Science AMA Series: Neil Brown here to talk about how fungal pathogens sense the 'touch and taste' of their plant hosts and if this can this be used to fight crop disease. AMA!

Dr$_{N}eil_{B}rown$[1]$andr/ScienceAMAs$[1]

[1]Affiliation not available

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Abstract

Hello Reddit! I'm Neil Brown, a fungal biologist and a BBSRC Future Leader Fellow at Rothamsted Research in the UK. In my school leavers book, my friends were asked "What will Neil end up doing?" They answered "saving trees", to which I laughed. But it appears that they knew more about me than I did, as I now devote my days to understanding plant diseases, contributing to the knowledge and innovation needed to develop new ways to protect our crops. New approaches to control fungal diseases that threaten our food security and health, through the contamination of crops with harmful toxins, are urgently needed. To achieve this, I am asking: how does a fungal pathogen landing on a plant decide if it is a suitable host; how does it know where to infect or where to find the best source of food; and how does it know when to deploy different virulence strategies, such as the secretion of toxins or hydrolytic enzymes? These are the questions I hope to answer in my study of fungal 'touch and taste' receptors, similar to those found on our tongue. I will focus on Fusarium, a fungal pathogen that cause disease on wheat, barley, rice and maize. The goal is to determine whether these fungal 'touch and taste' receptors are biological targets that can potentially be drugged to prevent a pathogen from causing crop diseases and toxin contamination. It would be great to discuss my research with you. So go ahead. Ask me anything. I will be back at 11am ET (4pm BST). In the meantime, you are welcome to find out more about me, and my international experiences as an early career researcher, in a blog entry I recently wrote for Rothamsted Research's 'A day in the life of a Research Scientist' blog series (http://www.rothamsted.ac.uk/day-life-dr-neil-brown). Hi everyone! Thank you all for this broad range of interesting questions. I will check back later to answer a any I missed. All the best, Neil

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DR_NEIL_BROWN R/SCIENCE

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Thank you for doing this AMA. I grow giant pumpkins competitively. Over the years I've noticed disease, including fusarium, usually shows up on the heels of insects that bite the plant. I've also heard that fusarium lives year to year in the soil. Are you suggesting that fusarium is an airborne infection? I really would like to know the best prevention strategy.

checkyminus

There are many Fusarium species which live in the soil. I work on Fusarium graminearum, which causes Fusarium Ear Blight on cereals. It also lives in the soil and produces resting spores that can survive many years. But it is the airborne spores which are released by the fungus that enable this pathogen to infect the wheat floral tissue. Therefore, yes I am saying that Fusarium Ear Blight is an airborne disease. But it is only a threat when rain coincides with flowering. However, other Fusarium species, such as Fusarium solani and Fusarium oxysporum, also attack plants directly from the soil,

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including pumpkins. Unfortunately, I am not an expert on pumpkin diseases and cannot advice on the best control strategy for this crop. However, the removal of crop residues and crop rotation should reduce the build-up of the pathogen responsible for your diseased pumpkins in the soil. Interestingly, dual aphids and Fusarium infections of wheat increases the severity of the disease and mycotoxin production (http://aem.asm.org/content/81/10/3492.short). Hence, the interaction between pests and pathogens that you mention are common.

How many candidate receptors have been annotated at this point? Is there any reason to think that any/all of these receptors are specific to Fusarium? Thank you.

RabidMortal

That is a great question. There are 123 predicted G-protein coupled receptors in Fusarium graminearum, which is an awful lot of genes to investigate. So, to narrow down on the genes that are most likely to be important to infection, I have looked at the expression of these genes throughout wheat infection. Among the Fusarium receptors predicted in the genome, 106 are of a particular type, which is specific to filamentous ascomycete fungi, so they are not just specific to Fusarium. These are the PTH11-type receptors. PTH11 was a fungal receptor identified in Magnaporthe oryzae (another fungal pathogen of rice) that senses hydrophobic plant surfaces. Now, during Fusarium infections of wheat, it was primarily the PTH11-type receptors that were highly expressed. This has therefore enabled me to focus on these highly expressed, fungal specific, receptors. The fact that these receptors are not present in plant or mammalian genomes, but conserved among several economically important fungal pathogens, only highlights their potential as targets to fight fungal disease.

Could a plant "harm" itself to prevent being targeted by a fungus?

mcChinglies

Excellent! In fact, plants naturally do this. Plant cells have receptors that can detect self-damage, so the breakdown of plant cell walls caused by a pathogen, or the presence of an invader, such as the detection of fungal chitin. Activation of these pathogen recognition receptors initiates a rapid response that causes localised cell death, called the hypersensitive response. This is an effective way to contain a microbe that requires live plant cells.

But pathogens have coevolved with their hosts and some have acquired mechanisms to prevent their recognition, through the secretion of proteins, commonly called "effectors". A good example would be fungal effectors that bind chitin and therefore mask the presence infection. However, plants have also evolved ways to detect fungal effectors. Hence, this evolutionary arms-race between pathogen and host results in a reoccurring cycle of susceptibility and immunity, called the Zig Zag model. Please see this link for an excellent summary (http://www.nature.com/nature/journal/v444/n7117/full/nature05286.html).

Also some pathogens thrive on dead plant cells. Hence, the hypersensitive response would not be a good option to fight these pathogens. In fact, some of these necrotrophic pathogens target the host plants receptors to induce plant cell death to their benefit.

Nonetheless, the knowledge now being generate on these interactions between pathogens and plants will enable us to develop new ways to fight fungal diseases, through conversional plant breeding and through the editing of the plant's pathogen recognition receptors, either to improve pathogen recognition or to prevent the pathogen's exploitation of the receptor.

What is the most useful (and practical) thing you have learned about preventing fungal contamination in crops to date?

dear_life

The most useful thing that I have learned is that the pathogen will always win. There is no single magical solution to prevent fungal diseases and if we do, the pathogen will quickly evolve. For example, within a few crop seasons a pathogen can acquire resistance to a new fungicide or breakdown plant resistance. Is this a good return for the time and money invested in the development of a new approach? Hence, only by stacking our approaches to fight infection, will we improve the durability of newly developed control methods.

But it is this dynamic situation that make plant pathology such an interesting and worthwhile topic to study. Now, with the progress being made in real time "in-field" diagnostics, plus new methods to improve plant resistance, such as gene editing and host-induced gene silencing, and the development of new fungicides, we are approaching exciting times for plant pathology. And I am hopeful that by combing modern biotechnology with the careful usage of new approaches we can improve the sustainable production of safe food.

1 - Is there potential for exosome secretion by invasive fungal pathogens to have a key role in the distribution of mycotoxins throughout a plant?

2 - DON has been known to be an inducer of inflammation in the human GI, as well as a stimulant for immune responses by macrophages. Does a similar event occur within plant physiology?

hkzombie

This is a really interesting area of fungal cell biology that requires more attention. At present it is known that the mycotoxin produced by Fusarium, DON, is synthesized within fungal toxiosomes, prior to the final biosynthetic step which make DON more toxic and its secretion. This is a self-protection mechanism. However, within the plant it is not bound within a vesicle. Please check out this reference (http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0063077).

The impact of DON on plant cells is diverse. At high concentrations it can induce host cell death, while at low concentrations it can actually inhibit cell death. As you probably know, DON binds to the small ribosomal subunit, inhibiting protein translation. My studies of Fusarium gene expression during wheat infection show that the genes responsible for DON biosynthesis are highly expressed during the initial phase of infection, when the pathogen is in contact with live plant cells. Also when Fusarium is not able to produce DON, by genetically disrupting its biosynthesis, the plant mounts an enhanced defensive response, confining infection. Therefore, the working hypothesis is that during the early stages of infection DON inhibits the plant immune response, but ultimately the DON levels become toxic to the plant cell.

If targeting the "touch and taste" receptors of the fusarium is an approach to reducing infection and toxic contamination, would an alternate approach be genetic modification of the wheat itself, to fool the fungal receptors? If so, what are the relative pros and cons of each approach?

mothslice

Yes, that is an excellent idea. So I am trying the generate the knowledge to permit both approaches to be taken forward. First we need to know the fungal receptors required for infection and mycotoxin production, then we need to know what are the cues within the host plant that the fungal receptor detects.

We will then be in a good situation where we can develop ways to drug these receptors to inhibit infection and mycotoxin contamination. But also ways to manipulate, partition or sequester the plant molecules that the fungal receptors detect.

The "pros" to targeting the fungal receptors is that approximately 40% of modern pharmaceuticals target GPCRs in mammalian cells, suggesting that these extracellular fungal proteins are accessible druggable targets and large compound libraries already exist. But the "cons" are that you would still have to spray your crop and in the UK, it is hard to predict when Fusarium will be a problem. This would lead you to the "pros" of the plant mediated approach, as this would not require crop spraying or disease forecasting. However, it is likely to involve GM or gene editing technologies which are an issue in some countries.

Hi Dr. Brown, thanks for being here! What are the best ways to manage harmful fungus on home crops? Industrial scale farms? What does it mean to "drug" a fungus, or am I misunderstanding your approach?

p1percub

I am afraid there is no simple answer on how to best manage harmful fungi on home crops or in an agricultural setting. It is very much dependent on the pathogen, the crop in question and the location. But at the risk of over generalising, the best ways to reduce pathogen pressure is to rotate your crops and reduce that amount of residues left in the field. Then to grow resistant, or partially resistant, crops and to apply fungicides when the conditions are right for infection.

Now, to your question concerning my use of the work "drugged". It is my objective to identify fungal receptors involved in infection and then to attempt to develop compounds that may inhibit or activate these receptors. Hence, I wish to see if these receptors are "druggable" targets to prevent disease. So these compounds will not kill the fungus, but just manipulate their signalling pathways, perhaps preventing it from entering invasive growth or from producing toxins required for disease.

What is the official name and mechanism of action of the "taste and touch" receptors? I am interested in finding out if something similar could occur in mammalian fungal infections.

misophonia

Yes, this is also an active area of research in fungal pathogens of mammals. It is the fungal receptors that detect the environment in the host organism. And this is central to determining fungal growth, metabolism and virulence. In addition to playing a central role in the interaction with the microbial community within the host.

I am now working on G-protein coupled receptors in the ascomycete fungus Fusarium graminearum. If you are working on a filamentous fungal pathogen of mammals, then it is most likely that your pathogen has homologous receptors. However, if you are working on a basidiomycete pathogen such as Cryptococcus, then there are significantly fewer G-protein coupled receptors.

But there are many other classes of receptors in a fungal cell. For example; transceptors which can dually transport nutrients and activate downstream signalling pathways, extracellular mucins which detect surfaces, and the stretch-activated channels involved in thigmotropism (changing direction after coming in contact with a hard surface).

Are there fungi that eat other fungi? How difficult is it to change food preferance of a species or is this

impossible?

Davidjhyatt

Yes, there are fungi that eat other fungi, called myco-parasites. These fungi have attracted increased attention over the last decade, due to their possible exploitation as biocontrol agents. For example, Trichoderma virens or T. atroviride (https://genomebiology.biomedcentral.com/articles/10.1186/gb-2011-12-4-r40), which live in the soil, and are able partially colonise plants, while also myco-parasitizing other fungi.

So, we would not need to alter a plant pathogen's "taste" for plants, to a liking for other fungi. But what researchers are doing is trying to increase the potential of existing myco-parasites as biocontrol agents and improve their capacity to induce systemic plant resistance (http://aem.asm.org/content/71/7/3959.full).

Interestingly, these myco-parasites also have the same types of fungal touch and taste receptors, and it is likely that these receptors also perform a central role in the parasitism of other fungi.

Do you know of any work of this type being done with Phytophthora infestans on tomatoes or potatoes? P. infestans is the big scary boogie-man of vegetable growers. Thanks for doing this AMA! Keep up the good work--we appreciate smart people working on difficult problems!

delphicblue

Phytophthora zoospores swim toward their host plant roots, via chemotropism, so sensing the smell or taste of chemicals released by the plant roots. As in fungi, oomycetes such as Phytophthora infestans and P. sojae have G-protein coupled receptors that play an important role in sensing the environment. Researchers have shown that the downstream signalling pathways and to a lesser extent the oomycete receptors are important to Phytophthora infections.

In another fungal pathogen of tomatoes, Fusarium oxysporum, similar work is ongoing (https://www.ncbi.nlm.nih.gov/pubmed/26503056). Here the researchers have shown that the sex pheromone receptors involved in fungal reproduction also detect compounds release from the tomato roots and contribute to infection. This interesting work shows how receptors can actually perform multiple functions.

Therefore, I hope that collectively in the future we will be able to help protect your tomato plants. I also failed with mine this year!

Good morning Dr. Brown. A few years ago I attended a fusarium workshop at Kansas State University with Dr. Leslie. Through out the workshop, it was my impression that we still don't completely understand the biological pathways required for mycotoxin production, and in some cases, we don't completely understand the biological function of the mycotoxins themselves. For example, what is the benefit to the fusarium of producing fumonisin, zearalenone, or DON? Have we made any headway in understanding the biological pathways required for aspergillus to produce aflatoxins? Thanks for hosting!

elCaptainKansas

Yes, Dr Leslie is right. The exact roles of the many toxins produced by Fusarium are unknown. In the context of plant infection, DON is the best studied example, and while we know it is required for infection, and that it can inhibit plant defences, while also inducing cell death, the exact mechanisms for these action are not clear.

The biochemical pathway for the production of DON in Fusarium is well understood, however, the cell biology of where, when and why it is produced is still under investigation. And that is where my research comes in. As I aim to discover what signals within the plant influence the pathogens decision to produce DON.

Far less is known about the biosynthetic pathways and biological functions of the other toxic and non-toxic metabolites. To date 13 metabolites have been characterised in Fusarium graminearum, some of which have been shown to be involved in infection, such as siderophores which scavenge iron from the host, and other which don't, such as aurofusarin. In addition, Fusarium is predicted to secrete up to 54 other metabolites. The role of these metabolites in the interaction with the host plant, or with the microbial community consisting of other fungi and bacteria, is an exciting area of research that is progressing.