TIMELINE

# A fortunate choice: the history of *Arabidopsis* as a model plant

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During the past 20 years, the flowering plant *Arabidopsis thaliana* has been adopted as a model organism by thousands of biologists. This community has developed important tools, resources and experimental approaches that have greatly stimulated plant biological research. Here, we review some of the key events that led to the uptake of *Arabidopsis* as a model plant and to the growth of the *Arabidopsis* community.

In 1976, 25 people attended the Second International Symposium on *Arabidopsis*[1]. Today, more than 12,000 people are registered as *Arabidopsis* researchers in The *Arabidopsis* Information Resource (TAIR). The growth in the use of this diminutive plant (FIG. 1) has significantly reshaped research in plant biology. Both the size and productivity of the *Arabidopsis* community were responsible for the sequencing of the *Arabidopsis* genome in 2000, and the community is now engaged in an international effort to determine systematically the function of the plant's 25,500+ genes by 2010 (REF. 2).

Because of the recent radiation of flowering plants from a common ancestor in the past 150 million years, *Arabidopsis* is closely related to several hundred thousand plant species and is, therefore, considered to be an excellent biological model for many aspects of plant biology. The widespread acceptance of *Arabidopsis* as a model plant is based on the genetic and genomic methods and resources that are available for it, which have facilitated the investigation of a range of biological problems. The small size and simple growth requirements of *Arabidopsis* make it easy to grow in laboratory conditions. The plant is a self-fertilizing diploid that produces thousands of seeds from a single individual, thereby facilitating the rapid production of many progeny from single mutants or transgenic plants; for a flowering plant, it also has a relatively short life cycle of ~8 weeks. Moreover, *Arabidopsis* is easily transformed by simply spraying flowers with bacteria that contain a gene of interest in a plasmid and by then selecting for the presence of the transgene in the succeeding generation. It has one of the smallest known genomes among flowering plants, and the presence of more than 50,000 polymorphisms between the two most commonly used ACCESSIONS has greatly facilitated the isolation of mutant genes by positional cloning. The genomic resources that are available for *Arabidopsis* include a large collection of sequenced insertion mutations and commercially available DNA microarrays that contain probes for all of the genes known to be expressed in the plant (see the Online link to Affymetrix's *Arabidopsis ATH1* Genome Array). A large collection of characterized mutations and transgenic plants is also available, in which most aspects of plant growth and development have been disrupted.

Some of the features that make *Arabidopsis* a powerful model for studying many aspects of plant biology were already evident 20 years ago when molecular biologists began to adopt the organism as an experimental system. However, some of its most useful features, such as the ease with which it can be transformed, could not have been anticipated and should probably be attributed to good luck and to the benefit of having many people working on the organism. Here, we provide a perspective on how and why *Arabidopsis* became established as the model plant. We hope that colleagues who are planning to obtain or to exploit the genome sequences of their favourite organisms will find this tale informative. (See also REFS 1,3–5 for other accounts of the history of this model organism.)

## The pre-molecular era

Before the era of gene cloning, genetic research in flowering plants was largely focused on plants of agricultural or horticultural importance, such as maize, tomato, barley, pea, petunia and snapdragon. These species attracted experimental interest because of certain features, such as colourful flowers in the petunia and snapdragon, large chromosomes in barley and kernel colours in

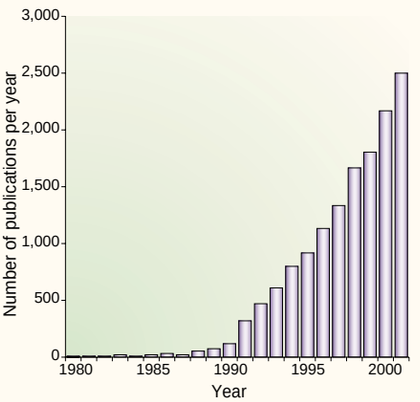



Figure 1 | **The number of articles published annually that describe research on *Arabidopsis*.** The numbers were obtained by examining the SciSearch citation index at Los Alamos National Laboratory using the keywords *Arabidopsis* or *thaliana*. SciSearch is an electronic database that is based on the Science Citation Index at the Institute for Scientific Information (ISI). (See the link to SciSearch in the Online links box for more information on this index.)

maize. The agricultural or horticultural usefulness of these plants provided funding for research, but also influenced the type of problems studied. So, for instance, although many interesting HOMEOTIC mutants were known to exist in maize, it was reportedly difficult or impossible to obtain funding for genetic studies on plant development before the mid-1980s (O. Nelson, personal communication). Also, in the days before gene cloning, there was apparently no pressing need and little funding[3] to work on an agriculturally unimportant species that had no unusual or overt features, such as *Arabidopsis* (FIG. 2).

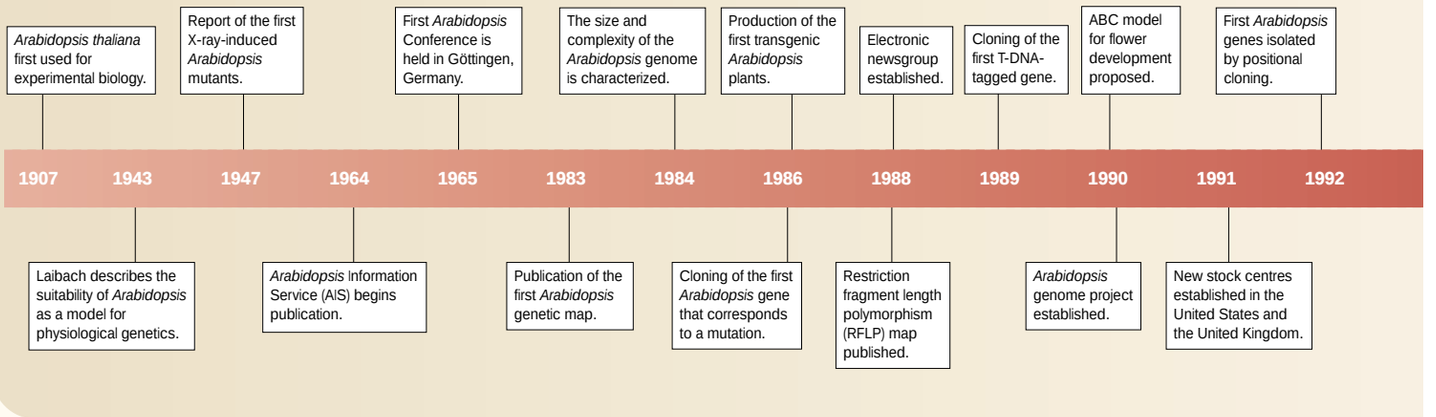
The first proponent of *Arabidopsis* as a suitable model for plant genetics was Friedrich Laibach, who had carried out cytological studies of various plants, including *Arabidopsis*, for his Ph.D. thesis in 1907 at the University of Bonn, Germany. His thesis was entitled *The Question of Individuality of Chromosomes in the Plant Kingdom*. He noted the presence of ten chromocentres, representing the heterochromatin that flanks the centromeres in interphase nuclei and also established that the number of chromosome pairs in meiotic cells is $n = 5$ (REF. 6). After a 30-year period studying other plants, Laibach, then Professor of Botany at the University of Frankfurt, returned to the study of *Arabidopsis*. He was particularly interested in natural variation and the effects of light quality and quantity on flowering time and seed dormancy. One of the features of *Arabidopsis* that attracted him was the large variation in physiological traits among accessions, which he started to collect systematically in 1937. In 1943, he outlined the suitability of *Arabidopsis* as a model for genetic and developmental biological research because it produced large numbers of progeny and developed rapidly, was easy to cultivate in limited space, had abundant natural variation, produced fertile hybrids and had a relatively low chromosome number[7]. In 1947, Laibach's student Erna Reinholz also showed that it was possible to induce mutations in *Arabidopsis* using X-ray irradiation[1] (TIMELINE).

Figure 2 | ***Arabidopsis thaliana*.** From a painting by Janet Wehr, 1995. Image courtesy of C. Somerville.

In the mid-1950s, *Arabidopsis* was adopted by other German scientists, including Klaus Napp-Zinn, who was interested in VERNALIZATION, and Gerhard Röbbelen, who studied mutants with reduced chlorophyll content[3]. Elsewhere, Peter Langridge in Canberra, Australia, and George Rédei in Columbia, USA, isolated the first thiamine AUXOTROPHS, which showed that biochemical mutants could be recovered in higher plants[8–10]. The fact that *Arabidopsis* was suitable for biochemical genetics also attracted people such as Michel Jacobs in Belgium and Wil Feenstra in The Netherlands, at the beginning of the 1960s. An active research topic among biologists in the 1960s was the identification of chemical mutagens. *Arabidopsis* was a useful organism for mutagenesis research because induced embryo-lethal mutations could be readily observed as a 3:1 ratio of green (normal) to white (lethal) seeds in developing siliques (seed pods)[11]. The small space requirements for *Arabidopsis* were also attractive because mutagenesis experiments required relatively large populations of plants[8,9].

Several *Arabidopsis* geneticists met at the XIth Genetics Congress in The Hague in 1963, and established an *Arabidopsis* Information Service (AIS) to exchange information on *Arabidopsis*. In this way, the *Arabidopsis* community started to become organized. Röbbelen was the driving force behind this initiative, and he published the first AIS newsletter in March 1964 in collaboration with Laibach, Andreas Müller, Rédei and Jiri Veleminsky. After Röbbelen left the *Arabidopsis* field, Albert Kranz took over the AIS newsletter in 1974, which was published annually until his retirement in 1990. The full text of the AIS series from 1964 to 1990 is available online at TAIR (see Online links box). Röbbelen and Kranz also established the AIS seed stock centre. This included the Laibach ECOTYPE collection and Röbbelen's

Timeline | Key events in the development and use of *Arabidopsis* as a model plant



own mutants, to which stocks from other groups were added. In 1965, Röbbelen also organized the first International *Arabidopsis* Symposium in Göttingen, Germany, which was attended by 25, mostly European, participants. Topics that were covered included physiological genetic studies of traits in natural populations, biochemical mutants and the first reports on genetic mapping and various methods of mutagenesis (see Online link to International *Arabidopsis* Symposium in Göttingen, Germany).

During the 1970s, interest in *Arabidopsis* declined, along with interest in mutagenesis and biochemical genetics, and several of the labs that had used it switched to other plants for which funding was more readily available. In retrospect, it seems that there was no compelling reason to choose *Arabidopsis* over other plants or other experimental systems, such as yeast or *Drosophila*, for genetic studies. *Arabidopsis* was not as attractive an organism for studying auxotrophy as were microorganisms, particularly because the only auxotrophs that could be recovered were thiamine deficient. Moreover, reports that thiamine auxotrophs could be complemented by *Escherichia coli* DNA[12] created scepticism rather than enthusiasm for *Arabidopsis* as a model.

During the 1970s, a few, relatively small, groups continued working with *Arabidopsis*. Among these was the group of Jaap van der Veen in The Netherlands. This group studied mutagenesis and chimerism in mutagenized plants, and also studied mutants in specific plant processes, such as flowering, and hormone production and function. Similarly, the work of Paddy Maher in the United Kingdom, on AUXIN-insensitive mutants, the work of Feenstra on nitrate-uptake mutants and that of David Meinke and Ian Sussex on embryo-lethal mutants in *Arabidopsis*[13] provided useful examples of the range of mutant types that could be generated in higher plants. These studies attracted the attention of young researchers, who recognized the usefulness of a model plant in which genetics and molecular biology could be integrated. However, as recently as 1983, there was a general lack of enthusiasm for *Arabidopsis* among plant biologists, which is exemplified by an anonymous reviewer of a paper describing the first linkage map of this organism. The reviewer wrote "Somehow *Arabidopsis* does not appear to have excited as many genetic researchers as one would have anticipated in the 1960s. I do not know why this is so". The paper, although originally rejected due to lack of interest, was eventually published[14].

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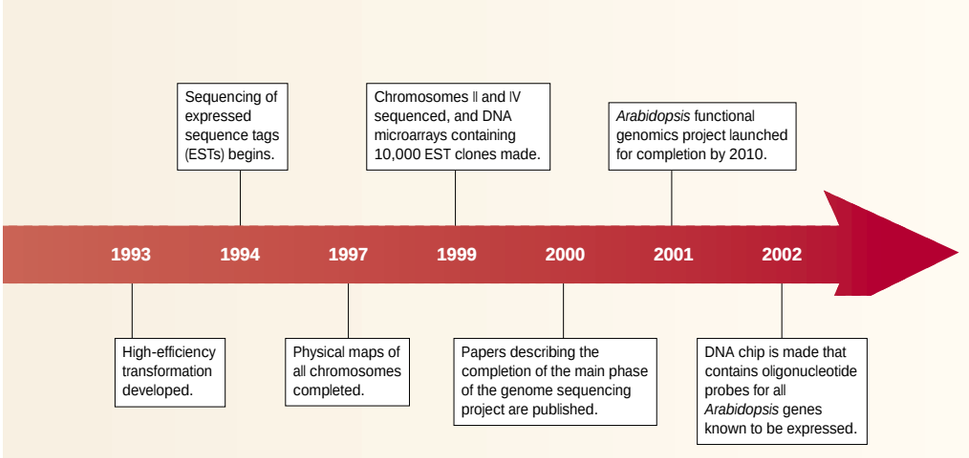
## The molecular era

The widespread adoption of *Arabidopsis* as a model plant began in the early 1980s. A few young biologists including Fred Ausubel, Elliot Meyerowitz, Dave Meinke, Randy Scholl, Shauna Somerville and ourselves were drawn to the organism because of its potential as a model plant. This group of researchers arose independently, came from various backgrounds and had little in common, except their enthusiasm for the use of genetics as a tool to analyse biological processes. A 1975 review by Rédei extolling the virtues of *Arabidopsis* as a model plant was influential in recruiting this group to the organism[10]. More importantly, perhaps, the dissemination of powerful molecular biology methods created a climate in which many biologists were looking for opportunities to make discoveries. There was a widespread sense that new approaches to previously intractable problems were possible. Finally, the discovery that *AGROBACTERIUM TUMEFACIENS* could transfer its DNA to the nuclear genome of higher plants indicated that gene transfer to plants was possible[15].

Most of the *Arabidopsis* papers published in the early 1980s described the isolation of mutants that affect various processes. Koornneef and colleagues identified a series of mutants that affect the response of plants to PHYTOHORMONES and to light, and also homeotic mutants, wax-deficient mutants and ANTHOCYANIN-deficient mutants[16–19]. These mutants elegantly showed the ease with which various processes could be disrupted by mutation. After the development of gene-cloning methods, these collections of mutants provided an important starting point for analysing many fundamental processes. The Somervilles characterized a series of mutants that would not grow in air but were relatively normal in atmospheres enriched in $CO_2$. These proved useful in resolving several biochemical questions about photosynthesis and photorespiration and exemplified the systematic use of genetics to analyse a process in higher plants[20,21].

One of the most influential *Arabidopsis* papers from the early 1980s was a report from the Meyerowitz lab that *Arabidopsis* had only ~70 Mb of nuclear DNA[22]. It had been reported previously that *Arabidopsis* had the smallest nuclear DNA content of any higher plant[23], but the paper that revealed this was either not widely known or not believed because it was based on FEULGEN MICROSPECTROPHOTOMETRY. In retrospect it seems that the reason that the Meyerowitz paper[22] was influential had almost nothing to do with *Arabidopsis* genetics or genomics. Instead, many people were excited by the low DNA content of *Arabidopsis* because of the technical difficulties of doing Southern blots on plants and of cloning genes from organisms with large genomes, which required the construction of genomic



libraries with millions of clones to obtain adequate genome coverage. The claim that the *Arabidopsis* genome could be represented in 16,000 λ-phage clones was very attractive to many people who were just learning recombinant DNA technology. The availability of high-quality genomic and cDNA libraries from the Meyerowitz and other labs was also an incentive to use *Arabidopsis*.

Fortunately for plant biologists, several distinguished non-plant biologists developed an interest in *Arabidopsis* during the formative period of the field. The yeast biologists Ron Davis and Gerry Fink were looking for new frontiers in the early 1980s and recognized that plant biology was in need of a change. Also, Howard Goodman, one of the founders of molecular biology, had become interested in *Arabidopsis*. The papers on *Arabidopsis* from the Davis, Fink and Goodman labs (such as REFS 24–29) carried with them an authority from outside plant biology that was very influential. Many young scientists, who might have been reluctant to work on plants because of a condescending and negative attitude towards plant biology by non-plant biologists, were emboldened by seeing such distinguished people working on *Arabidopsis*. They provided a seal of approval and examples of elegant work that were of great value at a crucial time in the growth of the field.

By the mid-1980s, a critical mass of biologists had adopted *Arabidopsis*, and the concept that *Arabidopsis* could become a model plant began to take hold[30]. At that point, the rationale for focusing on *Arabidopsis* rather than on other plants was still rather weak. Its rapid growth, small stature, high seed yield, diploid genetics and high frequency of self-fertilization were useful but not compelling. The characterization of genes that correspond to mutants had not yet yielded any interesting genes, and although it had been reported that *Arabidopsis* could be transformed[31], it was still difficult to do so. The maize community, with their thousands of mutants and elegant chromosome mechanics, considered *Arabidopsis* an annoying upstart. In response to a short review suggesting that *Arabidopsis* was destined to become the dominant model plant[32], a distinguished maize geneticist came to discuss the matter in person with one of the authors. He was astounded at the idea that several young people, who did not know anything about maize, could think that a weed of no economic importance and with few mutations or other genetic tools could become an important experimental organism.

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In 1987, Elliot Meyerowitz published an influential review article describing a vision for *Arabidopsis*[33]. He proposed that, because of its small genome, it would eventually be possible to clone any *Arabidopsis* gene by positional cloning. This paper was influential because it outlined a scientific strategy that integrated genetics and molecular biology into a systematic and universally applicable new way of doing things. It was a vision that set *Arabidopsis* apart from anything that had been proposed for any other plant, and it built on the unique technical advantages of the organism. Meyerowitz, Goodman and collaborators soon established genomic resources, such as restriction fragment length polymorphism (RFLP) maps[25,29,34], and Eric Ward, Erwin Grill, Joe Ecker and colleagues created YAC (yeast artificial chromosome) libraries[35–37]. Meyerowitz's vision was realized in 1992 with the map-based cloning of several genes by the Goodman and Somerville labs[38,39]. At that time, positional cloning was relatively time-consuming; the cloning of the *FAD3* gene by 'chromosome walking' required a two-year effort by three postdocs. However, it was liberating to realize that any mutant gene could be isolated by positional cloning and its function subsequently analysed. This was a qualitatively new way of approaching biological problems.

It is a truism that important discoveries are frequently not reported to the sound of trumpets. One of the most important technical innovations in *Arabidopsis* genetics was the discovery by Ken Feldmann and David Marks that the incubation of *Arabidopsis* seeds with *Agrobacterium* cultures resulted in the recovery of a few transformed progeny[40]. Because the paper lacked any insights into the mechanisms by which these rare transgenics arose, it was greeted with some scepticism. However, Feldmann and Marks produced a small but genuine collection of transgenic transfer DNA (T-DNA) insertion mutants. Feldmann then moved from Zoecon to DuPont, where he produced a much larger population of insertion mutants that was screened successfully by many labs. It was the cloning of genes from this collection that really initiated *Arabidopsis* into the molecular age[41–44]. By 1985, transformation protocols based on tissue culture methods had also been developed by Alan Lloyd and colleagues, and had been improved on by Valvekens and colleagues, which enabled genetic complementation tests to be carried out[31,45,46].

The seed-transformation methods pioneered by Feldmann and Marks underwent a series of incremental improvements. The greatest of these was the discovery by George Pelletier and colleagues that vacuum infiltration — a process in which plants were immersed in a culture of *Agrobacterium*, subjected to a vacuum for a few minutes, then grown to maturity — produced independent transformants in the progeny at a high frequency[47]. Today, it is possible to generate transformants by simply spraying *Agrobacterium* onto the plant's flowers. Several labs have produced tens of thousands of transformants using this method. Transformation has become such an easy and rapid aspect of the process of gene characterization that it is probably feasible to clone *Arabidopsis* genes by genetic complementation. Until other plants with fully sequenced genomes can be transformed with comparable ease, *Arabidopsis* is unlikely to be displaced as the plant of first choice for experimental molecular geneticists.

Although technical advantages convinced many people to choose *Arabidopsis* as their experimental organism of choice, the scientific context of certain programmes was undoubtedly also important. Young biologists were attracted by the success of others in solving interesting problems. In particular, its use in studying plant development was shown convincingly by Meyerowitz and colleagues, who developed the ABC model of floral morphogenesis[48,49]. Mutants that affect floral morphogenesis had been isolated by Van der Veen, and named and mapped by Koornneef, but their significance was not widely appreciated. Also, George Haughn published a speculative combinatorial model showing that as few as three genes (also named A, B and C) might account for the phenotypes of the floral organ identity genes[50]. However, Haughn did not know where and when the genes were expressed, and his model was not correct. The cloning of the floral-patterning genes, the analysis of their expression patterns by *in situ* hybridization and the analysis of double and triple

mutants led to a model that was elegant, simple and predictive[49]. In addition to the importance of the model for understanding floral morphogenesis, the design and execution of these experiments exemplified how a developmental process could be analysed and understood in plants. The beauty and power of these experiments attracted people to the field and created the impression that something qualitatively new was happening in plant biology. Complex biological processes began to look understandable, and students and postdocs began applying genetic methods to similar problems on a large scale. In much the same way that the elegant experiments of the Delbrück phage group mobilized the first generation of molecular geneticists in the 1940s, these experiments on floral organ identity genes mobilized plant biologists. People who had been reluctant to change from their favourite plant finally capitulated and switched to *Arabidopsis*.

By the late 1980s, it had become apparent to many in the field that *Arabidopsis* was an excellent model and that the field would continue to grow. An *Arabidopsis* conference in 1987 at Michigan State University, USA, was attended by 217 people. Most of the talks were about what researchers were planning to do, but they conveyed a sense of optimism. An *ad hoc* committee of established *Arabidopsis* laboratory leaders produced nomenclature guidelines and established an email newsgroup, which became one of the most active scientific newsgroups in the world. The newsgroup continues today, but is much less widely used because the information it distributed is now mostly available from *Arabidopsis* community web sites, such as TAIR, GARNET and MIPS.

In the late 1970s, James Watson, who was the Director of Cold Spring Harbor Laboratory (CSHL) at the time, recognized the need for a model plant and convened a Banbury meeting at CSHL to discuss the idea. However, most of the participants were unenthusiastic about *Arabidopsis* becoming the model plant because they believed that the tools of molecular biology could be applied to any species, and because of a widely held belief that research on non-crop species was largely unfundable. Watson persisted and persuaded Ausubel and John Bedbrook to organize a course at CSHL on plant molecular biology. Initially, they chose to focus on the petunia as a model because it was one of the few plants that could be transformed at the time. However, Ausubel was an early convert to *Arabidopsis*, and the course eventually became a course on *Arabidopsis*. This CSHL plant course and one organized by Czaba Koncz in Cologne, Germany, have been important for attracting young scientists into the field, and many prominent plant biologists are alumni of these courses.

Watson briefly became interested in *Arabidopsis* in the late 1980s and, in 1989, asked then director of the US National Science Foundation (NSF), Eric Bloch, to convene a small meeting to discuss the opportunities associated with *Arabidopsis*. At that meeting, attended by Ron Davis, Gerry Fink, Howard Goodman, Elliot Meyerowitz, Chris Somerville, Ken Feldman, Oliver Nelson, Vicki Chandler, Mary Clutter, DeLill Nasser, Bob Rabson, Machi Dilworth and several others, the concept of an *Arabidopsis* genome project was advocated by Watson. After the meeting, he explained in private that he did not particularly care about *Arabidopsis* but wanted to promote the development of model organisms in which gene function could be discovered more easily than in humans, to help with analysing the human genome. Because plants had been excluded from support by the US National Institutes of Health (NIH)-sponsored Human Genome Project, he thought that the NSF should take responsibility for supporting *Arabidopsis* research in the United States. Bloch and his colleagues at NSF, notably Mary Clutter, accepted the proposal, which led to the formation of both national and multinational *Arabidopsis* steering committees. The members of the first multinational steering committee were Marc van Montagu, Caroline Dean, Dick Flavell, Howard Goodman, Maarten Koornneef, Elliot Meyerowitz, Jim Peacock, Yoshiro Shimura and Chris Somerville.

The first report of the steering committee was published in 1990 and called for a series of developments that would culminate in the sequencing of the *Arabidopsis* genome in 2003 by an international team. At the time that this report was written, most of its authors were still struggling with sequencing single genes, and the idea of sequencing more than 100 million base pairs was ambitious in the extreme. The general feeling was that it was probably not realistic to obtain the complete sequence but that it was useful to have ambitious goals. The report advocated that a scientific knowledge base and infrastructure be created, through several steps, to take advantage of a genome sequence. These steps included the establishment of the *Arabidopsis* stock centres, the development of databases, polymorphism mapping, large-insert clone libraries and the characterization of many genetic mutations by FORWARD GENETICS. The goal of the proposal was to provide a blueprint for the international community to progress towards the genome sequence of *Arabidopsis*. Goals were revised each year by the multinational steering committee, which established an election process for committee candidates in which anyone with email could vote. This system continues today, and has created a cadre of leaders in the international *Arabidopsis* community who have a sense of

## Glossary

ACCESSION
A sample of a plant variety collected at a specific location and time.

*AGROBACTERIUM TUMEFACIENS*
A gram-negative soil bacterium that is used to transfer DNA into plant cells by a process similar to bacterial conjugation. The transferred DNA (T-DNA) randomly integrates into the plant genome to produce stably transformed plants.

ANTHOCYANIN
A flavonoid pigment. Anthocyanins are found in the cell vacuoles of plant organs and produce blue, red and purple colours in plants.

AUXIN
A plant hormone, also called indole-3-acetic acid, which is required for many aspects of plant development and for plant cell growth in culture.

AUXOTROPH
A mutant strain of a given organism that is unable to synthesize a molecule required for its growth. It, therefore, needs the molecule supplied in its growth medium to grow.

ECOTYPE
In the *Arabidopsis* literature, this term refers to a sample of a plant variety collected at a specific location and time.

FEULGEN MICROSPECTROPHOTOMETRY
A method for measuring cellular DNA content in which nuclei are stained with a DNA-specific dye and the amount of DNA per nucleus is measured by quantifying the absorbance of light by single nuclei in cytological preparations.

FORWARD GENETICS
A genetic analysis that proceeds from phenotype to genotype by positional cloning or candidate-gene analysis.

HOMEOTIC GENES
A class of genes that are crucial for controlling the early development and differentiation of embryonic tissues in eukaryotic organisms. The homeotic genes studied in *Arabidopsis* are frequently called organ identity genes.

PHYTOHORMONES
Plant growth and development is regulated by several small molecules, such as auxin, cytokinin, brassinosteroids, ethylene, jasmonic acid and abscisic acid.

VERNALIZATION
The induction of flowering by exposure of plants to a period of low temperature.

Figure 3 | **Second meeting of the *Arabidopsis* Genome Initiative, July 1998.** Standing from left to right: Richard Wilson (Washington University, USA), Steve Rounsley (The Institute for Genome Research (TIGR), USA), Marcel Salanoubat (Genoscope, France), Ellson Chen (Perkin Elmer Applied Biosystems, USA), Curtis Palm (Stanford University, USA), Rob Martienssen (Cold Spring Harbor Laboratory (CSHL), USA), Dick McCombie (CSHL), Elliot Meyerowitz (Caltech, USA), Nancy Federspiel (Stanford University), David Meinke (Oklahoma State University, USA), Ron Davis (Stanford University), Ian Bancroft (John Innes Centre, UK), Satoshi Tabata (Kazusa DNA Research Institute, Japan), Daphne Preuss (University of Chicago, USA), Sakis Theologis (USDA/UC Berkeley, USA), Gerd Jürgens (University of Tübingen, Germany), Francis Quetier (Genoscope), Michael Bevan (John Innes Centre) and Xiaoying Lin (TIGR). Photo courtesy of DeLill Nasser and Machi Dilworth, National Science Foundation.

common purpose and knowledge of how to work with government agencies to support the community.

Although an original goal of the genome project was to support the sequencing of the genome, the US component of the programme was focused initially on developing infrastructure and genomic resources rather than on sequencing *per se*. Several European programmes of the same era — such as the European Commission (EC)-sponsored BRIDGE programme, which funded *Arabidopsis* research in 33 laboratories from nine European countries[51], and a separate UK programme, which involved 41 laboratories — supported a broad range of basic research, including limited genomic sequencing. In 1991, several European plant scientists — Mike Bevan, Jerome Giraudat, Dirk Inze, Marc Zabeau and Jeff Dangl (some of them already involved in the BRIDGE programme) — issued a report calling for the sequencing of 3,000 kb of DNA by 2004. This led, in 1993, to a EC-sponsored project that involved 19 labs called ESSA (European Scientists Sequencing *Arabidopsis*), which had the goal of sequencing 2,500 kb from two contiguous regions. Soon after, Satoshi Tabata at the newly founded Kazusa DNA Research Institute in Japan decided to participate in sequencing the *Arabidopsis* genome. Subsequently, Rob Martiessen, Dick McCombie and Joe Ecker organized a Banbury meeting to develop a concrete US plan for sequencing the *Arabidopsis* genome. The NSF, in collaboration with the US Departments of Agriculture and Energy, provided the funds for this project. This resulted in three US groups being funded to participate in the sequencing project, together with the ESSA consortium led by Mike Bevan, a French programme led by Francis Quetier and the Kazusa programme. In 1996, a small meeting of the group leaders was convened in Washington, USA, to establish mechanisms of coordination and cooperation, and a committee called the *Arabidopsis* Genome Initiative was formed to support the interaction (FIG. 3). The completion of most of the genome sequence in December 2000 represented a landmark accomplishment for biology[52], and is a wonderful example of scientific cooperation and collaboration.

As the sequencing neared completion, the leadership of the *Arabidopsis* community in the United States turned to the next major goals. Joe Ecker convened a small workshop in December 1998 to discuss the matter; the result was a proposal to determine the function of all *Arabidopsis* genes by 2010. This proposal was validated and elaborated in a subsequent workshop convened by Ecker, Joanne Chory and Detlef Weigel in January 2001 (REF. 2). The essential elements of the proposal were adopted by the NSF as a blueprint for a ten-year functional genomics programme[53]. On the basis of past experience, the programme is likely to exceed the goals that were put forward. The key to the success of the programme will lie with giving voice to the aspirations of the community and with allowing the community to decide how to meet those goals.

## Conclusion

Our impression is that the *Arabidopsis* community has been an unusually successful collective enterprise that has provided a vehicle for the scientific inspiration of its members and has facilitated their work in ways not previously possible. Because of the genome sequence, the databases, the stock centres and the collegiality of the community, there are no technical barriers to the use of sophisticated genetic methods that were only available to a few large labs a decade ago. Whereas, in 1992, it took six postdocs several years to isolate one gene by positional cloning, today it requires as little as a few months. So, the community helps everyone. Of course, *Arabidopsis* was a fortunate choice. It is impossible to know how many other species could have served the same role equally well, but it seems likely that there are other equally amenable species. The key to the success of *Arabidopsis* was some good luck and the combined efforts of many people who shared a common purpose and a commitment to sharing resources and information.

The discoveries made with *Arabidopsis* during the past 20 years have fundamentally changed plant biology[54]. We predict that *Arabidopsis* will continue to be of central importance in plant biology for the foreseeable future. However, it is useful to remember that the goal of understanding *Arabidopsis* is to facilitate the understanding of all plants, in particular, and biological phenomena, in general. It seems likely that, because of the importance of agricultural species to human welfare, the coming decades will see a dialogue between those who propose to use limited resources to solve problems in agriculturally useful plants and those who advocate continued investment in a deep and basic understanding of plants. We hope that this account will provide a memory in the community of how we arrived at this point, and that this memory will help in making the many decisions that lie ahead.

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TIMELINE

# Conrad Hal Waddington: the last Renaissance biologist?

*Jonathan M. W. Slack*

Conrad Hal Waddington was a leading embryologist and geneticist from the 1930s to the 1950s. He is remembered mainly for his concepts of the 'epigenetic landscape' and 'genetic assimilation'. This article reviews his life and work, and enquires to what extent his ideas are relevant tools for understanding the biological problems of today.

Conrad Hal Waddington was a true twentieth-century polymath: he published research in palaeontology, population genetics, developmental genetics, biochemical embryology and theoretical biology. No modern funding agency would allow any individual to undergo so many changes of interest and direction. It is therefore a sign of the changes that occurred in the biosciences during the twentieth century that Waddington was awarded a series of research fellowships and academic positions in the 1930s and 1940s, culminating in the directorship of the Institute of Genetics in Edinburgh, UK. Most biologists under 40 years old have probably not heard of Waddington, who died in 1975. But to many of us who are a little older, he is