The John Innes Centre magazine
Winter 2017/18

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John Innes Centre
Unlocking Nature's Diversity

Advances

Welcome

Professor Dale Sanders introduces Advances

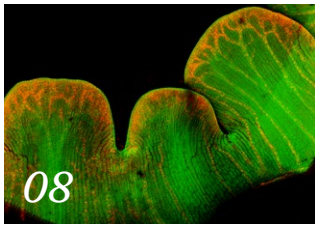
For scientific breakthroughs to have societal impact, often a relationship with a commercial or industry partner is necessary. Whether a project aims to improve crops, to uncover new valuable plant compounds, or to monitor global crop diseases, the translation of cutting-edge research into end use requires liaison and collaboration with partners who can provide technology scale-up, market knowledge and commercial viability.

In this issue of *Advances* we take a look at some of the ways that we promote the translation of our research to end use. In *George's Marvellous Medicines* (p3) we find out how investment in a translational facility, Leaf Expression Systems, gives a stepping stone to industry by providing proof of concept at a scale which is not possible in the research lab.

In our alumna section (p23), we talk to Dr Belinda Clarke, who studied for her PhD at the John Innes Centre. Her career so far means she can offer insight into how and why industry values academia, and why she is convinced that collaboration is the way forward.

At the heart of our science and innovation is support for individual researchers. Progress often relies on the hard work of teams, but it is important to recognise that teams are made up of individuals, be they PhD students, project leaders or scientific and laboratory support staff. The John Innes Centre values great ideas, irrespective of where they come from.

For instance, research assistant, Dr Martin Rejzek (p10) pursued a solution to a deadly algal problem on the Norfolk Broads – motivated by his love of angling he was supported to investigate further.



John Innes Centre
Unlocking Nature's Diversity

About the John Innes Centre

The John Innes Centre is a world-leading research centre based on the Norwich Research Park. Our mission is to generate knowledge of plants and microbes through innovative research, to train scientists for the future and apply our knowledge to benefit agriculture, health and well-being and the environment.

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Cover images clockwise from top left: tulips, infiltration of tobacco, Malca Schotten presents Lives in Science, green peach aphid, John Innes Centre Open Day 2017

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George's Marvellous Medicine

Bridge-building is a new preoccupation in the career of Professor George Lomonossoff, a virologist with a 40-year career in academic science. Not just any old bridge: this one spans the Valley of Death

Professor Lomonossoff says "The 'Valley of Death' has been spoken about since the biotech boom in the 80s and 90s, which saw the creation of a plethora of small start-ups – like the dot-com bubble. They didn't fail because the science was bad. But we couldn't scale it up. Investors want evidence if they are going to build a £100 million facility."

Early in 2017, the Norwich Research Park saw a significant first step in the right direction, with the opening of what Professor Lomonossoff playfully calls the "Facility of Dreams". Leaf Expression Systems is a John Innes Centre spin-out company at the Norwich Research Park, jointly owned by Plant Bioscience Limited (PBL) and the Biotechnology and Biological Sciences Research Council (BBSRC).

The company is an intermediate-scale facility, a transition point between academic discovery on one side of the Valley of Death and major investment on the other. The facility uses 'Hypertrans' transient expression technology developed in the Lomonossoff lab – a leafy production line using *Nicotiana benthamiana* plants, a relative of tobacco. Each plant represents a mini-green factory, its metabolism hijacked by soil bacterium, *Agrobacterium tumefaciens*, containing the necessary genetic information to produce proteins or secondary metabolites for pharmaceutical products. Batches of up to 42 plants are vacuum-infiltrated, then the products they express are purified in sufficient quantities to become vaccines and drug candidates which can be taken to commercial collaborators.

Advocates of using plants in this way say it's cheaper (plants need only sunlight, carbon dioxide and water to grow) and also quicker than established expression systems such as yeast, animal cells and bacteria.

A significant licensee of the Hypertrans technology is Canadian company Medicago. In North Carolina it has built a facility which covers the area of half a football field and houses 40,000 plants in a transient expression factory. Medicago has demonstrated it can manufacture the virus-like particles for an avian flu vaccine, reducing production times for ten million doses from nine months to 30 days. It is using the plants to develop a winter flu vaccine, with phase-three trials involving 10,000 people underway.

Another advantage of using plants is scale. The Hypertrans system enables labs, such as Professor Lomonossoff's working with proteins and that of Professor Anne Osbourn working with secondary metabolites, to produce scaled-up quantities of products. "Ten grams of proteins equates to about a million doses of vaccines, so it is not trivial," says Professor Lomonossoff. "It's a completely different scale to that of the lab. You need these quantities

for consistency, to demonstrate quality assurance and to be able to do reasonable-scale trials in animals for preclinical studies."

Like many of the best science stories, this all came about with one of those "lucky" accidents. Ten years ago, Frank Sainsbury, a postgraduate student working in the Lomonossoff lab, discovered a way of speeding up the clunky process of cloning into the expression vectors used in plants. By modifying the genetic instructions, Sainsbury discovered he could not only simplify the cloning process but, unexpectedly, could produce protein with a tenfold output increase (see graphic, right).

Professor Lomonossoff is happy to accept that a fortunate process set things in motion. But such fortune needs to be recognised for its significance and opportunities. The John Innes Centre team worked with PBL to get the Hypertrans technology patented. They improved the use of vectors and shared innovations freely with academic collaborators to raise the international profile of the technology. The turning point, says Professor Lomonossoff, came in 2012 when he and Sainsbury won the overall BBSRC Innovator of the Year Award. "This gave me the confidence to say, 'We really do need a way of scaling this up,'" he said. "We used that to knock on doors."

The result was the Leaf Expression Systems building, which was funded with a £5m grant and opened in January 2017. So what is the marker for success? "Success would be in five years' time, people going to get their flu vaccination and it would have been made in plants," says Professor Lomonossoff. "We want investors to do their research and development at Leaf Expression Systems and go and make their own facility, whether it's for small molecules or proteins. Leaf is not about commercial production, it's translational, it's the bridge."

REASONS TO BE CHEERFUL

One of the most exciting uses of breakthrough technology lies in creating a vaccine that would eradicate the age-old disease, polio.

In 2013 Professor Lomonossoff was asked to join a WHO consortium to investigate if his technique of using virus-like particles (VLPs) in plants would work as a way of producing a new polio vaccine. VLPs are engineered with the nucleic acid removed so they are not pathogenic – but contain enough material to stimulate an immune response. The collaboration was widely acclaimed when it made a plant-produced polio vaccine effective against Type 3 poliovirus in August 2017. It is hoped a vaccine produced in plants will be available in the next few years.

Polio was a global scourge until the middle of the last century. Well-known public figures affected by the virus included the singer Ian Dury, whose hit song *Reasons to Be Cheerful* was chosen by Professor Lomonossoff as one of his favourites on a local BBC radio show.

Effective vaccines have kept global levels of polio down to a few hundred. The vaccine currently uses a weakened version of the live virus which can cause poliomyelitis.

LEAN, MEAN TRITERPENE MACHINE

Recent work from the team of Professor Anne Osbourn has highlighted the role of the Hypertrans expression systems as part of a "step change" in the production of valuable small molecules with a host of medical, agricultural and industrial uses.

The Osbourn lab investigates triterpenes, natural products that are produced by plants and have a wide range of uses as drugs, agrochemicals, surfactants, and food and drink additives. The lab uses advanced genome mining approaches to scour the "dark matter" of plant genomes in order to search for new natural product pathways.

This has been greatly facilitated by the discovery, pioneered by the Osbourn laboratory, that the genes for many plant natural product pathways are organised in biosynthetic gene clusters, so making new pathways easier to find.

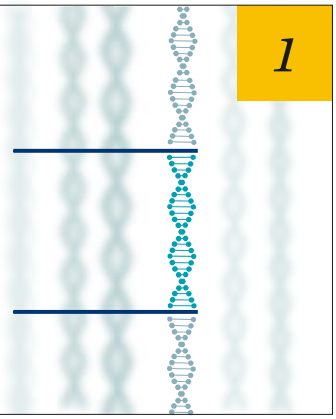
Alongside the Hypertrans technology, which allows valuable genes to be expressed in plants to deliver gram-scale amounts of molecules within weeks, Professor Osbourn says these advances represent a revolution for natural product pathway discovery and engineering, enabling the dark matter of plant genomes to be harnessed for medicinal, agricultural and industrial applications.

"Plant expression technology represents a whole new step change that could leapfrog microbial systems. We have shown that we can make gram-scale amounts of novel products rapidly. We are accessing chemistry that hasn't been accessed before."

1

ISOLATING GENES OF INTEREST

The gene or genes of interest are extracted from their host. In the case of producing the virus-like particles, the genes that produce and construct the virus shell (along with promoters needed to express these genes) are extracted.



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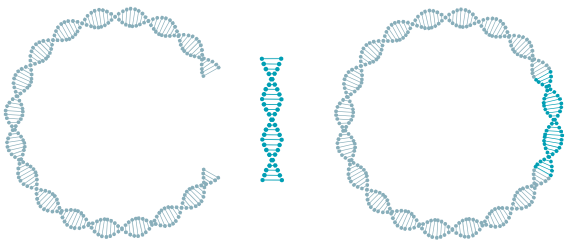


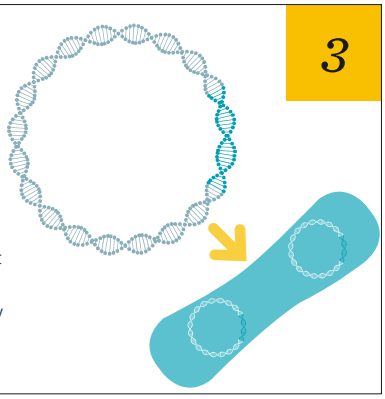
SPLICING INTO A VECTOR

The gene or genes of interest are spliced into a circular piece of DNA called a 'plasmid.'

3

INSERT VECTOR INTO BACTERIA

The plasmid containing the genes of interest is introduced into *Agrobacterium tumefaciens* using 'electroporation.' Electroporation is a technique that uses a burst of electrical charge to briefly increase the permeability of the bacterial cell membrane, allowing the plasmid to enter.



4

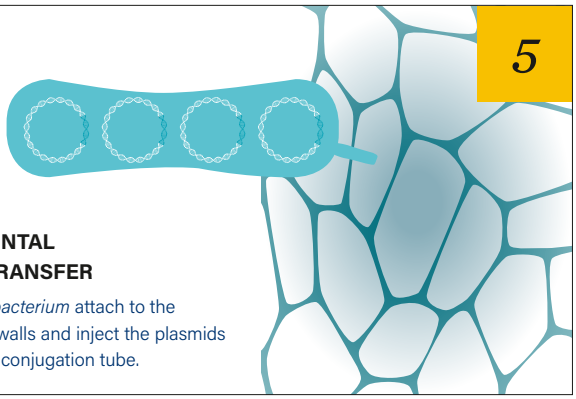
INFILTRATION

The liquid culture of *Agrobacterium*, now containing the engineered plasmids, is injected into the leaves of a plant. The plant most often used for Hypertans is *Nicotiana benthamiana*, a member of the tobacco family. The liquid fills the air spaces between cells in the leaf. This process is called 'infiltration.'

5

HORIZONTAL GENE TRANSFER

The *Agrobacterium* attach to the plant cell walls and inject the plasmids through a conjugation tube.



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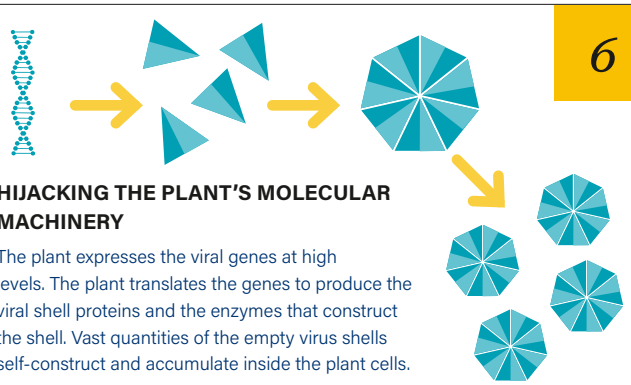
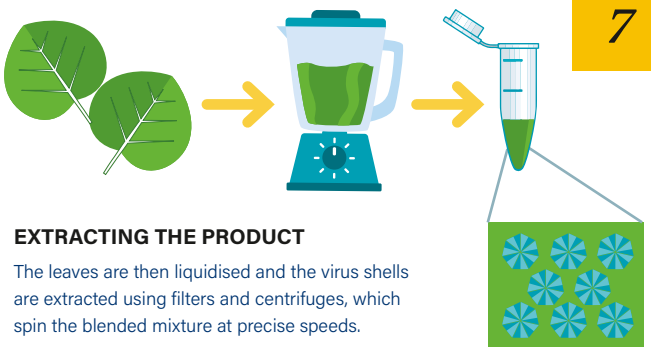


HIJACKING THE PLANT'S MOLECULAR MACHINERY

The plant expresses the viral genes at high levels. The plant translates the genes to produce the viral shell proteins and the enzymes that construct the shell. Vast quantities of the empty virus shells self-construct and accumulate inside the plant cells.

7



EXTRACTING THE PRODUCT

The leaves are then liquidised and the virus shells are extracted using filters and centrifuges, which spin the blended mixture at precise speeds.

WHAT'S SO SPECIAL ABOUT HYPERTRANS?

Taking genes from one organism and expressing them in another is known as 'heterologous expression.' In 2009, a breakthrough at the John Innes Centre by Dr Frank Sainsbury and Professor George Lomonossoff revolutionised the process. It had previously been thought that to get high expression levels of viral DNA in a plant host you needed to include promoters for both replication and translation of the transferred DNA. But when the promoters were left out, expression of the genes increased by around ten times. This change made the transferred DNA 'hyper-translatable,' which allows scientists to produce vastly greater quantities of valuable compounds, such as empty virus-like particles, using plants as a heterologous host.

Science Research Spotlight

A round-up of recent research from the John Innes Centre

Landmark discovery turns marathon of evolution into a sprint

A new way of rapidly generating medically significant natural products uses "Accelerated Evolution". A team including Isomerase Therapeutics Ltd, the University of Cambridge, Pfizer, Roche and DSTL inadvertently mimicked a process in bacteria that promotes the evolution of natural product biosynthesis.

The team aimed to produce a new version of rapamycin, used to treat cancers and prevent organ transplant rejection. This involved inserting a temperature sensitive replicon into the genes encoding rapamycin biosynthesis in the soil bacterium *Streptomyces rapamycinicus*. This introduced a genetic instability that activated the host's DNA repair process, making it "spit out" the replicon from the genome, along with varying amounts of the rapamycin biosynthetic genes. The resulting offspring produced rapamycin-like molecules.

Now the team plan to harness the Accelerated Evolution platform to generate "libraries" of new and potentially useful compounds.

+ ***Diversity oriented biosynthesis via accelerated evolution of modular gene clusters*** *was published in* Nature Communications.
DOI: 10.1038/s41467-017-01344-3

Plants use calcium to convey internal warning of attacking aphids

Aphids are a major pest, not only directly damaging plants but also acting as a vector, spreading damaging plant viruses. Professors Saskia Hogenhout and Dale Sanders have discovered how plants send internal warning signals in response to attack by aphids. They found that when an insect feeds on a leaf, it triggers the plant to admit calcium into the damaged cells. This small transport of calcium prompts the plant to signal that an attack is underway, and a larger amount of calcium is then mobilised from within the cell, initiating a localised defence response.

Calcium ions increase in plant cells in response to environmental changes. Before this study, the role of calcium in responding to specific biotic interactions, such as aphid feeding, was unclear.

The team used electrophysiological monitoring and a fluorescent reporter of calcium to reveal small elevations in plant calcium around initial-penetration sites. Combining these results with an evaluation of the genetic response, it was revealed that the elevation of calcium was dependent on the activity of specific cell membrane channels.

"Understanding the plant mechanisms involved in recognising the early stages of aphid feeding may provide information on how to stop the aphid in its tracks and prevent virus transmission," said Professor Hogenhout.

+ *The paper* ***Interplay of Plasma Membrane and Vacuolar Ion Channels, Together with BAK1, Elicits Rapid Cytosolic Calcium Elevations in Arabidopsis during Aphid Feeding*** *was published in* The Plant Cell.
DOI: 10.1105/tpc.17.00136

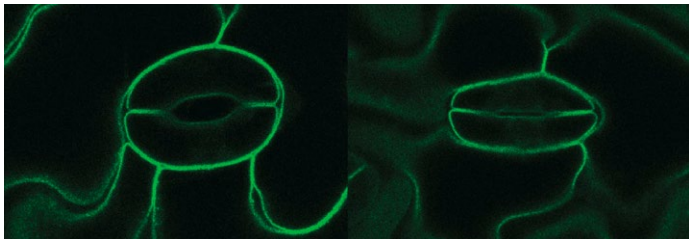
Changing of the guard: research sheds light on how plants breathe

A team led by Professor Richard Morris at the John Innes Centre, including partners from The Sainsbury Laboratory and the University of Madrid, has developed the first complete 3D model of a guard cell. Guard cells control the opening of stomata – tiny pores which plants use for gas exchange, water regulation and pathogen defence. Previous explanations of how stomata function have focused primarily on the characteristic thickening of the inner walls of guard cells, allowing the cells to balloon outwards as internal pressure increases.

Using a 3D simulation, the new research reveals the importance of three distinct characteristics that allow guard cells to function: internal pressure of the cells, elasticity of the cell walls and their kidney-shaped geometry.

Additional work with the University of Sheffield and the Sainsbury Laboratory in Cambridge using atomic force microscopy and computer modelling revealed a stiffening in guard cell poles. Polar stiffening reflects a mechanical pinning down of the guard cell ends which prevents stomata lengthening as they open. This leads to more efficient stomal opening.

These new insights could provide important clues for improving the resilience of crops to climate change.



The paper ***A 3-dimensional biomechanical model of guard cell mechanics*** *was published in* The Plant Journal. DOI: 10.1111/tpj.13665

Biofortified wheat could help to alleviate iron deficiency

A new biofortified variety of wheat, developed by a team at the John Innes Centre, contains twice the typical amount of iron – a feat which cannot be achieved by conventional breeding.

In modern wheat varieties iron accumulates in the outer parts of the grain, which are removed during production of white flour. Due to the low iron levels of the final product, many countries, including the UK, have made it a legal requirement to increase the iron content, often by adding iron-containing chemicals.

The team of scientists, including Dr James Connorton, Dr Janneke Balk and Dr Cristobal Uauy, used the recently published wheat genome to locate two genes that are responsible for iron transport. They then altered one of these to direct more iron into the endosperm, the part of the grain from which white flour is milled.

Breeders can incorporate this new understanding of iron transport into wheat-breeding programmes to produce wheat that gives white flour with enhanced iron content.

The paper ***Vacuolar Iron Transporter TaVIT2 transports Fe and Mn and is effective for biofortification*** *was published in* Plant Physiology. DOI: 10.1104/pp.17.00672

Green revolution genes promise additional yield

New research from Professor Robert Sablowski's team at the John Innes Centre has revealed that mutations selected during previous breeding for shorter stems can inadvertently result in crops with fewer flowers and seeds.

High-yielding semi-dwarf varieties of cereals were developed during the Green Revolution when plant breeders selected for individuals that were short-stemmed. Plants that have shorter stems are less likely to fall over in the field, and as a result greater yields are harvested.

When choosing shorter-stemmed individuals, breeders selected for variations in DELLA proteins. The team has now shown that the same DELLA mutations that cause shorter stems also reduce the size of the inflorescence meristem. The inflorescence meristem develops into the flowers, which in turn produce seeds, and therefore its size is a key factor in crop yield potential.

The new research also demonstrates how the negative effects of DELLA mutations on meristem size can be separated from the positive effects on plant height by additional mutations. Professor Sablowski said, "By separating the stem growth and meristem size effects, we could unlock further yield increases in widely used varieties."

This breakthrough exemplifies a way to mitigate the negative impacts brought about by trait trade-offs, potentially improving crop yields.

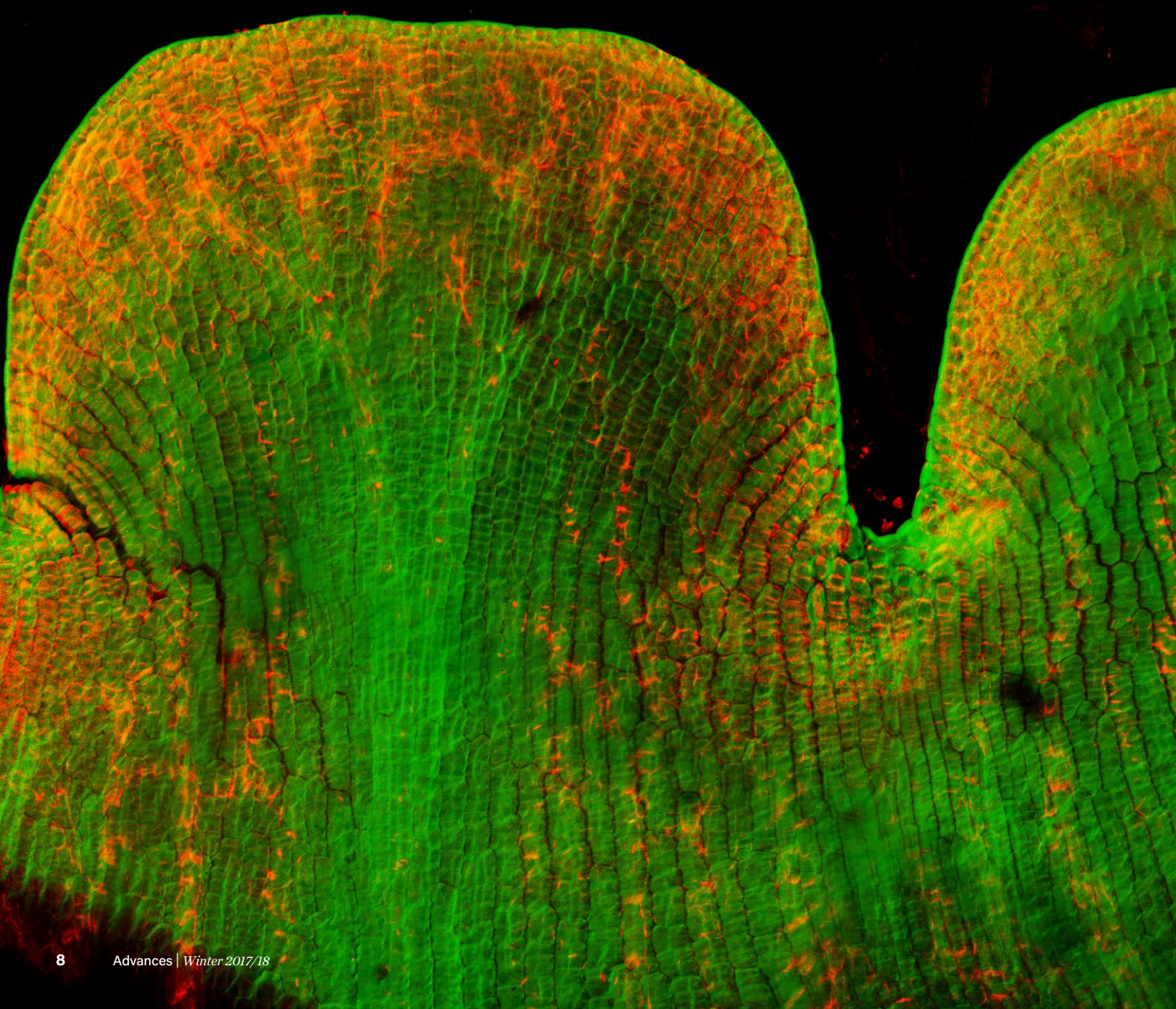
The paper ***DELLA genes restrict inflorescence meristem function independently of plant height*** *was published in* Nature Plants. DOI: 10.1038/s41477-017-0003-y

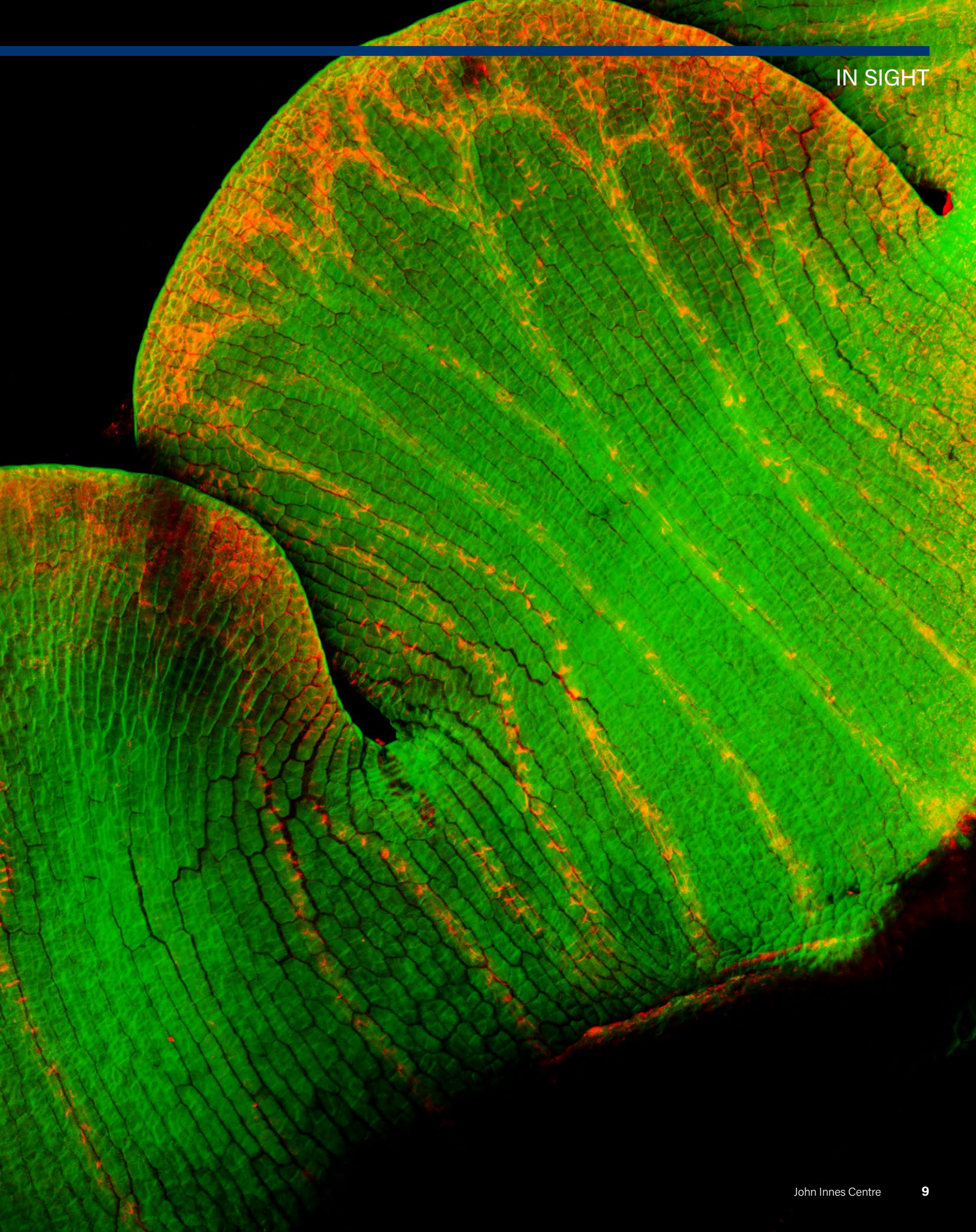
Glowing Review

Each plant cell contains the entire collection of genes for that individual, however, which genes are switched on may vary from cell to cell. A gene may be switched on in some cells and off in others, giving each gene a specific pattern of expression across tissues. Also the proteins produced by different genes may occupy distinct locations within each cell.

There are tools that can reveal where and when proteins produced by genes are located. One way scientists do this is by using fluorescently labelled antibodies which recognise and latch on to particular proteins. Then a specialised microscope can be used to see the pattern of where and when the fluorescence occurs. By visualising patterns of protein distribution it is possible to reveal how genes interact to produce a specific shape, or colour pattern, or response to an environmental stimulus.

In this image of an early stage of growth of a snapdragon (*Antirrhinum majus*) flower, a particular protein involved in hormone transport has been marked with red fluorescence.





At home in lab and landscape

As a boy in a small village close to Prague, Dr Martin Rejzek enjoyed a natural wonderland on his doorstep

Near his home was a lake and when he wasn't diving in, young Martin was on its banks casting a line as he nurtured a passion for angling. Arriving in Norfolk 17 years ago, Dr Rejzek, a natural product chemist at the John Innes Centre, struggled with life in a new landscape. So he set to work making a home from home.

Dr Rejzek joined the Norfolk branch of the Pike Anglers' Club, the biggest single fish species interest group in the UK. He recalls the warm welcome from a group of "proper Norfolk chaps" who agreed to take him out on to the Norfolk Broads. He says, "In a rowing boat you lose yourself in these awesome Broads, surrounded by reeds, the water and wild birds… At that moment, I became passionate about Norfolk."

But it soon became clear that Norfolk pike angling was experiencing troubled waters. "At meetings they would talk about regular fish kills caused by this alga called *Prymnesium parvum*. I had absolutely no idea what they were talking about," says Dr Rejzek.

Prymnesium parvum, the golden alga, is responsible for millions of fish deaths worldwide. Able to kill fish within hours, *Prymnesium* first causes chaos as the waters boil with the frantic activity of fish trying to escape. This is often the first sign of trouble from this stealthy killer, followed by thousands of dead fish clogging up the waterways (pictured right). John Currie, the general secretary of the Pike Anglers' Club of Great Britain, says, "Before the first *Prymnesium* wipeout in 1969, the Broads was one of the most important pike fisheries in Europe. But people had heard tales of *Prymnesium* and had started to give up on the place." Fortunately, for the £550m Broads tourism economy, things would take a turn for the better. Dr Rejzek researched *Prymnesium* and discovered it produces the toxin prymnesin, which previous studies had shown to be a highly complex organic molecule.

Professor Rob Field, project leader at the John Innes Centre, recalls: "Martin was desperate to help his angling colleagues in the Broads and smart enough to realise that here was an opportunity to bring all sorts of things together: fundamental science, engagement, economic and environmental outcomes. Maybe we could make a difference." He describes the toxin as a "beast of a molecule", a secondary metabolite with potential value as a natural product used for medicine and agriculture. "There were spin-offs in all directions: all sorts of biochemistry going on that we could use for industrial biotech."

An important breakthrough came when the team noticed what Dr Rejzek calls "some bizarre dots" in samples of the alga. These turned out to be a virus, which explained a mystery. The team had noticed that high *Prymnesium* cell counts did not necessarily lead to fish kills on their own. It was the presence of the virus, which at the end of its life cycle was causing cell lysis – with the alga spilling toxins into the water in one event – that was proving deadly.

Research continues to better understand the virus and the environmental conditions in which it flourishes. But for now, the greatest contribution of the John Innes Centre's team has been in finding a quick, cheap and readily available way of mitigating *Prymnesium* outbreaks. Research by John Innes Centre PhD student Ben Wagstaff and colleagues from University of East Anglia (UEA) revealed a candidate solution: hydrogen peroxide, the household chemical best known as hair bleach. "We developed a system in the lab using low enough concentrations that would kill algae but not affect fish or macroinvertebrates," explains Dr Wagstaff. "Then we took our lab understanding and sprayed a very small section of Hickling Broad which had been affected by blooms, and it worked brilliantly."

The breakthrough was hailed as a "lifesaver" by John Currie. "Thanks to this research we can save fish rather than observe them dying. To the local fishing fraternity, Martin and his colleagues at the JIC and UEA are heroes. It's hard to put into words how important this is for us."

It was also welcomed by the Environment Agency (EA), which has to pay the bill to deal with *Prymnesium* outbreaks. One operation to rescue 750,000 fish from Hickling Broad in 2015 took six weeks, costing just under £40,000 in staff time. "The John Innes Centre work on hydrogen peroxide shows how we can work together to translate research into real life," said EA Fisheries Technical Specialist Steve Lane.

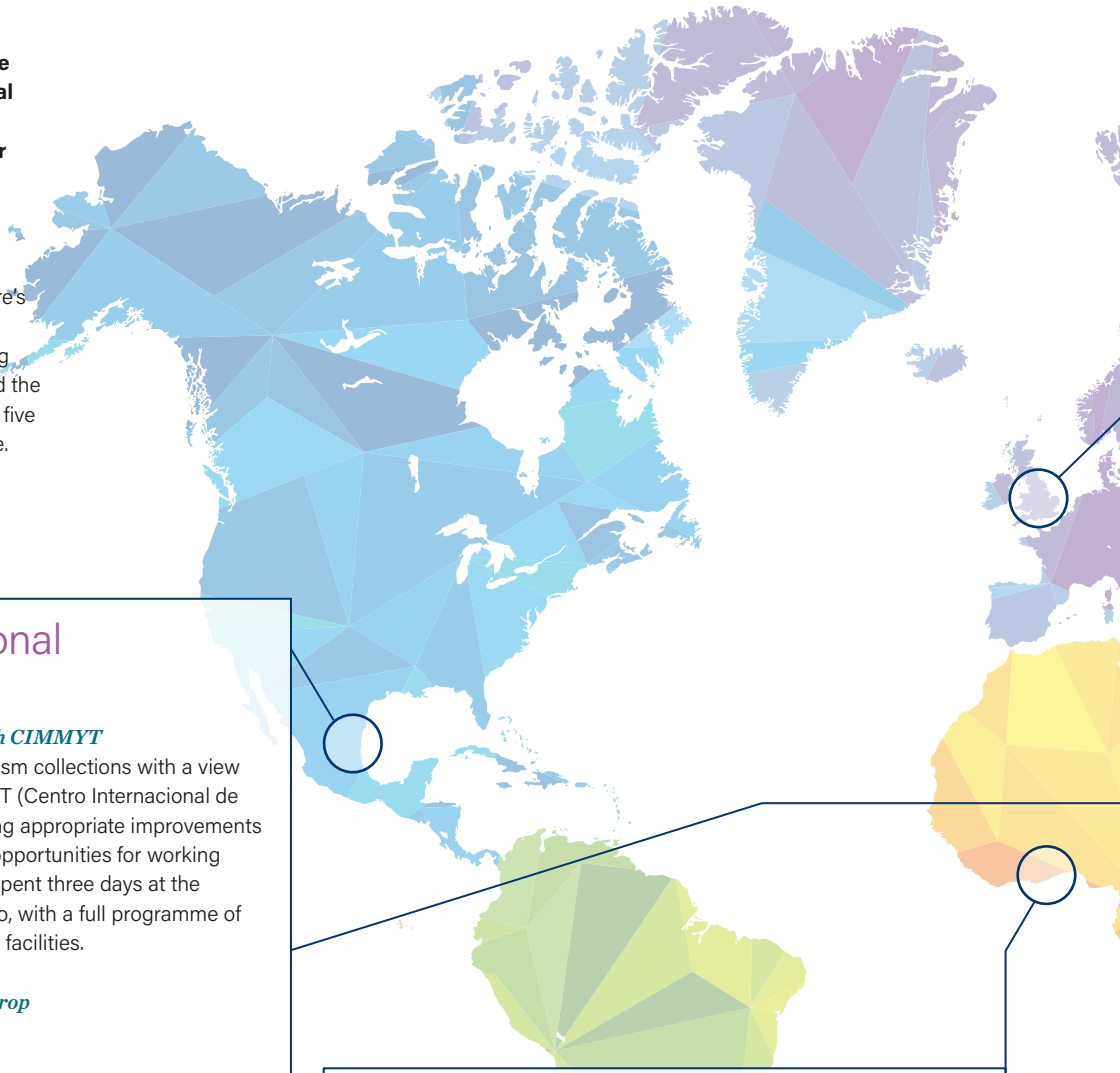
For Dr Rejzek, the Broads project speaks volumes about life in his lab and adopted landscape: "That is the beautiful culture of the John Innes Centre: it doesn't matter if you are a research assistant, or a project leader – if you come up with a good idea, then you will get the support. The Broads are a fantastic biological resource for seeking out natural products. We should study them, we should protect them."

> An important breakthrough came when the team noticed what Dr Rejzek calls “some bizarre dots” in samples of the alga. These turned out to be a virus

Accelerating our Impact

In 2016, the John Innes Centre was one of 23 UK centres to be awarded Global Challenges Research Fund support through a BBSRC 'Impact Accelerator Account' (IAA) to 'facilitate knowledge exchange and enable innovation in an international development context'.

The IAA strengthened the John Innes Centre's international development programme by supporting 17 projects across 22 developing countries in Africa, Asia, North America and the Middle East. The John Innes Centre set out five themes for the IAA, which are outlined here.



Deepening international partnerships

Case Study – Germplasm workshop with CIMMYT

The workshop was focussed on germplasm collections with a view to learning from best practice at CIMMYT (Centro Internacional de Mejoramiento de Maíz y Trigo), identifying appropriate improvements at the John Innes Centre and exploring opportunities for working together in the future. Six JIC scientists spent three days at the CIMMYT Head Office in El Batan, Mexico, with a full programme of presentations, meetings and tours of the facilities.

Case Study – Alliance for Accelerated Crop Improvement in Africa (ACACIA)

ACACIA was launched in June 2017, and will dramatically increase the range of partnerships between the BecA-ILRI Hub (Biosciences eastern and central Africa-International Livestock Research Institute), the John Innes Centre and the wider UK and African crop research communities. ACCACIA is an interdiscplinary partnership supporting African scientists to find solutions to local food security challenges by promoting research and building capacity.

Building research capacity

Case Study – Golden Gate training workshop

A workshop in March 2017 at the University of Ghana's Biotechnology Centre brought together scientists at various career stages from four countries for training in the use of 'Golden Gate' synthetic biology assembly techniques. The three-day programme, organised by the West Africa Centre for Crop Improvement (WACCI), in partnership with JIC, comprised lectures, lab work and Golden Gate exercises.

Improving understanding of international development challenges

Case Study – Meeting of Agricultural Scientist Support & Exchange Team (ASSET) in London

ASSET aims to increase effectiveness of agricultural scientists in the UK and sub-Saharan Africa by forming lasting collaborative partnerships. The programme pairs students from the two regions and supports them in their professional development through a peer-based network centred on peer-review exchange.

A year after the inaugural meeting in Kigali, Rwanda, the 16-person team, representing 12 nationalities met in London to share learning stories from a year of research and events, and develop tailored networking strategies to achieve specific goals for the coming year.

Broadening international partnerships

Case Study – Soft skills workshop

A four-day workshop hosted at the Punjab Agricultural University (PAU), India, aimed to coach early career scientists in science communication skills. The workshop brought together an array of international participants for a series of lectures and practical hands-on exercises covering important skills such as spoken and written scientific presentation skills, improving online presence, CV and fellowship applications and practical job interview experience.

Promoting development of interdisciplinary consortia

Case Study – Theory of Change workshop

The Theory of Change workshop was set up to develop new consortia between UK and African scientists, to develop shared objectives for agricultural research for development and to build a programme-level Theory of Change to inform the content of future projects. The workshop, which was held at the BecA-ILRI Hub in Kenya, was facilitated by the Agricultural Learning and Impacts Network (ALINe), part of Firetail Ltd.

Excellence, then relevance

Professor Dame Caroline Dean – who is a 2018 L'Oréal-UNESCO for Women in Science laureate – reflects on a memorable message

Excellence, *then* relevance. That was the constant message from the former Chief Executive at BBSRC Professor Julia Goodfellow in the late 90s. This fits well with the mission of the John Innes Centre – excellent fundamental research in blue-sky areas relevant to plant and microbial science, then maximising the impact of the new discoveries for societal good.

It is not always easy to predict what science will open new strategic opportunities. For example, who would have thought that the international genome sequencing project for *Arabidopsis thaliana*, which is not a crop, a pest or a pathogen, would be one of the most strategically important projects in plant science of the last 15 years? And it was coordinated by scientists from the John Innes Centre.

Professor Goodfellow's message has been very influential in my own research. As a postdoctoral researcher, there is always the question of what to work on when you get your own independent lab. I was a postdoc in California in the 1980's and I missed the noticeable seasons of my home in the north of England. I was intrigued by the different behaviour of the plants and began to investigate why. Then there was a moment that cemented my interest. I bought some tulip bulbs, and the man who sold them to me said, "Don't forget to put them in the fridge for six weeks before you plant them." That moment led me to my long-term research question of how plants align their development with the seasons.

So, when I applied to work at JIC (30 years ago!), I proposed to work on vernalisation – the requirement for prolonged cold for flowering. Commercial plant breeders have exploited this process to generate winter– and spring-sown varieties, but when I started we had no clue as to the molecular mechanism. It was the beginning of the arabidopsis era with the potential of cloning genes based on map position, with no other knowledge. They offered me the position and I arrived on 2 September 1988!

I began with three research questions: why do some varieties not flower until they have had cold? How does the plant know it's had prolonged cold? And how have those molecular mechanisms enabled adaptation to different climates – arabidopsis grows over a large range – from Cape Verde near the equator to northern Sweden. All three questions led to a focus on the regulation of a single gene, Flowering Locus C (FLC). FLC acts as a brake to flowering,

so if the plant is making the FLC protein, it won't flower. Conserved mechanisms regulating FLC expression, involving non-coding RNAs and chromatin (the interwoven DNA and protein that makes up our chromosomes), lie behind all three questions we had posed: how much the gene is expressed affects whether plants need to overwinter. Winter is registered by progressively switching off the gene in more and more cells. Adaptation is the result of small changes that affect the regulation of the gene.

So, after 30 years, my research has come down to a very detailed study of basic principles of gene regulation, important for human genes too. Instructions are given to genes in the embryo (human or plant), but the initial instructions don't stay around all the time; instead the instruction is remembered. The memory is passed down from mother to daughter cells by epigenetic regulation – through non-coding RNA and chromatin regulation. Epigenetics is being discussed everywhere at the moment – in the context of how the environment affects our genes. When memory mechanisms go wrong and genes turn on and off in the wrong place, disease is the result: most cancers carry genes expressed in the wrong place.

What is also amazing is that we can now build on our understanding of the vernalisation mechanism in arabidopsis to help plant breeders to produce commercial plant varieties that will respond to winter temperatures in predictable ways. New varieties could flower earlier, or be resistant to cold snaps, where previously premature flowering led to a glut of certain varieties at the supermarket. That's what the John Innes Centre is all about; discovering fundamental concepts, then translating the opportunities. Excellence, then relevance.

> That's what the John Innes Centre is all about; discovering fundamental concepts, then translating the opportunities

Celebrating 50 years in Norwich

In celebration of the 50th anniversary of this move to its spiritual home the John Innes Centre opened its doors to the public for the first time in eight years. Words from Andrew Lawn

The last time we opened our doors to the public was back in 2009, for our centenary celebration. Much has changed in the eight years since then and we were eager for another chance to tell the public about our research.

For the John Innes Centre, the support of our local community is very important, and equally important is keeping the public informed about our work, so in the build-up to the event we were delighted to appear on BBC Look East, Future Radio and in the Eastern Daily Press for the chance promote the event across Norfolk.

On the Thursday before the event, BBC Radio Norfolk's Thordis Fridriksson broadcast her show live from one of our laboratories. The three-hour morning show included interviews, hands-on demonstrations and guest appearances from Director Professor Dale Sanders and Professor George Lomonossoff.

Dr Anne Edwards captivated listeners with her animated telling of the invention of the famous 'John Innes' compost, and how the recipe was given away as part of the 'Dig for Victory' campaign in the Second World War. The show finished with a glorious hour of plant and science-themed songs requested by the listeners.

In the days and weeks before the event staff from across our site came together to transform the Conference Centre, greenhouses, seed store and grounds into an interactive, accessible, and fun-packed exhibition of our science. We have a large site, but we wanted to give visitors the chance to get up close and personal with our research.

Saturday dawned breezy and wet, but thankfully that didn't seem to dissuade the eager public from attending. Despite the doors officially opening at 10am, the Conference Centre was awash with visitors by 9:45.

All the volunteers were quickly in the thick of it, running busy activities, tours and exhibits spread across the site. The eagerness of staff to get involved was inspiring, matched only by the interest and enthusiasm shown by the visitors.

By 11am the whole site was buzzing as visitors got hands-on with all manner of activities including extracting DNA from a strawberry, making DIY lava lamps, listening to a tree drinking, tasting pea snacks, following the tree trail and exploring our greenhouses. At times it seemed as though half of Norfolk had turned up, from the very young to the

"Fabulous for my children. Hands-on, open dialogue. Please do it again."

"Brilliant family-friendly day. Accessible and fun but very rigorous and thought-provoking too."

"Lots more to see than I expected. I only came for an hour and stayed all day."

"The lab tours were great, really nice people. My daughter is a year 10 student and wanted to know about this environment for her future career."

"Very well structured event for all ages. The enthusiasm of the staff and volunteers was palpable – a triumph!"

"Lots to look at and learn whether you are 7 or 70."

"Loved the tour of microscopy."

"Eye-opening and very impressive."

very wise, and everything in between. Most amazing of all was how many young children came along, and how willing they were, not just to have fun (which they did in heaps), but also to learn.

Specialist tours of our seed store, historical collections, bioimaging and metabolomics departments proved more popular than expected and the limited spaces quickly filled up, unfortunately leaving some disappointed.

As the day wound to a close and staff came together to begin the clear up, there was a great sense of achievement among the tired feet and sore throats.

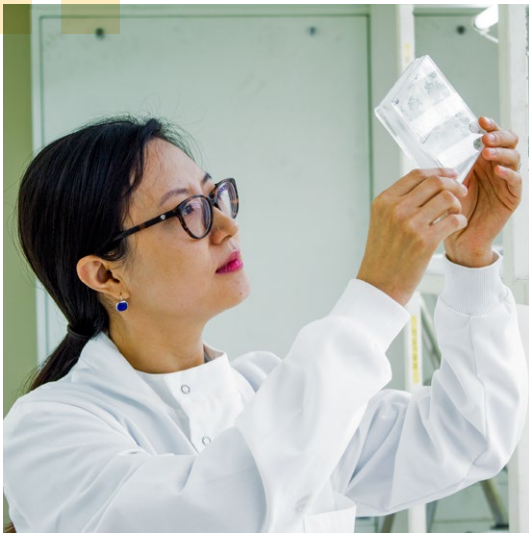
An estimated 3,000 people attended on the day, far exceeding our expectations. Most visitors came from nearby but we also welcomed visitors from as far afield as Devon, Nottinghamshire and even one group from Canada. The overwhelmingly positive response from the visitors demonstrates a great appetite for science among the general public. And with so many people asking, "When will the next open day be?", perhaps we won't wait eight years to do it all again.

NORWICH SCIENCE FESTIVAL 2017

The second Norwich Science Festival ran from 16-29 October 2017. Staff from the John Innes Centre took the opportunity to bring their work to the public and encourage visitors young and old to find out more about plant and microbial sciences. Displays included a history of pea genetics, barley for brewing and matching plants to foodstuffs.

The Crispr craze saw 600 DNA bases displayed on the floor of the Forum with visitors acting as guide RNA seeking target sequences in plant genomes. Alongside hands-on activities on stands, researchers Jacob Malone, Sarah O'Connor and Eugenio Butelli gave presentations about their work. These popular, accessible talks explored the potential of plants, the hidden life in soil and the value of colourful food.

Athena SWAN Gold Award



In October, the John Innes Centre became the first UK institution to win the Athena SWAN Gold Award – an achievement that reflects an ongoing dedication to becoming a workplace where everyone is treated with fairness, dignity and respect

The Equality Challenge Unit's Athena SWAN Charter was originally established to encourage and recognise commitment to advancing women's careers in STEMM, but has since been broadened to address wider gender equality issues, not just barriers to career progression that affect women.

"As an organisation, we have worked hard to introduce new family-oriented initiatives and to make current policies more inclusive," says Dr Carole Thomas, chair of the John Innes Centre's Inclusivity and Diversity Committee.

One standout success has been the introduction of 'Stop the Clock' for tenure-track scientists; a new initiative that offers some breathing space to new parents. Following the birth of her child, the new scheme gave Project Leader Dr Xiaoqi Feng the option to delay her tenure evaluation. "I find the support of maternity leave brilliant," says Dr Feng. "I feel that JIC respects my life choice of having a child, and went extra miles to make it easy for me to find my work-life balance."

Dr Xiaoqi Feng and Dr Siobhán Dorai-Raj

For Post-Doctoral Researcher Dr Siobhán Dorai-Raj, returning from a career break after starting a family could have been an intimidating transition, but a Daphne Jackson Trust Fellowship, partly sponsored by the John Innes Centre, supported her to return to work part-time while re-training in a new scientific field. "I find it an exceptionally supportive working environment," says Dr Dorai-Raj. "I have never felt anything but welcome and do not feel negatively judged for my part-time status."

The support she received during this time had a profound impact; she is now passionate about making it easier for parents to return to research after having children, and in February 2017 she started the Parents and Carers Support Group. Dr Dorai-Raj's burgeoning passion typifies a trend within the institute since receiving the Athena SWAN Silver Award in 2014. The intervening years have seen promising improvements under the framework of the ECU's Charter, including better policies, progress towards measurable targets and sharing good practice. But behind the headlines, another important but less easily measured outcome of the award has emerged.

"The enduring legacy of the Silver Award is a change in culture. Our staff are increasingly tuned in to equality issues and take a proactive role in addressing them," explains Dr Thomas. The new culture of consciousness means it's not only those directly affected who are spotting and raising issues of discrimination; an important step towards becoming a more inclusive and diverse organisation.

Equality and diversity is increasingly seen as more than an ethical obligation, and is now an integral part of competitive business strategy. "We believe that equality of opportunities is not only our duty to our staff and a moral responsibility, but is also key to achieving our institute goals," Dr Thomas explains. "Good science relies on open collaboration and cooperation, comprising diverse ethnicities, genders, ages and backgrounds."

Far from reaching the finish line, Dr Thomas insists achieving the Gold Award is just the shape of things to come. "This award demonstrates the progress we've made in our inclusivity and diversity journey, but we know that there is much more we can do.

"The next step is to better understand how to tackle discrimination holistically. We know that focusing on individual protected characteristics can compound equality issues, so future approaches must appreciate that individuals have complex, multi-layered identities."

An important aspect of the John Innes Centre's vision is ensuring that initiatives address career progression for all staff, not just scientists. Support is also provided to young students and peers locally and internationally through beacon activities such as the Women of the Future conference. For more information go to: www.jic.ac.uk/training-careers/equality-and-diversity

Lives in Science

With my project, Lives in Science, I wanted to inspire young people by telling stories about science through its scientists, finding out who they are, personally and through their practice. This project has been extraordinary and challenging: one of the biggest challenges I have faced in my artistic career

As an artist, I am inspired and driven by my love of drawing and my passion to reflect what matters in our lives through subjects that raise public awareness of key issues. By exhibiting thought-provoking projects in public spaces I hope to reach a wider audience and bring art into the public domain.

Lives in Science was a different sort of project for me, and I had come out of a dark place with a sick child since 2013 (thankfully, he is now fine and studying at Leeds College of Music). My last project was also in 2013, and while I never stopped drawing altogether there have been fallow periods. Working on this new and ambitious project, I was heading straight into a world that, for me and many others, is pretty intimidating.

When I first arrived at the John Innes Centre, I was both excited and terrified. With every project I do, my normal and rather unfortunate first response is to have a small meltdown, panic and tell myself I can't draw. My way of dealing with this is to face these demons head-on in an intense period of drawing in some form.

The time I had to complete this project was very tight. It took me almost two years to apply and receive funding for this project (partly because I am dyslexic and grammar isn't my forte. 'But this article is so beautifully written,' I hear you say!). Once funding was finally confirmed in March 2017, I only had six months to learn about the science and scientists, to draw them, and create the pieces.

After talking to scientists in many departments I drew up a list of six teams to become large, narrative, full-colour drawings for exhibition at JIC's '50 Years in Norwich' open day on 16 September 2017. The drawings would then travel to the Norwich Science Festival with a brochure, postcards and blog (*livesinscience.blog*) following the story of the project; I had lots to do.

There would be many frustrating occasions in which I would arrive, with sketch book, camera and audio recorder hoping to catch some science action and be told, 'oh this is a really busy time; you won't find anyone now,' or 'this is a really quiet time, they are mostly

MALCA SCHOTTEN

on holiday' or 'this is conference season, they are all away.' It was like fishing in the dark – I didn't have a clue where I was, what I was dealing with and whether I would even get a bite. Drawing scientists at work was proving to be a massive challenge!

If that golden opportunity – to draw a scientist – did offer itself, I would often find myself sweating and my hand shaking. When your head is telling you that you can't do something it has the power to disable you from the task in-hand. The thought translates like an electric charge from brain straight through to the finger tips, and can make drawing very difficult. The trick is to hang on for dear life until the joy of drawing kicks in again.

Timing in science is critical, and as a result, when a scientist tells you they will meet you in the lab, it can quite often be a movable feast. When they are there, their heads are

often bent over their work or they are jumping from one bench to the next. Talking was tricky; the concentration on their faces impossible to sketch – a major problem owing to the restricted time. Reluctantly, I found a solution in swapping my sketchbook for a camera to capture the energetic and assiduous activity.

My experience at the John Innes Centre was not at all what I expected, not that I'm even sure what that was. I was so pleasantly surprised by how very normal and approachable the scientists were. There were a few moments in which, at last, I found my comfort zone. Drawing Mike Ambrose was a sheer delight. As I shadowed him moving through the pea enclosure on a sweltering summer day, I found a happy place, Mike striking an assured pose and chatting about his life – perfect!

I have come out of this experience with my first real understanding of areas of science and its people, which I feel is a great achievement. Looking back, with more time and the freedom to work with my sketch book, I feel I could have really got under the skin of a life in science. So far, I feel I have only skimmed the surface.

As with most artists, I will always be critical of what I have done. In this whirlwind journey, I have met some extraordinary people from all over the world working together in a common cause for improving world health and food production. The rich diversity of cultures, language and learning is a distinct feature at the John Innes Centre, and it is one to be celebrated.

For more information, visit livesinscience.blog

> In this whirlwind journey, I have met some extraordinary people from all over the world working together in a common cause

Awards & achievements

Scientists at the John Innes Centre are recognised for their contributions to the research community, both nationally and internationally

Iceni Diagnostics

EDP Business Awards: Knowledge Catalyst Award

John Innes Centre and UEA spin-out company, Iceni Diagnostics, founded by Professor Rob Field and Professor David Russell (UEA), has won an EDP Business Award for developing a diagnostic tool designed to detect microbial and viral pathogens. The device uses a simple colour-change test to rapidly diagnose infections, consequently reducing the unnecessary prescription of antibiotics.

The EDP Business Awards are aimed at ambitious businesses and organisations that are underpinned by the acquisition, implementation, and exchange of knowledge. The judges look for a sustained commitment to acquiring and embedding new ideas in business planning and structure.

Professor Claire Domoney

Awarded an MBE

Professor Claire Domoney, Head of the Department of Metabolic Biology, was awarded an MBE in the Queen's Birthday Honours list for services to crop science and improvement to the UK pea crop. "I feel very honoured and humbled in receiving this award," said Professor Domoney. "I thank everyone who has worked with me to ensure that research outcomes are translated to benefit stakeholders and UK agriculture."

Professor Domoney is the UK's leading academic researcher on the pea crop. Her innovative research and leadership enables the breeding and development of improved crops with superior quality for food and animal feed. Her research also promotes knowledge transfer and has initiated three major platforms: the Pulse Crop Genetic Improvement Network, QDiPS and ProtYield, funded by DEFRA, BBSRC and Innovate UK.

Professor Sarah O'Connor

Elected as a member of EMBO

Professor Sarah O'Connor has been elected as a member of the European Molecular Biology Organisation (EMBO), joining a group of over 1,700 of the best researchers around the world. Professor O'Connor's team study the metabolic pathways that construct plant natural products with diverse applications, such as the anti-cancer agents vinblastine and taxol, and the anti-malarials artemisinin and quinine.

EMBO members are actively involved in the execution of the organisation's initiatives by evaluating applications for EMBO funding and by serving on the EMBO Council, committees and editorial boards.

Professor Dame Caroline Dean

2018 L'Oréal-UNESCO For Women in Science Laureate

Professor Caroline Dean has been named as a 2018 L'Oréal-UNESCO 'For Women in Science' laureate in life sciences for her "ground-breaking research on how plants adapt to their surroundings and climate change, leading to new ways for crop improvement."

Each year the L'Oréal Foundation and UNESCO name five outstanding female scientists – one from each continent. The awards celebrate women in science all over the world, with a particular emphasis on exposing the under-representation of women in prestigious awards.

Roger Castells-Graells

UEA Engagement Award

Roger Castells-Graells, PhD student at the John Innes Centre, is one of four students to be awarded a 2016/17 UEA Engagement Award. Roger has communicated his science at local, national and international events, including Pint of Science, the International Advances in Plant Virology conference, and "WhatIf"; an innovative educational project that Roger himself founded aiming to bring science outreach activities to students and high school children in Spain.

Dr Belinda Clarke

We caught up with Dr Belinda Clarke, Director of Agri-Tech East, who did her PhD at the John Innes Centre and continues to work closely with the Norwich Research Park organisations

How did you get into your area of research?
I did my PhD with Professor Alison Smith at the John Innes Centre, researching starch production in peas and potatoes. Starches have many important uses: in paints, thickeners, lubricants and the food industry including the sugar coating on jelly babies. Before that, I worked with Professor Anne Osbourn in The Sainsbury Laboratory as a lab technician investigating avenacin, the compound that gives oats protection from the take-all fungus. One morning, she said she had been reading about a tomato compound, tomatine, and that she had a hunch it would help her understand how oats create avenacin. She was right, and her epiphany has helped open up the field of plant natural product metabolism – the study of how plants make compounds with useful properties. Seeing how exciting it was to make new discoveries inspired me to study for a degree.

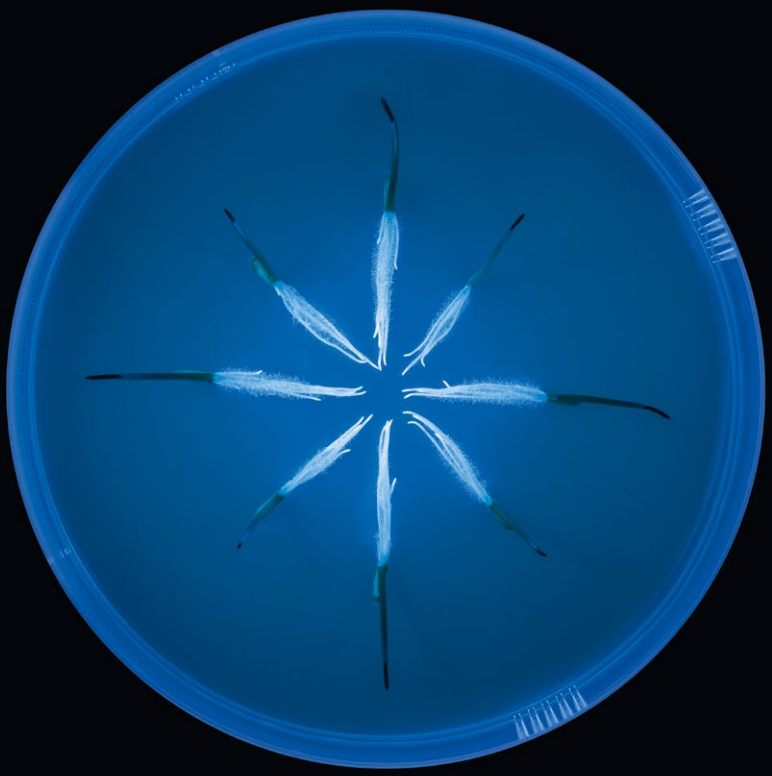
What persuaded you away from the lab?
During my PhD I experienced a second turning point in my life. The John Innes Centre created a stand for the Royal Norfolk Show and Alison's lab technician and I spent a very happy time making an interactive display to show how plants make starch. We tooled up with bricks, spray paint, Velcro, pipe cleaners and all sorts of fun things. I realised that I wanted my career to be about enabling science to have a wider impact, more than pushing the boundaries as a research scientist. When I was finishing my PhD, many research organisations and universities were encouraging people into communication, but I struggled to see a long-term career path, and how it would make a direct impact. I was far more interested in taking great science and putting it to use. I realised that I needed to operate at the interface of research, industry and government to ensure I could better understand the whole process and be directly involved.

What have you learnt from working with the industry sector?
I'm more convinced than ever of the need for collaboration – from discovery to industrial application. Discovery research is critical for the UK to retain its world-leading knowledge base. At the same time, we must not underestimate the appetite with which industry is looking to academia for solutions. Industry is made up of large and small businesses on whom careers, employment, pension funds and mortgages all depend. When science helps to reduce waste or to improve productivity and efficiency, our health, wealth and the environment all benefit. The expectations of industry and academia can sometimes start out of sync, but when they come together the impact can be tremendous.

How do we encourage academia and industry to work together?
There are a lot of tools and incentives to help academia and industry work together, but it can still be tricky to get the relationships set up. Very often people "don't know who they don't know" and expectations of outcomes, timescales and funding are not always aligned between the two groups. Sometimes a boost of "activation energy" is needed, often provided by a third party, to help overcome some of the barriers. I have always been excited by trying to provide that energy. Helping all parties understand the needs and drivers and expectations of the others from the outset can really speed up the connections and establish common goals.

As Director of Agri-Tech East, what is your vision for the organisation?
Our vision is to be a globally recognised catalyst for open innovation in agri-tech. The "open" aspect is crucial: looking outside one's existing or traditional network for solutions or partners, and thinking laterally around a challenge. Our existing relationships with plant researchers, breeders, farmers and other members of the supply chain will still be critical, but we're also interested in bringing the "non-traditional" players into the discussions, such as software engineers, materials scientists, imaging technologists and computer modellers – many experts in these disciplines are interested in working with crop biologists and growers to help develop new on-farm innovations.

> I wanted my career to be about enabling science to have a wider impact



Glowing oat seedlings

Aymeric Leveau (JIC), Gemma Farré Martinez (UDL), Andrew Davis (JIC)

Young oat seedling roots glow under UV due to the accumulation of the antimicrobial triterpene avenacins. Oats naturally produce avenacins exclusively within the root tip epidermal cells, which protects them from soil pathogens. Image supplied by researchers in the Osbourn laboratory at the John Innes Centre on the Norwich Research Park.

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