The Nottingham Arabidopsis Stock Centre

The Nottingham Arabidopsis Stock Centre (NASC) provides researchers with access to a unique collection of over 800,000 seed stocks from the model plant *Arabidopsis thaliana*[1]. These stocks underpin the UK's world-leading position in plant sciences research and are used in fundamental plant science research in laboratories around the world. They also play an important role in the development of new crop varieties by enabling researchers to work with the simpler genome of *Arabidopsis* before translating their results into more complex crop species. These new varieties will help address the challenges of climate change and the need for increased food yields for the world's growing population.

IMPACT SUMMARY

Resources provided by the BBSRC-funded Nottingham Arabidopsis Stock Centre help maintain the UK's world-leading position in plant science research, and have contributed to the development of new crop varieties.

The NASC maintains a collection of over 800,000 unique seed stocks from the model plant *Arabidopsis thaliana*. Those seeds are made available to researchers around the world.

- **NASC stocks underpin the UK's world-leading plant science research, and have done so since the NASC was founded in 1990. The UK is ranked first amongst G8 countries for plant science.**
- **Work on *Arabidopsis*, which depends on NASC stocks, enables research to develop new varieties of economically-important crop species, such as wheat, to increase yields and reduce susceptibility to changing climates.**
- **The NASC has led the way in encouraging researchers to share seed stocks and to see a benefit from doing so, supporting global plant science research.**
- **Globally, researchers using the NASC have access to validated genetic resources from other laboratories around the world, creating a level playing field for research.**

Over 800,000 stocks

The NASC holds a collection of seeds from over 800,000 genetically distinct lines of *Arabidopsis* donated by the global research community (see 'The NASC catalogue').

"*Arabidopsis* has an extremely sharing community," says Professor Sean May, Chair of Plant Cyberinfrastructure at the University of Nottingham and Director of the NASC[2]. "We've got stocks from the UK, from Germany, from the USA, from Singapore."

"We generate publications, but our biggest impact, the strength of the NASC, is in encouraging people to use standards, encouraging people to share, and making that happen."

Arabidopsis flowers. The NASC holds more than 800,000 *Arabidopsis* seed stocks, which underpin plant science around the world. Image: BlueRidgeKitties/Flickr. CC BY-NC-SA 2.0

Submitting stocks to the NASC offers several benefits to researchers in academia and industry. Maintaining stock collections requires time and resources, and sending biological material overseas can be complicated. By donating seeds to the NASC, researchers can concentrate on their scientific work, leaving the curation, management and validation of stocks to the Stock Centre.

According to Professor Simon Turner at the University of Manchester[3], "We deposit stocks with [the NASC]. It saves us a huge amount of effort. I'm obligated to send stocks [to other researchers who request them], but if we've already put it in the stock centre I can tell people to contact them."

Stocks held by the NASC are stored securely in dedicated seed facilities. They are made available to all, creating a level playing field for researchers, and all seed stocks are maintained and validated to ensure users receive precisely the genetic variant they require. (For an example, see 'Supporting Research').

Together with the Arabidopsis Biological Resource Center, or ABRC, at The Ohio State University in the US[4], the NASC provides an independent back-up for researchers in case valuable stocks are accidentally lost or destroyed.

The NASC supplies seed to researchers in Europe, while its sister-centre, the ABRC, supplies the Americas. Researchers from elsewhere can request seed from whichever stock centre they choose, and NASC users include researchers from Australia, China, Malaysia and elsewhere.

"We distribute around 130,000 seed tubes per year, which is a lot of seed," says May.

Arabidopsis seedings. *Arabidopsis* is the dominant plant used in research globally due to its small size, short generations and and small genome.

THE NASC CATALOGUE

Each seed stock held by the NASC represents a unique *Arabidopsis* genome. Two of the largest collections held by the stock centres are the GABI-Kat stocks from Professor Bernd Weisshaar's laboratory in Germany[5], which has provided thousands of stocks per year for the last few years, and the SALK stocks from Professor Joe Ecker at the Salk Institute in California[6].

Other important stocks include those donated by the 1001 Genomes Project[7], and mapping lines provided by Professor Caroline Dean[8], a Project Leader at the John Innes Centre, which receives strategic funding from BBSRC[9]. The NASC also holds stocks donated by companies such as Syngenta[10].

An online catalogue allows scientists to search for stocks by phenotype, location in the genome, or by other criteria. "Over the last fifteen to twenty years, we now have a mutant available for pretty much every *Arabidopsis* gene. You can order… a mutant along with information about how the mutant affects the phenotype of that organism. You can link it to expression profiles – what genes are being expressed and how they affect other genes," says May.

SUPPORTING RESEARCH

Professor Simon Turner at the University of Manchester has made extensive use of 'T-DNA insertion' lines from the NASC to identify genes responsible for producing a compound called xylan. Xylan forms part of the cell wall that gives plant cells their rigidity and strength. It occurs in the majority of plants, making up 30% of the biomass of some species, meaning it plays an important role in food crops and in plants grown for bioenergy. Despite this, little was known about how it is made.

"Xylan is probably the third most abundant biopolymer on the planet, but no-one had ever identified any genes involved in its synthesis. In that one study we discovered around half a dozen," Turner explains[11].

Each T-DNA insertion line contains a single mutation in a single gene, which prevents that gene from working correctly. The mutation is caused by inserting a length of DNA, called 'T-DNA' into the middle of the gene's DNA sequence. As it is relatively easy to insert T-DNA into the *Arabidopsis* genome, some researchers have generated hundreds of thousands of such insertion lines.

"What someone has done is to make these huge numbers, thousands of these T-DNA insertion lines, which have all been mapped. The stock centre holds all those lines. We can look online, decide which are going to be useful to us and the stock centre sends them out," Turner explains.

Turner and colleagues began by identifying genes they thought were involved in xylan production. By growing plants from seed stocks containing a T-DNA insertion in each of those genes, the researchers could show that mutations in some of the genes they found did result in defects in the cell wall and that those defects were caused by a lack of xylan.

"We rely on NASC supplying us with the T-DNA insertion lines that are the background of that work," says Turner. "There is no other easy alternative. We could try to down-regulate [reduce the activity of] that gene ourselves, which doesn't work as well, or use TILLING[12] or something, which would take months, just to get one mutant."

A global impact on research

In 1991, a report by a multinational steering group of scientists, supported by the US National Science Foundation and including several UK representatives, laid out the international role of *Arabidopsis* stock centres, including the newly-founded NASC[14].

One of the six objectives proposed by the steering group was to establish two 'biological resource centres'. According to the report, "Having a central location to deposit and distribute seeds, cloned DNA fragments, libraries etc. will make generally and immediately available the results of research, and will serve as central organizing points for the genetic and molecular studies that will provide for and make use of the results of the genome sequencing efforts." Since then the NASC has continued to support global research efforts in *Arabidopsis* and in a range of crop species.

"I can't stress enough how important NASC has been to our research," says Professor Ian Small, Director of the ARC Centre of Excellence in Plant Energy Biology at The University of Western Australia in Perth from 2006-2013. "Over the last eight years we have obtained over 1000 seed stocks from NASC and published around 360 papers on *Arabidopsis*, many of which relied directly on material from NASC."

TRANSCRIPTOMICS

In 2002 the NASC began offering a transcriptomics service to researchers, known as 'GeneChip'.

Transcriptomics is the study of the complete set of RNA molecules produced (or 'transcribed') from a genome under specific conditions or in a specific type of cell. This requires specialist high-throughput technology, which NASC implemented and offered to the research community.

The service enabled plant science researchers to send samples to NASC where they were analysed. However, one of the conditions for using the service was that the data were released into the public domain, and was an early example of an open resource in the biosciences.

So far, GeneChip has released over 4,000 public data files and users include plant and crop scientists, computer scientists and bioinformaticians, as well as veterinary, medical and bioenergy researchers[13].

"We obliged people to be altruistic by giving them a low-cost service where they would be happier to come to us to do the experiment [rather than do the work in-house] because of the cost savings, and we then obliged them to release their data into the public domain," says May. "We gave *Arabidopsis* researchers, and crop researchers, and some animal researchers, the ability to get data they might not otherwise have been able to access very easily,"

A field of wheat in Bedfordshire, UK. Research into important crops such as wheat depends on knowledge gained in *Arabidopsis*.

"To my knowledge everybody working with *Arabidopsis* needs specific mutants and genotypes for mapping traits (mapping populations and accession collections)," says Professor Maarten Koornneef, Director at the Max Planck Institute for Plant Breeding Research in Germany and a regular donor and user of NASC and ABRC stocks. "This is what the stock centres provide and it would be very difficult to do it without them."

"The only alternative is contacting individual researchers who, when they have generated large collections of materials in general, often do not have the facilities and man-power to distribute seeds and DNA at the large scale that the stock centres do."

Supporting world-class UK plant science

The resources provided by the NASC also underpin world-leading plant and crop science research in the UK, much of which is funded by BBSRC[15]. A report by Elsevier for the Department of Business, Innovation and Skills (BIS) showed that the UK is ranked first for bioscience (as measured by citations per article published) amongst the G8 countries[16]. Within that, the UK is also ranked top for plant sciences[17].

"The UK is really very strong in *Arabidopsis* [research] internationally, and I think it is because of the efficient and early establishment of all those resources," says Professor Caroline Dean, a Project Leader at the John Innes Centre. "The research outputs from the UK need to be supported by the resources required for that research." adds May. "You invest in infrastructure [like the NASC] and it improves your competitive ability."

The NASC arose from the need to coordinate the work of the newly-established *Arabidopsis* research community in the UK. In 1989, BBSRC's predecessor, the AFRC, initiated the Plant and Molecular Biology initiative, which provided funding for 34 research projects on *Arabidopsis*, around 40 % of the total investment[18].

Dean was one of the programme coordinators for the *Arabidopsis* elements of the Plant and Molecular Biology initiative, alongside Dr Bernard Mulligan from the University of Nottingham. Together they identified a need for a stock centre to provide a central repository for the resources needed by the UK *Arabidopsis* community. The fledgling NASC, established in 1990 and managed by Dr Mary Anderson, first acquired hundreds of stocks from the *Arabidopsis* Information Service managed by Dr Albert Kranz at the Botanical Institute of Johann Wolfgang Goethe University, Germany. Anderson then began accumulating seed stocks from individual research groups.

"At the beginning, what was so important was that 34 labs were suddenly funded to work on *Arabidopsis*. No-one had any seeds, no-one knew how to grow the plant. It could have been three years of wasted effort. We managed to coordinate that. Having [the NASC] here, having it set up and pulling the resources, the T-DNAs, the Kranz collection, together, meant that researchers in the UK could see they were available and use them, much earlier than they would have done had it been somewhere else."

From model to crop

The stocks held by NASC are valuable not just for fundamental plant science, but also for research into economically-important crop species (see 'The model plant').

"Breeding strategies for many crops build on fundamental research in *Arabidopsis*. Breeders map all of the *Arabidopsis* genes for their trait of interest onto the genetic map for the crop species. This provides molecular markers and helps them to understand how much the known genes contribute to the traits of interest," explains Dean.

Dean studies flowering and how environmental cues – in particular the need for a period of cold weather – influence the timing of the transition to reproduction. Dean and colleagues have developed a detailed understanding of these processes[19] and are translating that knowledge into crop plants such as the brassicas (a group that includes broccoli, cabbage, cauliflowers, Brussels sprouts and oilseed rape).

Although researchers now know many of the genes involved in regulating the transition to flowering, they still do not fully understand the detailed mechanism by which plants integrate exposure to multiple environmental cues. "We need that detailed mechanistic understanding in order to effectively manipulate flowering time in crops," says Dean.

In the 1990s, other researchers at JIC used *Arabidopsis* to identify the 'Green Revolution' gene in wheat, which was the basis for the new dwarf varieties that boosted wheat yields during the global Green Revolution in the 1960s and 1970s. The JIC researchers, led by Professor Nick Harberd, first identified a similar gene called GAI in *Arabidopsis*[20]. The work relied on stocks from the *Arabidopsis* Information Service, which were subsequently added to the NASC holdings, as well as from individual researchers and the ABRC. Based on that study, in 1999 they were able to find their target gene in the wheat genome[21]. That discovery is now used by all wheat breeders around the world to produce high-yielding varieties.

More recently, researchers at the Institute of Biological, Environmental and Rural Sciences (IBERS), JIC and the University of Birmingham identified a gene in *Arabidopsis* similar to a wheat gene called Ph1. Manipulating Ph1 allows wheat breeders to introduce traits such as pest and disease resistance to domesticated wheat from wild wheat species. The discovery of a similar gene in *Arabidopsis* allows researchers to study the properties of Ph1 more easily than working in wheat directly[22]. The study used stocks, including T-DNA insertion lines, from the NASC.

At the University of Manchester, Professor Simon Turner is also using information about *Arabidopsis* to improve the yield of wood from poplar trees, which can be used to generate energy. "[The poplar work is] to do with yields. It will be using all of the information we've gathered over several years working in *Arabidopsis* to make trees grow faster, so basically they'll give a higher yield of wood more quickly."

New varieties of crops such as wheat, oilseed rape, and the brassicas are helping to address food security, ensuring there is enough food to feed the world's growing population. Research and plant breeding to produce these new varieties depends on robust, easily-accessible genetic resources in the model plant *Arabidopsis*. As populations continue to grow, and the climate changes, there will be a pressing need for new and improved crops based on a solid understanding of fundamental plant science, highlighting the continuing need for genetic resources in *Arabidopsis*, such as those held by the NASC.

THE MODEL PLANT

Since the late 1980s researchers have used *Arabidopsis* as a 'model' or 'reference' plant. It is now the dominant model plant in use in plant science research globally.

Arabidopsis has very short generations, going from germination to seed production in the laboratory in around six weeks (in contrast, many trees take several years). It can also be grown in a relatively small space. *Arabidopsis* also possesses the majority of the tissues found in other plants. Although it lacks certain specific features of some plants, such as soft fruit and root nodules, it does have closely-related genes.

Arabidopsis genetics are also amenable to research. *Arabidopsis* was the first flowering plant to have its genome sequenced. The genome is quite small (e.g. the wheat genome is 17Gb, compared to 140Mb in *Arabidopsis*[23,24]) and the stretches of DNA between genes are relatively short, making it easier for researchers to study *Arabidopsis* genetics. *Arabidopsis* plants are also relatively easy to 'transform' i.e. to insert foreign DNA into their genome[25]. Thanks to resources such as the NASC, researchers now have access to mutants for almost every gene in *Arabidopsis*.

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