brassica* resulted in broad-spectrum potyvirus resistance (Nellist et al. 2014). CRISPR/Cas9-mediated mutations of *eIF4E* have been shown to be a viable strategy for engineering resistance to multiple potyviruses in cucumber (Chandrasekaran et al. 2016). Similarly, knockout of *eIF4E* in tomato provided resistance to two potyviruses; however, plants remained susceptible to other potyvirus strains (Piron et al. 2010), indicating further research is needed to understand potyvirus-*eIF4E*/*eIF(iso)4E* interactions to inform exploitation and development of durable resistance. However, these pathosystems illustrate the potential of S loci as sources of resistance.

The identification of effector targets also provides opportunities for detection and targeting of new plant S genes. Multiple *Xanthomonas* transcription activator-like effectors enhance the expression of genes encoding *SWEET* sugar transporters, which are attractive targets for genome editing (Streubel et al. 2013). The wild type *MLO* gene in barley suppresses defenses against powdery mildew disease and is conserved across the plant kingdom. Natural and induced loss-of-function *mlo* alleles have been generated in multiple species using a variety of approaches including radiation and genome editing (Luo, Gilbert, and Ayliffe 2016). However, mutation of *MLO* can have deleterious physiological consequences requiring analysis over multiple environments and possibly introgression into an appropriate genetic background (Hulbert and Pumphrey 2014; van Schie and Takken 2014). Pathogen lifestyle should also be taken into account when targeting S genes and stacking different resistance genes. An R gene against a biotrophic pathogen can function as an S gene during infection by necrotrophic pathogen (Lorang, Sweat, and Wolpert 2007). Enhancing the foundational understanding of QDR and S genes provides an opportunity to expand our understanding of the mechanisms controlling both resistance and susceptibility. This information can then be translated into effective disease control strategies, especially with the advent of genome editing.

Modulating Plant-Microbe Interactions

Altering host-pathogen interactions using small RNAs (Blake Meyers, Wenbo Ma, Roger Innes)

Small RNAs are central players of RNA silencing, which is a universal and fundamental mechanism of gene regulation in eukaryotes. Extensive studies have established small RNAs as essential regulators of growth and development; moreover, accumulating evidence implicates small RNAs as having an integral role during plant-pathogen interactions that influences the outcome of pathogen challenge (Baulcombe 2015; Fei et al. 2016). Specific plant and pathogen small RNAs are activated during infection and there is bi-directional trafficking of silencing RNAs between multiple filamentous pathogens and their hosts (Baulcombe 2015; Weiberg et al. 2013). The importance of host small RNA pathways in plant defenses is evidenced by the multiplicity of effectors produced by viral, bacterial and oomycete pathogens that target host RNA silencing pathways (Pumplin and Voinnet 2013; Toruño, Stergiopoulos, and Coaker 2016). Our understanding of the involvement of small RNAs in pathogen/pest interactions is far from complete; for example, additional foundational studies are needed to address the regulation of immune-related host genes via endogenous microRNAs (miRNAs) and small interfering

RNAs (siRNAs) or other silencing pathways, with potential implications in epigenetics (Fei et al. 2016). There is also an urgent need to understand the mechanisms by which small RNAs are transferred from pathogens/pests to host cells and *vice versa*.

As our understanding of small RNA function and evolution advances, the number of novel opportunities to deploy this knowledge to safeguard plant health will increase. Pathogen suppression of host silencing pathways may be mitigated to maintain or enhance endogenous resistance. Host-induced gene silencing (HIGS) and RNA interference (RNAi) are being demonstrated in an increasing number of biotrophic, hemibiotrophic, and necrotrophic interactions (Baulcombe 2015). The efficacy of these approaches should be tested in numerous pathosystems, particularly against insects, pests, and parasitic weeds for which there are currently few alternative control measures. Constitutive ectopic expression of small RNAs can profoundly affect endogenous small RNA profiles with potentially deleterious consequences; research is needed to fine tune approaches such as HIGS. Research is also needed to determine if exogenous application of small RNAs is an efficacious approach to pathogen control and if so, what is the most effective way to deliver small RNAs exogenously. Because HIGS and RNAi can be targeted against vital pathogen/pest processes, they are anticipated to be durable; however, research is necessary to investigate the potential of pathogens and pests to counteract control strategies based on small RNA-centric approaches and to identify optimal targets to reduce the chances of evolution of resistance.

Multiple technological advances can facilitate a greater foundational understanding of small RNAs as well as aid in the deployment of translational approaches to utilize small RNAs for crop improvement. High-resolution imaging will enable investigations of transfer and localization of RNAs, both *in vitro* and *in vivo*, at tissue and subcellular levels, throughout the dynamic process of infection. Similarly, sequencing and quantification of small RNA, mRNAs, and small RNA targets in single cells will allow informative dissection of small RNA biology in plant-pathogen/pest interactions. Continued increases in genome sequences of both crops, models, and their pathogens, coupled with detailed molecular and biochemical experiments, will enable studies of the diversity of mechanisms by which plants and pathogens deploy and manipulate small RNA pathways to enhance resistance or avoid disease.

Immunomodulating chemicals: opportunities for chemical biology (Jean Greenberg, Alisa Huffaker)

Plants produce diverse small molecules that have the potential to significantly impact plant health. These compounds can collectively be considered metabolite immunomodulators. Their characterization could lead to breeding or engineering efforts to enhance plant health; also, some modulators may be useful for direct application to plants either as sprays or soil additives. Both beneficial and pathogenic microbes and pests also produce chemical-based effectors/toxins that might be exploited. Examples of activities of potentially useful metabolites include direct antimicrobials/antipests (Ahuja, Kissen, and Bones 2012; Christensen et al. 2015), signaling intermediates and pathway modulators (Shah, Chaturvedi et al. 2014), secreted compounds that can impact the phyllosphere or rhizosphere microbiomes (Huang et al. 2014), and pest/microbe chemical effectors that modulate plant behavior and resistance (Ma and Ma 2016).

To successfully exploit chemical immunomodulators, we need to define the chemical repertoires of plants and interacting organisms under diverse conditions, infer processes impacted by diverse sets of metabolic outputs, identify biosynthetic and regulatory mechanisms, and identify targets and modes of action. Furthermore, plants have diverse chemistries, some of which are family- or species-specific. Therefore, screening broad taxonomic groups is warranted. This will require collaborations with analytical chemists for natural products analysis and synthesis for proof of concept and/or deployment. A finer understanding of the roles of these metabolites will be gained when single cell metabolic analyses are feasible in order to dissect their roles in space and time during the infection process. An important goal will be to identify pathways for synthesis and action using biochemical genetic screens, metabolite-based genetic mapping, and expression based analyses; however, to fully realize the opportunities for identifying metabolites with potential value as control agents, additional assays may need to be developed. Opportunities also exist to generate novel compounds through using combinations of biosynthetic enzymes that may not occur naturally together (Wurtzel and Kutchan 2016).

At present, comprehensive metabolite analysis is not routine, especially when mixtures are complex, chemical libraries are limited, and there are many unknown compounds. Investments in national/international repositories for plant/microbe/pest metabolite identification and analysis are needed. Several approaches can be used and combined to identify immunomodulating chemicals. These include exploiting differing chemistries among diverse genetic backgrounds and mutant collections, informatics-led searches for novel predicted enzymes and activities (e.g. (Rajniak et al. 2015)), and bioassay-based approaches for discovery of new activities (e.g. anti-pest, anti-microbial, defense priming). As the sensitivity of instruments for chemical analysis improves and chemical libraries expand, it will become increasingly feasible to survey root exudates, vascular exudates, apoplastic extracts, plant-pathogen interface sampling, secreted molecules from microbes and pests to identify high value metabolites. As new activities and compounds are inferred, partitioning can be used to reduce the complexity of metabolite extracts. For this, it will be important to utilize multiple and complementary methods of extraction, derivatization, separations, and analysis. Once isolated, high-value unknowns can then be synthesized to determine their direct biological activities and mobility. Additionally, they can be more finely monitored to discern their spatial distributions.

There will be several translational opportunities stemming from these efforts. Biosynthetic pathways could be engineered to produce new bioactive metabolites into plants or other organisms; these could be useful beyond plant health applications. Furthermore, for pathogen/pest-derived chemicals, a next step will be to develop strategies such as HIGS to abrogate pest/microbe chemical effectors. As noted above, chemical immunomodulators could be applied in the field or plants with altered chemistry could be bred/engineered as part of a disease control strategy. Knowledge of the chemical repertoires of plants and their associated microbes/pests could allow the design of sensitive metabolite biosensors that would act as sentinels for perturbations.

Exploiting Organismal Interactions with Plants

Pathogen effector molecules as tools for accelerated production of disease resistant crops and dissection of plant biology (Sebastian Eves-van den Akker, Jean Greenberg, Wenbo Ma, John McDowell)

Diverse pathogens, pests, parasites, and symbionts deploy large repertoires of secreted proteins known as effectors to modify host processes for their benefit. Effector activities range from the suppression of plant immunity to the manipulation of host biochemical and developmental processes. In addition to these virulence activities, effectors can trigger immunity following recognition by cognate receptors, often NLR proteins (Lee et al. 2015). Effectors are thus central in dictating the outcomes of plant immunity and disease development. Comprehensive characterization of effector repertoires and determination of their modes of action should therefore be a high priority. Understanding effector biology offers several opportunities for disease control, as well as tools for manipulating plant biochemistry and development in the absence of disease.

Effectors that trigger immunity can expedite the discovery of R genes (see above and (Vleeshouwers and Oliver 2014). Selection of breeding material with individual effectors is an informative alternative to marker-assisted selection that can facilitate pyramiding multiple R genes, each of which confers resistance to most or all strains of a pathogen by allowing selection of each R gene individually. Effectors have been effectively used in resistance breeding to control diseases caused by diverse classes of pathogen (biotrophs, hemibiotrophs, and nectrotrophs) (Vleeshouwers and Oliver 2014). Effector-directed breeding also provides the possibility of identifying and prioritizing R genes that recognize core effectors that are broadly conserved within the species and play important roles in virulence. R genes that recognize core effectors are potentially more durable to pathogen co-evolution, because deletion or silencing of the effector would impose a fitness penalty on the pathogen; however, the caveats regarding possible second site compensating mutations and redundancy in effector function need to be considered (see section on durable resistance above). In addition, effector-based screens can be used to identify sources of resistance in plants that are non-hosts for the pathogen of interest.

Effectors are also needed for comparative functional studies of the biophysical/biochemical basis of immune-receptor activation (see above) (Maqbool et al. 2015). This will address how many ways there are to activate NLRs and how receptor complexes are impacted biochemically and biophysically by immune modulating effectors. Having this information will provide opportunities to re-wire activation mechanisms to facilitate resistance.

The roles of effectors that target host processes to enhance pathogenicity are less well understood relative to their roles in triggering immunity. However, it is already clear that effectors from divergent pathogens and pests target conserved pathways, such as flagellin and chitin mediated immunity, vesicle trafficking, and RNA silencing. Effector-targeted pathways reflect the strategies used by particular pathogens to overcome host defenses and establish disease. Mechanisms by which effectors alter host physiology, cell biology, signaling, and nutrition are profoundly under-explored. Multiple effector target genes identified so far encode susceptibility factors (Boevink et al. 2016; Yang et al. 2016). Such host factors can potentially be manipulated to provide resistance. Genome editing technologies can be employed to alter effector targets such that they retain function but no longer act as susceptibility factors (e.g. *SWEET* genes activated by *Xanthomonas* TAL effectors) (Li et al. 2012; Streubel et al. 2013).

Large scale sequencing and functional screens are leading to characterization of effector repertoires of an increasing number of pathogens and pests; however, this is far from comprehensive. Motif-based sequence analyses (e.g. the RXLR peptide motif of oomycetes) (Bhattacharjee et al. 2006) and the DOG box promoter motif of cyst nematodes (Eves-van den Akker et al. 2016) as well as structural similarity to fungal MAX and RALPH proteins (de Guillen et al. 2015; Spanu 2015) have revealed extensive repertoires of effectors. However, these searches only detect a subset of effectors and in the case of insect pests no such predictive motifs have yet been identified. Therefore, additional criteria are needed to identify effectors (e.g. prevalence, evidence for selection, reasonable levels of expression, and ideally, demonstration of a contribution to virulence or fitness). Furthermore, downstream functional analyses would be greatly facilitated by routine transformation, gene knock-out, and allele replacement technologies. All plant-parasitic nematodes, insect pests, and many fungi and oomycetes remain refractory to transformation, at least in part due to a lack of resources directed to this goal. Genome editing mediated by CRISPR/Cas9 has recently been reported in the oomycete *Phytophthora* and this technology holds promise as a tool for pathogen transformation (Fang and Tyler 2016). In addition, high-content screening (phenomics), in conjunction with reporters for alterations in host biological processes/metabolism/pathways (Qiao et al. 2013), could revolutionize the detection of causal relationships between effectors and non-immunity related phenotypes.

Effectors honed over millennia of host-pathogen co-evolution also provide tools for the finely tuned and exquisitely-specific manipulation of plant processes. Such tools may aid our fundamental understanding of plant biology, ultimately facilitating novel biotechnological applications (Li et al. 2012). The extent of host physiological manipulation during infection can be substantial. Some parasites, pests, pathogens and symbionts are able to induce the formation of novel organs in which the number and/or size of organelles is modified (e.g. giant cells formed by root-knot nematodes or galls formed by *Agrobacterium tumefaciens* or *Phylloxera*), while others can greatly modify source-sink relationships (e.g. green islands surrounding rust pustules). The ability to harness these effector functions and engineer the proliferation of chloroplasts, mitochondria, or even amyloplasts in specific tissue types has clear potential for biotechnological utility. In addition, effector biology has facilitated the discovery of biological processes. Examples of recently discerned effector biochemistries include: a newly identified mechanism of PTM (Zhang, Ma, et al. 2016), novel PTMs (e.g. uridylation of several receptor like-cytoplasmic kinases by AvrAC, (Feng et al. 2012); acetylation of histidines, (Lee et al. 2015) and novel metabolites (Schuebel et al. 2016). Consequently, knowledge of effector functions enables foundational research into the biological processes of the plant cell.

A detailed understanding of effector functions can have translational applications far beyond the plant sciences. For example, the sequence specific DNA binding activity of TALENs, discovered from *Xanthomonas* effectors acting as transcription factors, has been exploited for genome editing (Boch, Bonas, and Lahaye 2014). Such applications could not have been predicted using classical DNA-binding protein identification algorithms and highlight how many potentially useful functions may remain in the largely uncharacterized portions of effector repertoires.

Phytobiomes: Exploiting knowledge of organismal interactions to increase plant health (Duncan Cameron, Toby Bruce, Jeff Dangl)

In addition to improving genetics of a crop itself to enhance resistance against deleterious organisms, there are multiple opportunities to use beneficial plant-associated organisms as allies (Phytobiome_Roadmap 2016). These include many types of microbes, arthropod predators and

parasitoids, companion crops, and other organisms. Beneficial microorganisms play a central role in maintaining plant health in terms of both nutrition and defense. For example, arbuscular mycorrhizal fungi (AMF) and plant growth-promoting rhizobacteria (PGPR) not only enhance plant nutrient capture but also can directly modulate plant defenses (Cameron et al. 2013; Hiruma et al. 2016). The advent of high-throughput DNA and RNA sequencing technologies and increased capacity for characterizing small molecules from soil samples have driven a rapid expansion in environmental genomics directly germane to plant productivity (Blaser et al. 2016). However, virtually nothing is known of the principles of evolution and biochemistries that determine the composition of plant-associated microbiota above and below ground. Robust experimental systems are crucially needed to investigate principles of microbiota structure and function, from reductionist settings, through increasingly complex ecological settings, to deployment. Most crops have been bred independently of many of their rhizosphere- and phyllosphere-associated organisms, potentially due to loss of microbe diversity and intensity in agricultural ecosystems as a result of tillage and chemical inputs (Helgason et al. 1998). Traditional breeding programs may have inadvertently selected against beneficial microbial associations due to their use of high nutrient conditions and pesticides, which decrease opportunities for microbial benefits. For example, under ample soil nutrient conditions, the carbon drain of AMF can present a fitness cost, potentially selecting against traits favoring mycorrhizal associations. Research is required to evaluate the performance of different crop genotypes under low input conditions, including their ability to attract and sustain beneficial microorganisms.

There is a dearth of knowledge as to how intra- or inter-specific plant genetic variation impacts the plant-associated microbiota. Current results support the existence of a core microbiome that may be tuned by specific plant genotype x microbiome and genotype x environment interactions (Vorholt 2012, Bulgarelli, Schlaeppi et al. 2013, Hacquard, Garrido-Oter et al. 2015). For example, plant root exudates contain signaling chemicals that influence the species composition of the rhizosphere but little is known of natural genetic variation influencing the support of beneficial rhizosphere microbes. Harnessing beneficial microbes will be increasingly important as low-till, low-input agricultural systems are adopted (Cameron 2010). Foundational research is also needed to identify appropriate combinations of beneficial organisms that can be used to develop cocktails of plant growth promoting or biocontrol organisms. Addressing this difficult challenge is dependent on deriving associations of microbes that provide diverse benefits to plants and are also able to invade and persist as complex microbial communities in the target environment, potentially in a co-dependent manner.

Research is needed to investigate trade-offs involved in hosting potentially beneficial microorganisms. Priming is a long-lasting memory that provides potentiation of faster and stronger defense responses (Bruce et al. 2007; Conrath et al. 2015). Beneficial microorganisms have been demonstrated to induce defense; well-studied examples include root-colonizing bacteria that promote plant growth and provide enhanced broad spectrum resistance (Induced Systemic Resistance, ISR) to several types of pathogens (Biere and Goverse 2016). Pathogens can also activate resistance distant from the site of infection (Systemic Acquired Resistance, SAR) (Cecchini et al. 2015). Some signaling components are involved in both of these long-distance responses. The challenge is to ensure that plants have the capacity to be well-colonized with ISR-promoting microbes and also capable of adequately activating these signaling pathways for resistance. Priming or induction of plant defenses, particularly SAR, may incur a yield penalty, which is yet to be fully understood. Germplasm should therefore be screened to find genotypes amenable to beneficial colonization. Plant genes that regulate responses to different microbial populations should also be characterized to identify input genotypes for breeding programs to enhance beneficial associations. Progress towards implementing these strategies will require extensive sequencing for microbial characterization, high resolution metabolomics, the ability to culture and maintain promising organisms, and the ability to assess many plants rapidly for a variety of responses.

It is important to develop interventions for improving plant health that go beyond altering crop genetics. Small molecule signals generated in response to beneficial microorganisms could be commercialized for external application, in a similar manner to chemicals inducing SAR (e.g. azelaic acid and BABA (Cecchini et al. 2015; Jung et al. 2009)). Both biological control and biopesticides have much scope for development. There are multiple approaches to improving biological control by boosting

populations of natural enemies of pests, pathogens, and weeds. Classical biocontrol involves recruiting biological control agents from the areas of origin of invasive pests and weeds and introducing them to the areas where they have invaded. This approach has had several impressive successes as well as some inconsistent results. It requires long-term research efforts to find candidates, determine likely effectiveness, and verify safety. Conservation biocontrol involves exploiting resident populations of natural enemies of pests, weeds and pathogens as an ecosystem service; interventions to improve the effectiveness of conservation biocontrol are required to support natural populations. Again, the new tools for determining microbial community structure and identifying insect pest population structure help to build mechanistic understanding of the ecosystems, leading to more reliable predictions. This requires food resources and suitable habitat. Considerable progress has been made with field margins to support populations of natural enemies of insect pests; however, there is often insufficient movement of beneficials into the crop where they are needed. Lure and reward strategies to attract beneficials with semiochemicals coupled with food rewards that enhance their fitness and performance are required (Stenberg, Heil et al. 2015). A greater foundational understanding of the ecology of tritrophic interactions and signaling is needed to enable better recruitment of natural enemies of pests (Stenberg et al. 2015; Tamiru, Khan, and Bruce 2015), perhaps by breeding. Companion cropping can both repel pests and attract their natural enemies; a successful example of this is the push-pull system in Kenya (Khan et al. 2010). The development of biopesticides involves formulation of living organisms, for example an entomopathogenic fungus or a virus that affects insects, can kill the pest target and can be sprayed or applied like a pesticide. Research priorities include discovery of new agents, development of new biopesticide delivery methods, and approaches in which a killing agent is formulated with an attractant semiochemical.

Novel opportunities to control viral diseases (Lesley Torrance, Wenbo Ma, Savithramma Dinesh-Kumar)

Because viruses are obligate intra-cellular pathogens with small genomes, they are completely dependent on cellular host factors to complete their life cycle and on vectors such as insects, nematodes, or plasmodiophorids for dissemination. Plant viruses are comprised of either RNA or DNA genomes, which typically encode only four to ten proteins and differ in replication strategies (den Boon, Diaz, and Ahlquist 2010; Hanley-Bowdoin et al. 2013). Several aspects of viral biology remain insufficiently characterized. The last decade has seen major advances in characterization of host factors involved in replication and movement and virus manipulation of host gene regulation (Wang 2015). Viruses also modify host and insect vector behaviors (Blanc and Michalakis 2016; Casteel et al. 2014). However, the knowledge of the underlying mechanisms is still lacking. In addition, virus-plant and virus-vector interactions as well as regulatory host small RNAs are affected by environmental factors such as temperature and light (Blanc and Michalakis 2016; Ghoshal and Sanfaçon 2014; Sunkar 2010). A greater understanding of environment-mediated regulation of viral infection is needed. The basis of virus specificity for certain cell types and tissues and why some viruses have wide or narrow host ranges are also not understood. It is known that hormone and defense pathways are affected by viruses, but information on spatial and temporal restriction of viruses at the cellular level is lacking. Discovery of the underlying reasons may enable the development of novel strategies that restrict virus infection. The drivers of virus evolution and the mechanisms by which vector population complexity influences viral population composition and transmission remain incompletely known.

Multiple studies are needed to address these gaps in our knowledge. Single-cell genomics and transcriptional profiling may reveal molecular details of viral restriction, cell autonomous and non-autonomous virus responses, basis of seed transmission, and the influence of environmental factors and host developmental stage on virus infection. Development of anti-viral peptides targeting key components is needed to determine the basis of host and tissue specificity. Cryo-EM is providing previously unobtainable, high-resolution structures of plant viruses and it holds promise for resolving intracellular macromolecular virus-associated complexes (Hesketh et al. 2015; Kuhlbrandt 2014).

Approaches such as RNA-seq, small RNA sequencing, metabolomics, and proteomics should facilitate dissection of molecular signatures that are altered in the vector during virus acquisition and in the host upon infection. Furthermore, understanding of vector and host factors that facilitate virus replication and vector-mediated immune response on the virus is fundamental to engineering resistance to vector-transmitted plant viruses.

Post-transcriptional gene silencing (PTGS) or RNAi is fundamental to defense against RNA viruses. RNAi-mediated transgenic resistance strategies are effective against RNA viruses (Fondong, Nagalakshmi, and Dinesh-Kumar 2016), but not DNA viruses, which present different challenges for control. CRISPR/Cas9 has recently been used to engineer resistance against DNA viruses (Fondong, Nagalakshmi, and Dinesh-Kumar 2016; Ji et al. 2015); additional editing strategies need to be evaluated, including modification of susceptibility factors as has been used against potyviruses (see above) (Zaidi et al. 2016). Since mixed infections by multiple viruses are common in field settings, CRISPR/Cas9-based approaches should be evaluated for the feasibility of engineering broad-spectrum resistance against multiple viruses.

Minimizing and Monitoring Weed, Pathogen, and Pest Challenges

Weed control (Duncan Cameron, Rob Edwards).

The control of weeds is rapidly emerging as a major challenge to sustainable agriculture due to the rapid evolution of herbicide resistance in both conventional and GM production systems (Cummins et al. 2013). The problem has been further compounded by both the loss of many types of herbicide through stricter regulation and the lack of research and development of new modes of action for herbicides; this situation is unlikely to improve over the coming decade.

Herbicide resistance arises through two mechanisms. 1) Target site resistance (TSR), where the protein functions targeted by herbicides become insensitive to chemical disruption. This can arise through selection for genetic changes resulting either in reduced binding or in increased expression of the target. 2) Non-target site resistance (NTSR), where the activity of herbicides in weed tissues is reduced to sub-lethal levels either by neutralizing the herbicide, or through metabolic responses that reduce chemical injury. Our understanding of both types of resistance, their plasticity and evolution, is currently constrained by the lack of genome information for major agronomic weeds. In the case of NTSR, we lack fundamental understanding of the multiple mechanisms associated with this complex quantitative trait.

The opportunities for counteracting herbicide resistance can be broadly divided into developing strategies for the better use of existing chemical control measures, changing cultural practices, and developing new approaches to weed control based on new crop traits. In reality, durable weed control will likely require integration of all of these approaches. Immediate opportunities will be built on foundational research in the biology of major weed species, including the application of the technologies now in place for functional genomics of crops such as genome sequencing, transformation, and editing. Studies should be aimed at understanding the mechanisms underpinning the plasticity of resistance and the molecular basis of NTSR. Outcomes would include better diagnostic and predictive tools for the stewardship of existing products and the identification of new targets for intervention such as 'resistance-busting' synergists (compounds that restore the efficacy of the herbicde; Cummins et al. 2013). Changes in cultural practice, such as alterations in rotations and the use of cover crops as well as precision and robotic weed control, offer the most immediate opportunities for counteracting resistance; these will be best implemented through expanding training programs for agronomists and agricultural engineers. Public funding for field research programs to objectively test the efficacy of different approaches to weed control along with their life cycle analysis will be required to ensure rapid adoption.

To date, the use of genetic improvement as a route to weed control has relied on developing resistance to specific herbicides in the crop, the most well-known example being Round-Up Ready technology. This approach was initially projected to be durable; however, it has not proven durable due to over-dependence on a single herbicide and the resulting selection on weeds to develop resistance. Transformation of crops with new herbicide resistance genes still offers useful opportunities if used carefully in the field. For example, glyphosate-resistant wheat (which could be derived from non-GM classified transformation) would be a very useful tool to counteract NTSR in wild grasses in Europe.

In the longer term, the introduction of novel weed control traits into crops has great potential for future integrated management. There are multiple reports of weed-suppressive crop varieties. The underpinning mechanisms such as allelopathy, plant vigor, and nutrient use efficiency require greater foundational understanding prior to effective translation. Our advancing knowledge of plant pathology may also provide new strategies for weed control, including new herbicides based on microbial pathogens or mechanisms used by them, matched with crops bred to be resistant to these biologicals.

Control strategies developed for pathogens are also relevant to controlling weeds that directly parasitize other plants. Parasitic weeds including *Striga* in sub-Saharan Africa and *Orobanche* spp. in the Mediterranean can significantly limit crop yields both in the tropics and temperate regions. Traditionally, chemical control of parasitic weeds has been difficult because parasitic plant lifecycles are complex and the host and parasite have similar physiologies (Gressel and Joel 2013). In addition, resistant germplasm has been difficult to develop. Modern approaches have resulted in a deeper understanding of host resistance to parasitic plants (Timko and Scholes 2013). This makes introgression of R genes to current commercially desirable crop varieties now possible and hence a priority for future research and control efforts. Host-induced gene silencing targeted against vital parasite genes should be explored as a control strategy where transgenic crops will be accepted (Baulcombe 2015; Nowara et al. 2010).

Monitoring of pathogens, pests and weeds (Diane Saunders, Michael Shaw)

The implementation of any control strategy imposes selection pressures to overcome it. Recent disease outbreaks in plants have been associated with expansions of pathogen geographic distribution and increased virulence of known pathogens, such as in the European outbreak of ash dieback and wheat stem rust in Africa and the Middle East (MacLean et al. 2013; Singh et al. 2015). The scale and frequency of emerging diseases have increased with the globalization and industrialization of food production systems (Firth and Lipkin 2013). In the past it has been difficult to monitor for breakdowns in control. Current surveillance and diagnostic systems are reliant on lengthy and costly in-lab processes, such as PCR or ELISA based protocols. Genomic-based surveillance and diagnostic tools are still in their infancy; however, advances in remote sensing and sequencing technologies and increases in computational power are allowing unprecedented opportunities for real-time assessment of pathogen, pest, weed, and symbiont populations and the rapid implementation of interventions. Following the influenza paradigm of continual adjustment of the intervention, deployment of control measures should be driven by knowledge of the variability and evolution of pathogen/pest populations (Michelmore, Christopoulou, and Caldwell 2013).

High throughput sequencing is revolutionizing population genetics with further advances on the near horizon. This has stimulated the development of genomic-based surveillance techniques. One example is the development of “field pathogenomics” for surveillance of pathogen populations (Hubbard et al. 2015). This can be based on high-resolution transcriptome data acquired directly from field-collected samples of infected plant tissue. This approach was recently employed to determine the identity and origin of a *Magnaporthe oryzae* lineage that caused the first severe outbreak of wheat blast in Asia within just six weeks of sample collection (Islam et al. 2016; Malaker et al. 2016). Selective sequence capture of virulence and resistance associated genes could also improve the cost-effectiveness and resolution of field pathogenomics. Monitoring of human pathogens has capitalized on the recent advances in sequencing technologies; the deployment of portable real-time genome sequencing for surveillance of the Ebola virus in Guinea using the MinION platform provided sequence data that could be immediately exploited for guiding control measures (Quick et al. 2016). Similarly, genome surveillance for Zika virus using portable genotyping in Brazil enabled tracking of viral spread into new geographical regions. Widespread deployment of such devices will allow real-time monitoring of plant pathogen variation as long as it is accompanied by adequate reference sequence information. Detailed surveillance of pathogens and pests will reveal their population structure and effector repertoires at the individual and pan species levels. Genome analyses can reveal the center(s) of pathogen diversity, which could be the basis a network of phenotyping centers to analyze germplasm resistance. Furthermore, genomic-based surveillance can also be employed to improve the diagnosis and differentiation of pathogens present that are often misdiagnosed or present in mixed infections (e.g. Dothideomycete pathogens).

There are several challenges to robust monitoring. Sampling is a major problem. Recent work has shown that adaptive sampling can improve the efficiency of management of some diseases (Parry 2014; Parnell 2014, 2017); however, effective control requires detailed, intensive sampling of host populations which may not be showing symptoms (Cunniffe et al. 2016). The distinction between severe, explosive invasions and minor outbreaks which require less expensive intervention is challenging (Thompson et al. 2016). Foundational research on both theoretical and actual population dynamics on a landscape scale is essential. Therefore, new ideas and technologies are needed to detect pathogens and

pests at very low frequency. This is critical for plant hygiene and preventing introductions in the context of increasing global trade. Monitoring for volatiles that are either produced by the pathogen/pest or produced as a consequence to the plant defense response may help with the detection of certain diseases. This could enable the capture of latent diseases and would be deployable in shipping-based trade routes. Latent disease could be detected by machines or dogs. This could be an excellent opportunity for international collaborations to lead the development of diagnostic tools and testing their implementation.

Sensitivity is another challenge. Resistance to fungicides is hard to combat because much of the evolution has already happened when detected at the currently typical threshold levels of a few percent. Also, some fungicides are still effective even when some level of resistance exists (Oliver 2014). Loci likely to be involved in development of resistance are often known when a new fungicide class is introduced; it would be desirable to detect very low levels of change at these loci. The challenge is to find efficient, inexpensive, ways of sampling and to tackle the bioinformatics challenge of heterogeneous samples with many loci being sequenced and examined simultaneously. Monitoring generates very large datasets. Research is needed into methods for efficient data gathering from large numbers of locations and integration with meteorological data to allow accurate epidemiological modelling.

Remote sensing from drones or satellites is also providing vast amounts of data with increasing resolution and opportunities for monitoring crop health. Initiatives such as the aggregation of information from CABI “Plant clinics” (Bruce 2016) with specialists able to analyze overall patterns are of great value, but require research in both population biology and social science rather than only biological understanding at the molecular level. Weeds, viruses, nematodes, soil fungi that have limited capacity for movement and produce patches observable from a distance are well suited to remote sensing. Research is needed to link image analysis with data on field performance and genotype, including ground observation of suspicious patches. There is the opportunity for integration of remote sensing with grower observation and response; however, this will require strong partnerships with growers and pest control advisors.

Impacts of climate change on pathosystems and pathogen evolution (Becky Bart, Jagger Harvey)

As we move towards lower input, sustainable agriculture under changing climatic conditions, it is critical that disease and pest control strategies be considered in the context of the environmental variation and uncertainties resulting from climate change. Climate change models project a range of potential scenarios; as climates change, pathogens, pests and vectors will spread into new areas and new diseases may emerge more frequently. While accurate climate modeling is still under development, the opportunity now exists to investigate how temperature, humidity, CO_2 levels, light quality, soil quality, and other environmental factors will affect plant health in the context of diseases and pests.

Experimental systems have advanced to the point that they can inform the pathogen/pest layer of climate change models. Investigations can be conducted using high-throughput, sophisticated phenomics approaches to track pathogen and pest interaction with hosts in controlled environmental chambers (Mutka et al. 2016) as well as in field settings (Chakraborty and Newton 2011; Fahlgren, Gehan, and Baxter 2015). Nonetheless, individual pathosystems need foundational studies before impact will be realized because our current predictive ability on decadal scales is severely limited (Shaw and Osborne 2011). There is a dearth of funding for studies of relationships determining long- and medium-term dynamics of plant disease; current understanding of host-pathogen-weather relations rarely extends to comprehension of changes in pathogen populations.

Complementary to studies on ecosystem and population dynamics, it is possible to study how environmental conditions that affect immune signaling at the molecular level. In cases where existing resistance genes are functional only within specific temperature ranges, approaches facilitating the expansion of this functional range could be explored. Additional molecular and genetic approaches to optimizing responses to biotic and abiotic stresses should also be investigated (Fujita et al. 2006; Whitham, McCormick, and Baker 1996). Climate change could also influence food safety; it is predicted to increase the prevalence of mycotoxin contamination, with new areas becoming at risk and current hotspots having more frequent and severe episodes (Battilani et al. 2016). Consequently, research into multiple avenues for reducing mycotoxins in human and animal food should be a high priority.

Because many diseases and pests are highly mobile and climate change will result in changes in cropping systems, global approaches to management must be deployed across national boundaries. In terms of food security, the effects of climate change may hit developing nations hardest, as these countries will have less nimble crop improvement programs and therefore will be less able to respond to climate change within existing breeding programs. Studying pathogen evolution on a global scale will allow developed and developing countries alike to better anticipate and respond to emerging and potential threats. Investments and collaborations with developing countries are critical to secure future harvests worldwide.

Translational Opportunities, Needs, and Challenges

The foundational research described above will provide a plethora of possibilities, including immediately implementable opportunities, for improving plant health in the field. No single intervention will provide a complete solution to disease problems; rather, each intervention should be considered as a component of integrated agricultural systems aimed at providing sustainable, high quality yields. This integration will require considerable coordination between academic, government, and private sector entities. Most developed countries have long traditions of translational research, for example through the Agricultural Experiment Stations in the US; however, state support for the continuum of foundational to translational research has progressively been eroded in both the US and UK as well as elsewhere. This trend must be reversed if the beneficial impacts of foundational research on global food security are to be realized. There is a fiscal “valley of death” between innovation and effective deployment at scale. This valley should be spanned by adequate public sector funding mechanisms to support pre-competitive translational research, possibly by stimulating collaborations of academic and government labs with small and large biotech and plant breeding companies, both nationally and internationally. It is also critical to have mechanisms, such as the cooperative extension system, to engage with end-users to increase the adoption of newly available solutions. Professional societies such as the American Phytopathological Society (APS) and the British Society for Plant Pathology (BSPP) should continue as effective advocates for funding translational research and implementation at the local, national, and global levels.

There are several challenges to implementation of control strategies. One is the handling of unprecedented amounts of data. Tools are needed to acquire, curate, query, store, and distribute vast datasets as well as integrate plant health information with other datasets, such as climate data, soil characteristics, agricultural activities, and crop performance. We are transitioning from a data poor to a data (over)rich situation. We should be more concerned about false positives than false negatives because the new technologies will present far more potential leads than can be pursued. Consequently, intelligent algorithms based on machine learning are needed to enable decision making in the context of precision, data-driven agriculture. These computational needs are far from unique to the plant health area. Bioinformaticians and computer scientists who are tackling these challenges in other areas need to be recruited to the plant health area.

Another key to successful implementation will be the two-way knowledge exchange and partnerships with all constituents in the food production and distribution chain, particularly growers, extension personnel, pest control advisors, and breeding company staff as well as consumer advocates and policy decision makers.

Capacity building and knowledge transfer for developing countries (Jagger Harvey, Toby Bruce, Becky Bart, Rebecca Nelson)

Translational research to enhance food security in developing countries was given specific consideration at the workshop. Developing countries face additional substantial challenges compared to developed countries. The US and UK plant health research communities have been engaged in mutually reinforcing collaborations and cultivation of the rising generation of plant health researchers as part of programs funded by USAID and DIFD as well as foundations such as the Bill and Melinda Gates Foundation (BMGF) and the CGIAR Consortium. This has resulted in significant cross-fertilization of ideas and exchanges of expertise and experience. In an era in which population growth, climate change, and emerging diseases demand a more global focus, models for integrating developing country partners as effective and equal collaborators are essential. These should be developed by scrutinizing extant and past collaborations for effectiveness, capacity-building of national systems, outcomes, and impact.

Strategies for focusing, integrating, and evolving such efforts are necessary to leverage the collective expertise and resources. Such efforts should result in a more responsive, integrated and proactive global community.

Although many developing countries in the tropics and subtropics have enhanced their human and infrastructural capacities over the past few decades, these efforts must be improved and accelerated because current capacity is inadequate to tackle the environmental, agroecological, socioeconomic and biodiversity (including pathogens and pests) complexities faced by agricultural systems in these regions. As an example, the USAID-supported CRSP and Innovation Lab efforts have trained ~3,500 developing country MSc and PhD scientists in the past 30 years. However, there have been limited efforts to evaluate and leverage this investment by tracking the alumni pool and supporting them in their home countries. The opportunity to access this quiescent expertise should be exploited to integrate these and a rising pool of researchers and other actors in collaborative efforts, and to generate a more global enterprise. Broader collaborations to recruit and support researchers in developing countries would be a major, feasible consequential action.

Key considerations for effective capacity building and knowledge transfer include:

- Giving national partners platforms and background information needed to assess and articulate national and regional plant health issues so as to develop national strategies and priorities.
- Constructing collaborations and capacity building programs around priorities and strengths of national partners that include complementary expertise from developed countries to address key challenges to improving food and nutritional security.
- Establishing equitable, bidirectional partnerships where developing country participants have leading roles in major components of the research, including developing capacities in their own labs.
- Assessing human and infrastructure capacity of in-country partners and where it can be effectively enhanced to inform plans as to where components of research programs should be conducted. Over the course of projects, national partners should be empowered to conduct increasing proportions of the research.
- Enabling reciprocal exchanges of researchers at multiple levels from senior researchers to postdocs and grad students as well as communications officers and agricultural economists. This applies to all stages of the project from formulation to final reporting.
- Developing appropriate technologies for end-point use. For example, high throughput DNA sequencing, RNA-Seq, small RNA-seq, or LC-MS/MS may be used by partners with the necessary infrastructure. As the project progresses, diagnostic tests should be developed that can be used in developing country labs or fields.
- Engaging other actors along the pathway to impact, including government (agriculture, health, trade), regulatory, private sector, and extension personnel, while being sensitive to the way both societies work.
- Developing international networking opportunities (match-making) to help interested scientists in developed countries identify and engage with partners in developing nations and *vice versa*. This could be achieved by conducting planning and workshop grants to help groups with common interests come together, likely facilitated by web-based platforms to help interactions and catalyze linkages; this could have multiple levels, including extension information exchange.

A key component for successful implementation of disease management strategies will be knowledge exchange with farmers. Farmers need to be engaged to ensure that they are aware of innovative approaches and that there is buy-in and adoption. This has to be a two-way process so that researchers are aware of the farmers' needs and priorities that lead to co-designing of solutions. There are huge opportunities to use information technology to engage with farmers. This is not a substitute for face-to-face meetings, but is complementary to them and keeps contacts active. With resource constraints to reach a very large number of smallholder farmers (estimated to be 33 million in sub-Saharan Africa) with poor transport links and few extension personnel, there are opportunities to use mobile phones to crowdsource information about plant health priorities and collect feedback on what works and does not work; the CABI Plantwise initiative might serve as a model (www.plantwise.org). Sharing information about potential solutions will target plant health interventions to hotspots where the problems are the most serious. Creation and support of village-based advisers as well as farmer to

farmer networks are important because farmers are more convinced when they see another farmer successfully using an approach than if an outsider tells them about it.

Acceptance of genetically modified crops (Jonathan Jones, Andrew Bent)

GM crops have the potential to make major contributions to food security. In the area of biotic challenges to plant health, they provide means to facilitate control of pests and pathogens for which current control options are inadequate, while greatly reducing the use of chemical protectants and thus reducing the environmental impact of agriculture (NAS, 2016). GM crops will be increasingly important to prevent a crisis in a more highly regulated pesticide/fungicide world. The commercialization of GM crops has so far been limited to a few crops, focusing primarily on herbicide or insect resistance (Giller 2016). GM trait development and deployment should be expanded for traits that directly benefit the consumer and that provide additional sustainability traits, including disease resistance. A more rigorous science-based system of risk assessment and an accordingly adjusted regulatory system are needed, to maintain stringent standards where appropriate while lowering the extreme economic cost of making benign and societally beneficial GM crop traits available to farmers and consumers. The ultimate release of GM crops with new traits will depend on advances in research and development, changes in public perception, regulatory requirements, and health and environmental assessments (Ricroch and Hénard-Damave 2015). Adoption will also be facilitated by detailed cost-benefit analyses of economic and societal factors.

The opposition to GM organisms (GMOs) is mostly an ideological issue (Herman and Raybould 2013), while consumer antipathy is largely due to a lack of understanding of crop improvement methods and zero tolerance of perceived risk. It is crucial to communicate better with the public and decision makers so as to allay poorly founded concerns about GM technology and to counter emotion-based opposition. It must be effectively conveyed that food crops are the result of breeding that involves a suite of technologies including chemicals, radiation, and molecular tools as well as conventional cross breeding. Transfer of R genes between closely related plants may offer a precedent-establishing an example of GM utilization that a broad sector of the public sees to be low-risk, beneficial, and also achievable but with far more costs, constraints, and reduced efficacy if done by traditional plant breeding. Genome editing that results in transgene-free genetically improved plants, with useful DNA inserted or deleterious DNA deleted at specific genomic locations, could help promote consumer acceptance of GM crops (Luo, Gilbert, and Ayliffe 2016). Efforts to foster communication among consumers, policy makers, industry representatives, and researchers should be continued so that GM crops benefitting all parties can be more readily brought into use. The potential benefits of GM crops to human health (e.g. camelina producing omega-3 fish oils) and environmental health (e.g. insect and disease resistant crops) need to be communicated more effectively to the public. Novel approaches toward changing public opinion could be deployed through collaborations between social scientists and those engaged in crop improvement. Considerable diplomacy is required because the opposition to GMOs is well funded and organized and resonates with public concerns about the environment and food safety. International collaborations could help provide evidence-based counter-arguments and examples to support a balanced and science-based regulatory policy that would benefit the public, researchers, and the agricultural industry. Britain's exit from the EU may provide an opportunity for development of its own science-based regulatory framework that is more consistent with those in the US, Australia, and Canada.

It is important that farmers and consumers continue to have options for both GM and non-GM crops and food, at a reasonable price. Issues surrounding intellectual property protection of crop cultivars apply to both GM and non-GM crop cultivars. Public sector crop improvement programs could make multiple contributions (for example, improvement of minor crop species, novel trait combinations for major crops, and training of the next generation of plant breeders in the use of transgenics) and may help allay various concerns (such as concerns over intellectual property and monopolistic control due to consolidation of the seed and biotechnology industries). It may become essential for governments to enact policies so that publicly beneficial GM crop varieties can become more widely available.

Conclusions

There is great potential to increase food production, reduce the environmental impacts of agriculture and enhance global food security, if adequate investments are made. However, this is a time-sensitive issue; climate change will likely cause plant health to worsen, reducing food security, and

leading to civil strife and mass migrations. Both short term and sustained longer term support for plant health research is necessary to enable both immediate translational implementations and foundational research to address major challenges for which there are currently no solutions. Some funding resources should be designed for flexibility to allow rapid responses to plant health crises when and where they inevitably arise. Global monitoring of the health of major crops modelled on that being conducted for stem rust (http://rusttracker.cimmyt.org/) should be implemented to minimize the vulnerability of the food supply to biotic challenges.

There are a broad variety of options for intervention strategies that maximize the evolutionary hurdles that pathogens, pests, or weeds must overcome before they evade control measures. However, development of alternative pest, weed, and disease management strategies is currently not happening fast enough to fill the gap left by losses of chemical protectants due to legislation and evolution of insensitivity. Current and imminent technologies could provide flexible interventions and reduce response times. Control strategies need to evolve at least as fast as the pathogen, pest, or weed; if they do not, then it is an ineffective use of time and resources to pursue those strategies. After further development, genome editing-based allelic replacement and gene insertion hold great promise for accelerating introduction of disease and pest resistance genes into elite cultivars that will be more durable.

There are multiple barriers to rapid and effective implementations. These include not only a lack of detailed foundational knowledge but also restrictions on germplasm exchange, legal and financial obstacles to deployment of GM crops, uncertainties surrounding IP and regulatory status of genome editing technologies, a dearth of plant breeders to exploit the wealth of new knowledge and technologies, and inadequate data handling capabilities.

The Green Revolution of the last century was largely based on the development of crop cultivars that responded well in terms of yield to high levels of inputs that included fertilizers and control chemicals. The challenge now is to develop crops and agricultural systems that will continue to provide good yields in the face of continuous evolution and global dissemination of pests, pathogens, and weeds as well as changing and more stressful growing environments. Sustaining the world food supply requires excellence in both foundational and translational research in parallel with agriculture becoming more data-driven. The necessary technologies and expertise are available such that, with sufficient investment, the future is bright for improving plant health as part of integrated and sustainable agricultural systems.

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Summary of Workshop Deliberations on Improving Plant Health

Area	Needs/Gaps	Opportunities	Approaches[1]	Immediate priorities & short term deliverables	Long-term Deliverables	Opportunities for Collaboration: Between US & UK	Opportunities for Collaboration: With Developing Countries	Opportunities for Collaboration: Other International
Foundational Research Needs, Opportunities, and Challenges								
Improving genetic resistance:								
Increasing the durability of resistance to pathogens and pests	Identification of resistance (R) genes that are likely to be durable. Improvement of genome editing technologies to enable pyramiding.	Development of strategies that maximize hurdles to pathogen virulence.	Pyramiding of resistance genes, preferrably with multiple modes of action.	Development protocols for testing durability under experimental conditions of accelerated pathogen evolution. Identification of R genes that detect conserved effectors. Techniques for rapidly stacking genes at single chromosomal sites.	Pyramids of resistance genes in adapted germplasm of crop species.	Studies in model pathosystems defining pathogen components recognized by R genes. Comparative functional genomics to identigy commonalities or novelties with non-model interactions.	Field studies characterizing pathogen evasion of R genes. Characterization of pathogen diversity and evolutionary potential.	Expansion of types of pathosystems studied. Widespread translational trials to evaluate durability of R gene resistance in diverse locations.
Identifying and engineering pathogen-recognition receptors	Identification of large numbers of R genes, including cell surface and apoplastic receptors. Detailed understanding of R gene function.	Characterization of R gene repertoires in crop species and function of multiple types of R genes.	Mining of wild species for canonical R genes. Structure-function studies of natural and designed R proteins, including use of synthetic biology, cryo-EM, and high resolution cell biology.	High-throughput screens for novel recognition abilities of R proteins. Expression systems to produce R proteins for structural studies. Structures of R proteins and complexes.	R gene catalogs from wild relatives of crop plants. R genes available for pyramiding. Engineered R genes with novel specificities.	Synthetic and structural biology approaches to understand structure-function relations of NLR proteins.	Screens of biodiverse plants and crop wild relatives for novel recognition capabilities.	Prospecting wild plant species for novel resistance functions. Development and deployment of field-scale, high throughput phenotyping platforms for gene discovery. Coordination with international genome projects.
Identifying and deploying diverse R genes	Detailed understanding of quantitative disease resistance and infection processes to identify opportunities for interventions.	Molecular characterization of polygenic resistance, responsiveness of defense response pathways, susceptibility genes, and effector targets in major and minor crop species.	Genome mining, expression analyses, high resolution cell biology, genome editing.	Evaluation of genetic materials at locations where variation can be assessed. Development of resistant cultivars with pyramids of R genes through marker-assisted breeding. Manipulation of S and defense response (DR) genes in crops using genome editing technologies.	New targets for interventions. Genes with different modes of action for incorporation into gene pyramids. Dissection and exploitation of large effect QTLs in major and minor crops for marker-assisted and genomic-informed breeding.	Experiments to transfer known resistance mechanisms to new crop species. Increased interaction with programs such as Rosbreed II for durable disease resistance in speciality fruit crops.	Develop (improved) transformation protocols for locally important crops. Testing of variability in efficacy of QDR in target crops at multiple locations.	Widespread translational trials to evaluate efficacy and durability of QDR under diverse conditions. Engagement with EU FP7 and H-2020 programs. Excellent opportunities exist for collaboration with Australia, New Zealand, Canada and Brazil.
Modulating plant-microbe interactions:								
Manipulating small RNAs to alter plant-pathogen interactions	Better understanding of the roles of small RNAs in regulating plant disease resistance and pathogen virulence and how they move between plant and pathogen.	Manipulation of regulatory pathways to enhance resistance. Identification of points of pathogen vulnerability .	High resolution detection of small RNAs. Characterization of small RNA dynamics by sequencing. Host-induced gene silencing (HIGS) of pathogens.	Identification of host-pathogen small RNA transfer mechanisms. Identification of targets for HIGS. Assessment of HIGS efficacy against different classess of pathogens; field tests with crop plants.	Novel intervention strategies. Crops with HIGS-mediated resistance. Assessment of durability of HIGS.	Evaluation of HIGS and RNA interference for efficacy against hard-to-control pathogens.	Deployment of crops with HIGS.	
Exploiting immunomodulatory chemicals	Identification and detailed knowledge of immunomodulatory repertoires from both plants and pathogens. Development of a chemical registry of metabolites.	Leveraging state of the art analytical instrumentation. Integration of metabolomic profiling with genomic and genetic resources.	Bioassays, genetic and chemical analyses to resolve activities and compound identities at biologically relevant levels. Spatial imaging of chemicals.	Profiling of plant and microbe immunomodulatory metabolites coupled with assays for bioactivity. Elucidated regulatory and biosynthetic mechanisms for metabolite production.	Deployment of molecules modulating resistance. Engineered biochemical defence pathways. New bioactive chemicals. Metabolite biosensors.	Integration of high-quality metabolite databases. Identification of mechanisms underlying metabolite-mediated resistance. Technology transfer to multiple cropping systems.	Bioassay-based screens for identification of candidate immunomodulatory metabolites. Deployment of crops with optimized biochemically-based immunity.	Collect diverse samples for profiling metabolites, bioactivity and underlying genetic control. Assess durability of resistance mechanisms in diverse environments.
Exploiting organismal interactions with plants:								
Characterizing pathogen effectors	Comprehensive characterization of effector repertoires from multiple pathogens and their modes of action. Knowledge of effector function outside of defense suppression.	Availability of genome sequences and high-throughput sequencing technologies to characterize effector repertoires. High resolution imaging to identify common subcellular targets exploited by effectors.	Large scale genome sequencing and mining. Determination of effector expression patterns. Genetic and biochemical functional screens and analyses.	Improved transformation technologies to support rapid functional analyses in pathogens/pests and vectors. Identification of conserved effectors and shared effector targets.	Expedited discovery, functional analyses, and stacking of R genes. Understanding of plant resistance and pathogen virulence. Tools for manipulating plant processes.	Reporter-based phenomics screens for biological pathways targeted by effectors. Development of novel functional assays. Organize collaborations based on pathways targeted rather than by pathogen.	Screens of non-host plant species for detecting effectors to identify novel resistance genes. Rapid genome/transcriptome sequencing of emerging pathogen lineages to identify effector repertoires and inform R-gene deployment.	Screens of diverse pathosystems to expand the repertoirs of effectors from disparate types of pathogen. Coordinate systematic genome sequencing of emerging pathogens.
Exploiting phytobiomes to enhance plant health	Characterization of the composition, evolution, and function of phytobiomes, and approaches to modulate the phytobiome for plant benefit.	Sequencing and analytical technologies to identify components of complex microbial communities, signaling cues, and interactions that influence plant health.	Metagenomic analyses of microbial communities above and below ground in heathy and diseased states using reductionist and natural settings. Co-analysis of genotype performance and phytobiome composition/ function.	Identification of major drivers of plant microbiome structure and function. Identification of management practices that favor beneficial phytobiomes. Deciphering of cross-kingdom signaling within the phytobiome.	Agricultural biologicals, including microbial inoculants and bio-based chemicals as novel biostimulants and biopesticides. Plant genotypes that enhance beneficial associations.	Co-screens of genotype performance and beneficial phytobiome recruitment potential under low input conditions.	Screens of microbes, microbial mixtures and bio-based chemicals for biocontrol, biopesticides and biostimulation.	Commercialization of agricultural biologicals, including microbes and small molecules for exogenous applications.
Modifying virus-plant interactions	More complete knowledge of mechanisms underlying viral evolution, replication, movement, and virulence.	New high resolution techniques such as single-cell genomics, high resolution imaging, and RNA sequencing for analysis of viral activities in plants and vectors.	High resolution cell biology. Cryo-EM. Single cell RNA and DNA sequencing. Genome editing of genes critical for viral infection.	Elaboration of the molecular signatures of vector and plant responses to infection. Single cell approaches to identify common sRNA/microRNAs that influence pathogenesis of multiple viruses. Optimization of approaches for engineering resistance to DNA viruses.	Identification of new opportunities for intervention and engineering resistance to both RNA and DNA viruses. Genome editing to alter S genes to effect viral but not plant processes.	Identification and manipulation of vector, host, and phytobiome factors that limit viral repication and vector dissemination.	Development and deployment of viral and vector control strategies.	International collaborations to obtain genome sequences of important vector species such as plasmodiophorids.
Minimizing and monitoring weed, pathogen and pest challenges:								
Controlling weeds	Genomic information on major weeds. Understanding of beneficial and deleterious plant-plant interactions.	Minimizing herbicide resistance through a better understanding of its genomic basis in weeds. Development of precision agriculture and integrated management practices.	Functional genomic studies of weeds. Research into cultural practices. Crop phenotyping for weed control traits.	Genome sequencing of major agronomic weeds including resistant biotypes. Screening plant germplasm for weed suppression and microbes and microbial products for weed control.	Understanding of the evolution and basis of herbicide resistance. Better diagnostic and predictive tools for durable herbicide use. New strategies for controlling weeds and parasitic plants. Reduced reliance on herbicides.	Identification of mechanisms of herbicide resistance.	Development of cultural practices that maximize weed control and herbicide durability.	Expansion of traning programs focused on optimized cultural practices for weed control and durable herbicide use.

Monitoring pathogens, pests, and weeds.	Real-time monitoring of pathogens. New detection technologies to diagnose and quantify diseases. Gobal collections of pathogen isolates/ecotypes/biotypes.	Advances in remote sensing, sequencing technologies, and computational power. Opportunities to test germplasm using relevant pathogen isolates.	Development of global networks for monitoring key pathogens of major crops. High throughput sequencing of field samples of pathogens and crops. Integration with remote sensor data. Establishment of global pathogen collections.	Linking remote sensing data with ground-truthing data on disease and pathogen presence. Identification of pathosystems requiring investment in monitoring.	Deployment of control measures driven by knowledge of pathogen variation. Germplasm with widespread efficacy.	Development of cost-effective, high-resolution diagnostic methods for field pathogenomics for surveilling major crop pathogens.	Development of partnerships to integrate data from farmer observations with remote sensing data. Development of disease assessments appropriate for each area.	Implementation of (volatile) detection methods for detecting pathogens during global trade. Exchange of data for development of science-based regulations for pathogen detection/validation and quarantine restrictions.
Assessing the impacts of climate change on pathosystems.	Understanding the impacts of climate change. Data to inform the pathogen layer of climate models.	Advances in tools for organism level measurements. Increasing sophistication of climate models.	Detailed phenomic and molecular analyses under controlled perturbations and field experiments.	Characterizing the impact of environmental conditions on pathogen epidemiology and on resistance in major crops.	More accurate predictive models. Global approaches to disease management. Modified R genes with efficacy under future climatic conditions. Attenuated increases in mycotoxin contamination of food.	Generation of data for climate change models using high-throughput characterization of environmental impacts on biotic stresses. Analysis and prediction of pathogen and vector responses to climatic change.	Generation of data for climate change models using field-based characterization of environmental impacts on biotic stresses.	Global integration of disease data to better predict and respond to existing and emerging pathogen threats.
Translational opportunities, needs and challenges:								
Translational activities.	Two way knowledge exchanges. Tools for handling unprecedented amounts of data. Development of decision trees. Coordinated efforts of multiple entities.	Tools for handling big datasets from electronic social media.	Recruitment of bioinformaticans and computer scientists to the plant health area.	Meta-analysis of plant, pathogen, and phytobiome compnents influencing crop productivity.	More effective translation.	Development of disease resistant potato, wheat, barley, and sugar beet varieties. Development of HIGS systems that target rust fungi and nematodes.	Translation to perennial crop systems (e.g. banana). Translation to minor (orphan) crops of local importance for food security.	Development of disease resistant wheat, corn, and soybean cultivars.
Building capacity in developing countries.	Increased capacity building. Models for successful partnerships in knowledge transfer.	Social media capabilities. On-going activities of professional societies, foundations, research universities, and government agencies.	Establishment of bidirectional partnerships. Two-way exchanges of information between partners. Engagement of extension and farmer networks.	Training of graduate students from developing coutries. Short-term training of research scientists from developing countries in collaboration with CGIAR.	Targeting relevant interventions to hotpsots.		Identify needs in priority crops. Collaborations facilitated by e.g. multiple national BBSRC, DFID, NSF, USDA, USAID and BMGF programs.	
GMO deployment.	Increased discourse to promote GMO acceptance. Rational, evidence-based decisions. Public appreciation and enthusiasm for improved crops.	Traits that appeal to consumers. Genome editing as a non-GM technology.	Improved communication with decision makers and general public.	Assistance for publicly-funded projects and those aimed at minor crops to comply with regulatory hurdles.	More efficient path to deployment of GM and edited crops. Increased consumer trust. Reduced environmental impact of agriculture.	Collaborate to develop science-based regulatory framework for GMOs. Share experiences and informational materials.	Involve existing and nascent regulatory agencies in GMO framework discussions.	
Genome editing.	Efficient methods for allele replacement and knock-ins. Technologies for reagent delivery that do not involve tissue culture.	Generation of stacks of R, DR, and/or S genes.	Technology development through multi-institutional collaborations with private sector and exchange of information and protocols.	Technologies for non-DNA-mediated genome editing of crops. Non-tissue culture based protocols.	Genome-edited, non-transgenic crops with enhanced disease resistance.	Exchange of methods and protocols. Collaborations with the private sector.	Targeting crops and cultivars relevant to developing countries.	

[1] Approaches: These are some of the most salient that could be applied and are not comprehensive. There are also overlaps and redundancies between areas that are not repeated.

Due to space constraints, the term "pathogen" in this table is inclusive of all types of biotic interactors including viral, bacterial, fungal and oomycete pathogens, insect pests, nematodes, parasitic plants, and where appropriate beneficial symbionts and weeds.

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