34. Lexer, C., Welch, M. E., Durphy, J. L. & Rieseberg, L. H. Natural selection for salt tolerance quantitative trait loci (QTLs) in wild sunflower hybrids: implications for the origin of *Helianthus paradoxus*, a diploid hybrid species. *Mol. Ecol.* **12**, 1225–1235 (2003).
35. Peichel, C. *et al.* The genetic architecture of divergence between threespine stickleback species. *Nature* **414**, 901–905 (2001).
36. Aparicio, S. *et al.* Whole-genome shotgun assembly and analysis of the genome of *Fugu rubripes*. *Science* **297**, 1301–1310 (2002).
37. Beldade, P., Brakefield, P. M. & Long, A. D. Contribution of Distal-less to quantitative variation in butterfly eyespots. *Nature* **415**, 315–318 (2002).
38. Frary, A. *et al. fw2.2*: a quantitative trait locus key to the evolution of tomato fruit size. *Science* **289**, 85–88 (2000).
39. El-Assal, S. E.-D., Alonso-Blanco, C., Peeters, A. J. M., Raz, V. & Koornneef, M. A QTL for flowering time in *Arabidopsis* reveals a novel allele of *CRY2*. *Nature Genet.* **29**, 435– 440 (2001).
40. Dilda, C. L. & Mackay, T. F. C. The genetic architecture of *Drosophila* sensory bristle number. *Genetics* **162**, 1655–1674 (2002).
41. Robin, C., Lyman, R. F., Long, A. D., Langley, C. H. & Mackay, T. F. C. *hairy*: a quantitative trait locus for *Drosophila* sensory bristle number. *Genetics* **162**, 155–164 (2002).
42. Zhang, X. S. & Hill, W. G. Joint effects of pleiotropic selection and stabilizing selection on the maintenance of quantitative genetic variation at mutation-selection balance. *Genetics* **162**, 459–471 (2002).
43. Holub, E. B. The arms race is ancient history in *Arabidopsis*, the wildflower. *Nature Rev. Genet.* **2**, 516–527 (2001).
44. Jakob, K. *et al. Pseudomonas viridiflava* and *P. syringae* — natural pathogens of *Arabidopsis thaliana*. *Mol. Plant Microbe Interact.* **15**, 1195–1203 (2002).
45. Grant, M. R. *et al.* Independent deletions of a pathogen-resistance gene in *Brassica* and *Arabidopsis*. *Proc. Natl Acad. Sci. USA* **95**, 15843–15848 (1998).
46. Brakefield, P. M. & Liebert, T. G. Evolutionary dynamics of declining melanism in the peppered moth in the Netherlands. *Proc. Royal Soc. Lond. B* **267**, 1953–1957 (2000).
47. Clegg, M. T. & Durbin, M. L. Tracing floral adaptations from ecology to molecules. *Nature Rev. Genet.* **4**, 206–215 (2003).
48. Watt, W. B. Avoiding paradigm-based limits to knowledge of evolution. *Evol. Biol.* **32**, 73–96 (2000).
49. Feder, M. E. & Watt, W. B. in *Genes in Ecology* (eds. Berry, R. J., Crawford, T. J. & Hewitt, G. M.) 365–391 (Blackwell Scientific, Oxford, 1993).
50. Fay, J. C., Wyckoff, G. J. & Wu, C. I. Testing the neutral theory of molecular evolution with genomic data from *Drosophila*. *Nature* **415**, 1024–1026 (2002).
51. Swanson, W. J., Zhang, Z. H., Wolfner, M. F. & Aquadro, C. F. Positive Darwinian selection drives the evolution of several female reproductive proteins in mammals. *Proc. Natl Acad. Sci. USA* **98**, 2509–2514 (2001).
52. Riley, R., Jin, W. & Gibson, G. Contrasting selection pressures on components of Ras-mediated signal transduction in *Drosophila*. *Mol. Ecol.* **12**, 1315–1323 (2003).
53. Schulte, P. M. Environmental adaptations as windows on molecular evolution. *Comp. Biochem. Physiol. B Biochem. Mol. Biol.* **128**, 597–611 (2001).
54. Watt, W. B. & Dean, A. M. Molecular-functional studies of adaptive genetic variation in prokaryotes and eukaryotes. *Ann. Rev. Genet.* **34**, 593–622 (2000).
55. Fields, P. A., Kim, Y. S., Carpenter, J. F. & Somero, G. N. Temperature adaptation in *Gillichthys* (Teleost: Gobiidae) A(4)-lactate dehydrogenases: identical primary structures produce subtly different conformations. *J. Exp. Biol.* **205**, 1293–1303 (2002).
56. Farrell, B. D. *et al.* The evolution of agriculture in beetles (Curculionidae: Scolytinae and Platypodinae). *Evolution* **55**, 2011–2027 (2001).
57. Oleksiak, M. F., Kolell, K. J. & Crawford, D. L. Utility of natural populations for microarray analyses: isolation of genes necessary for functional genomic studies. *Marine Biotechnol.* **3**, 203–211 (2001).
58. Boffelli, D. *et al.* Phylogenetic shadowing of primate sequences to find functional regions of the human genome. *Science* **299**, 1391–1394 (2003).
59. Zdobnov, E. *et al.* Comparative genome and proteome analysis of *Anopheles gambiae* and *Drosophila melanogaster*. *Science* **298**, 149–159 (2002).
60. Charlesworth, D., Charlesworth, B. & McVean, G. A. T. Genome sequences and evolutionary biology, a two-way interaction. *Trends Ecol. Evol.* **16**, 235–242 (2001).
61. Ureta-Vidal, A., Ettwiller, L. & Birney, E. Comparative genomics: genome-wide analysis in metazoan eukaryotes. *Nature Rev. Genet.* **4**, 251–262 (2003).
62. Cooper, T. F., Rozen, D. E. & Lenski, R. E. Parallel changes in gene expression after 20,000 generations of evolution in *Escherichia coli*. *Proc. Natl Acad. Sci. USA* **100**, 1072–1077 (2003).
63. Elena, S. F. & Lenski, R. E. Microbial genetics: evolution experiments with microorganisms: the dynamics and genetic bases of adaptation. *Nature Rev. Genet.* **4**, 457–469 (2003).
64. Ideker, T., Galitski, T. & Hood, L. A new approach to decoding life. *Annu. Rev. Genom. Human. Genet.* **2**, 343–372 (2001).
65. Wittbrodt, J., Shima, A. & Schartl, M. Medaka — a model organism from the far East. *Nature Rev. Genet.* **3**, 353–364 (2002).
66. Kocher, T. D., Lee, W.-J., Sobolewska, H., Penman, D. & McAndrew, B. A Genetic linkage map of a cichlid fish, the tilapia (*Oreochromis niloticus*). *Genetics* **148**, 1225–1232 (1998).
67. Pennisi, E. Recharged field's rallying cry: gene chips for all organisms. *Science* **297**, 1985–1987 (2002).
68. Whitfield, C. W. *et al.* Annotated expressed sequence tags and cDNA microarrays for studies of brain and behavior in the honey bee. *Genome Res.* **12**, 555–566 (2002).
69. Davidson, E. H., McClay, D. R. & Hood, L. Regulatory gene networks and the properties of the developmental process. *Proc. Natl Acad. Sci.* **100**, 1475–1480 (2003).
70. Bradshaw, H. D., Ceulemans, R., Davis, J. & Stettler, R. F. Emerging model systems: poplar (*Populus*) as a model forest tree. *J. Plant Growth Reg.* **19**, 306–313 (2000).

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TIMELINE

An everlasting pioneer: the story of *Antirrhinum* research

Zsuzsanna Schwarz-Sommer, Brendan Davies and Andrew Hudson

Despite the tremendous success of *Arabidopsis thaliana*, no single model can represent the vast range of form that is seen in the ~250,000 existing species of flowering plants (angiosperms). Here, we consider the history and future of an alternative angiosperm model — the snapdragon *Antirrhinum majus*. We ask what made *Antirrhinum* attractive to the earliest students of variation and inheritance, and how its use led to landmark advances in plant genetics and to our present understanding of plant development. Finally, we show how the wide diversity of *Antirrhinum* species, combined with classical and molecular genetics — the two traditional strengths of *Antirrhinum* — provide an opportunity for developmental, evolutionary and ecological approaches. These factors make *A. majus* an ideal comparative angiosperm.

"*Antirrhinum* has always allowed new, and frequently surprising, insights to be made into the nature, variability and manifestation of genetic substance and, even today, the rich variety of appearance in the genus *Antirrhinum* offers an inexhaustible resource for genetics-based studies in developmental biology, biochemistry and evolution". With this sentence, Hans Stubbe[1] justified his motivation to write a comprehensive monograph on *Antirrhinum* in 1966; this article shows that his assessment of *Antirrhinum* is as valid today as it was half a century ago.

It might seem surprising that such a familiar ornamental plant could be used as an experimental system. In fact, *Antirrhinum* was used in the earliest studies of inheritance by Darwin and Mendel, and became established as a model by Erwin Baur (FIG. 1) during the first decades of the twentieth century (TIMELINE). Interest in *Antirrhinum* declined after 1930, because of the emergence of

Figure 1 | **Erwin Baur.** Oil painting of Baur by Schaumann (1950). Reproduced with permission from the Centre for Agricultural Landscape and Land Use Research (ZALF), Müncheberg, Germany, where the original is displayed.

other model systems, such as *Drosophila*, which were better suited to study some aspects of inheritance in higher eukaryotes. Its comeback during the early years of plant molecular biology in the 1980s was celebrated with the molecular isolation of transposons.

Antirrhinum research has made important contributions to the understanding of pigment biosynthetic and photosynthetic pathways and their regulation. However, here we focus on how it has contributed to building the fundaments of plant developmental genetics by providing molecular access to the HOMEOTIC control of floral-meristem identity and floral-organ identity, as well as leaf development, organ growth and floral asymmetry. Reviewing recent work in these areas, and the extent to which genetic mechanisms in *Antirrhinum* are conserved in other model species, notably *Arabidopsis*, illustrates the importance of comparative approaches. Looking to the future, we draw attention to the potential of the genus *Antirrhinum*, with its 19 highly diverse and yet interfertile species, as a resource for studies in development, biodiversity and evolution.

A classical object for genetic studies

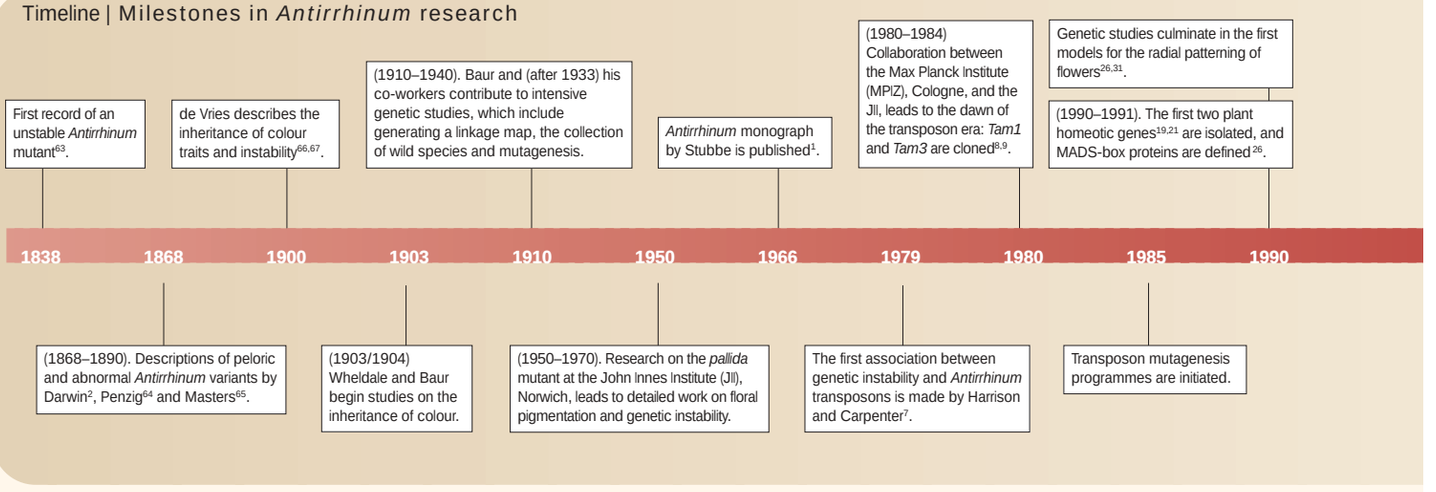
Antirrhinum majus is native to the western Mediterranean and has few recorded medicinal uses. Despite this, its association with ancient Roman sites outside its natural range indicates an early cultivation[1], presumably owing to the attractiveness of its large red bilaterally symmetrical flowers (FIG. 2).

By the mid-nineteenth century, several morphological and colour variants of *Antirrhinum* were widely available as garden varieties. These included double-flowered forms in which the reproductive organs were replaced by extra petals and PELORIC radially symmetric forms, which had lost the bilateral floral symmetry of the wild type. Although hybridization with other species might have contributed to some variation, mutagenic transposable elements undoubtedly had a role in generating diversity. The high level of phenotypic variation, combined with hardiness, a relatively short generation time of three months, and ease of selfing and cross-pollination, made *Antirrhinum* attractive to the earliest students of variation and inheritance, including Mendel and de Vries. Charles Darwin famously described crossing a peloric mutant of *Antirrhinum*, which he had shown bred true, with the wild type. He observed that the peloric character was lost in the progeny, but recurred in 29% of the subsequent generation (behaviour that was later shown to result from a monogenic recessive trait).

It was, however, the pioneering work of Bateson, Wheldale and particularly Erwin Baur, coinciding with the rediscovery of the research of Mendel, which established *Antirrhinum* as a model species in the early twentieth century. Baur began his work with *Antirrhinum* in 1907 and characterized *Aurea*, the first documented case of Mendelian segregation of a dominant lethal mutation[1]. Along with his students and colleagues, he maintained *Antirrhinum majus* at the forefront of plant genetics for several decades. Their discoveries included the first confirmation of genetic linkage, the identification of cytoplasmic inheritance, the quantification of the effects of environment on recombination and mutation rates, and the correlation of recombination with CHIASMA formation[1]. Baur was also one of the first researchers to appreciate the potential of evolutionary genetics, and used *Antirrhinum* species to identify and map genes that are responsible for evolutionary differences in flower colour and morphology[1]. Most of this research, together with short descriptions of the 550 mutants that were available in 1966, was compiled by Hans Stubbe, the founder and director of the Institut für Kulturpflanzenforschung (IPK) in Gatersleben[1,3], where the collection is still maintained.

The genetic instability of many mutations (BOXES 1,2), and their ability to give rise to a series of different alleles became a recurring theme throughout classical *Antirrhinum* research. This anomalous behaviour attracted the attention of William Bateson, the Director

Timeline | Milestones in *Antirrhinum* research



of the John Innes Horticultural Institution — subsequently known as the John Innes Institute (JII) and now the John Innes Centre (JIC) — in the United Kingdom, and was revisited by many of his successors.

The present *Antirrhinum* community originated from interest in transposition in Germany and the United Kingdom, and emerged from contacts between Heinz Saedler at the Max Planck Institut für Züchtungsforschung (MPIZ), Cologne, and David Hopwood, Brian Harrison and Rosemary Carpenter at the JII, Norwich. The first collaboration between the Norwich and Cologne groups included an exchange of mutant material and, in 1984, a visit by Cathie Martin and Enrico Coen to the laboratory of Hans Sommer in Cologne to learn molecular techniques.

Small meetings were organized in Cologne and Norwich for the exchange of information on transposable elements. These meetings were the progenitors of the Annual *Antirrhinum* Meetings that started in Cologne, in 1991, and continue to take place at different locations in Europe every year, reinforcing scientific contacts and the friendly relations between the groups. The annual meetings are typified by their informality and are managed in a disciplined way without a Chair. They attract scientists, not only those now working with *Antirrhinum*, but also former postdoctoral researchers and co-workers, irrespective of their present research areas. The *Antirrhinum* meetings are increasingly attended by population biologists, systematic biologists, evolutionary biologists and comparative biologists, in response to the enthusiasm and interest in the *Antirrhinum* community to extend understanding in these areas. The forthcoming meetings are advertised on the *Antirrhinum* DragonDB web site.

Transposons and the molecular era

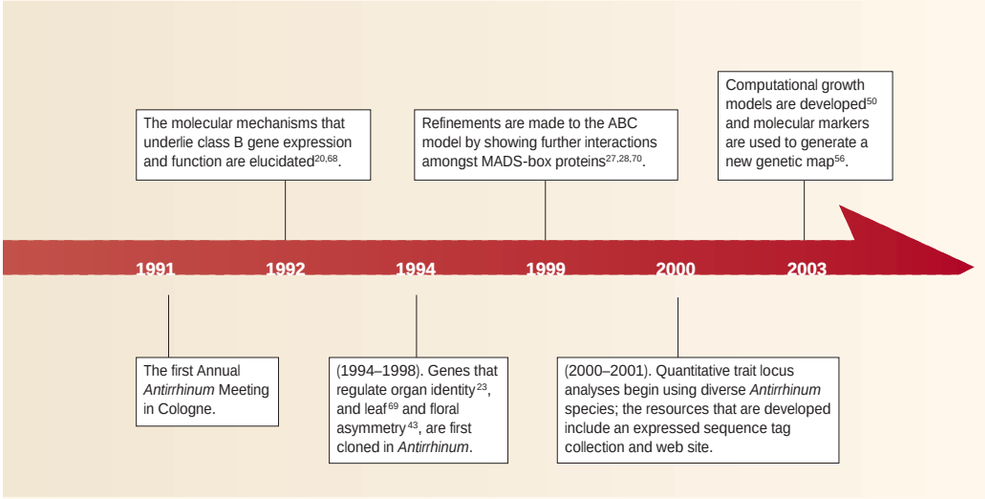
Long before transposable elements were cloned, McClintock proposed that they were responsible for the instability and variegation of some maize mutants[4]. Similar variegation was known in several horticultural species, including rose, morning glory and snapdragon. A variegated mutant of *Antirrhinum majus* had been in cultivation since the nineteenth century and further unstable mutations were isolated and characterized by Baur and his colleagues during the first decades of the twentieth century (FIG. 3). Between the 1950s and the 1970s, Harrison, Carpenter, Stickland and Fincham began working with unstable mutations in two genes — *NIVEA* (*NIV*) and *PALLIDA* (*PAL*) (BOX 1) — both needed for ANTHOCYANIN pigmentation of the flower. They showed that *NIV* probably encoded the biosynthetic enzyme chalcone synthase[5] and that unstable alleles differed in their sensitivity to temperature and a genetic stabilizer, which indicated that they might carry different transposable elements[6,7]. Heinz Saedler recognized that the *Antirrhinum majus NIV* gene could be isolated using the newly identified parsley chalcone synthase gene as a probe. This led to the cloning of *NIV* in the group of Hans Sommer[8] and the first isolation of an AUTONOMOUS TRANSPOSON from a plant, Tam1, from an unstable *niv* allele[9]. This was the overture to an exciting era during which, as a result of collaborative Anglo–German efforts, several other transposons were isolated from the *NIV* locus including Tam3, which was used as a molecular tag to isolate *PAL*[10,11].

Transposons facilitated the isolation of genes by transposon tagging — perhaps their most significant contribution to the initiation of plant molecular studies. In turn, genes for which molecular probes were available could be used as 'transposon traps' to assist the isolation of many transposable elements. Two classes of transposons were defined in this way[12]: the CACTA elements, which include Tam1 and its relatives in *Antirrhinum* and En/Spm in maize, and the Ac/Ds-like Tam3 elements. The availability of information on different groups of *Antirrhinum* transposons was fundamental for a better understanding of the structure and function of homologous transposons in maize[13].

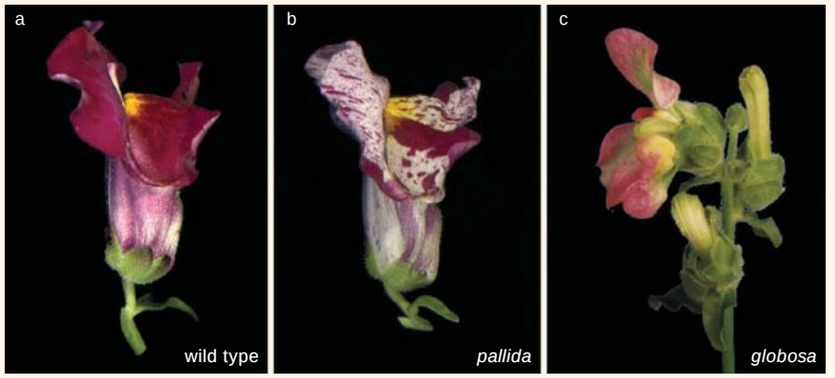
Antirrhinum transposons have proved to be versatile and efficient tools for the study of many aspects of plant developmental genetics and molecular biology. Precise and imprecise excision events, for example, have been used in several different ways including the study of cell–cell communication (BOXES 1,2). In the 1980s, promoter analyses were carried out, mostly using promoter-deletion constructs in transgenic tobacco. A more elegant way to identify functionally important promoter regions was developed in *Antirrhinum*, making use of stable mutants that resulted from the imprecise and germinally heritable excision of transposons that were located in promoters[14,15]. Correlating changes in the level and pattern of colour expression in flowers with different transposon-induced mutations revealed the function of different promoter sequences.

Analysis of new alleles that were generated by transposition led to a model in which excision of the transposon is followed by ligation of each end of the host DNA to form a hairpin intermediate[14]. A remarkably similar mechanism was later found to operate in the V(D)J recombination system that generates immunoglobulin diversity in vertebrate

Figure 2 | **Size comparison between mature *Antirrhinum* and *Arabidopsis* flowers.** Despite differences in size and shape, *Arabidopsis* (white) and *Antirrhinum* (red) flowers share a similar overall organization. The similarities and differences between the species are important for comparative studies.



Box 1 | Interpretation and consequences of transposon excision events



Insertion of a transposon into a gene can impair its structure and function. Transposons cause gene instability — their integration disrupts gene function and their subsequent excision restores it. Excision events are not necessarily precise and can result in mutations that alter or abolish gene function. The juxtaposition of neighbouring cells carrying active and inactive genes creates a genetically mosaic structure, named a sectorial mosaic or MERICLINAL CHIMAERA.

Panel **b** shows a mericlinal chimaera with respect to colour. It carries the unstable *pal-rec* allele of the *PALLIDA* (*PAL*) gene. The white/ivory background colour is observed when the *PAL* gene is inactivated by transposon (Tam3) insertion in the *pal-rec* mutant. Magenta pigment (typical for the wild-type flower shown in panel **a**) is produced when *PAL* gene activity is restored after Tam3 excision. Cells in individual revertant sectors are clonally related, because they are derived from a single revertant progenitor cell. The shape and size of coloured areas in the *pal* flower mark the subsequent developmental fate of individual revertant cells. Such somatic excision events have been recently used to develop a new dynamic model of petal growth[50].

Panel **c** shows a mosaic with respect to the identity of petals. The inflorescence carries an unstable allele of the homeotic B-class *GLOBOSA* (*GLO*) gene. Impaired *GLO* function in the mutant, as seen in the two lower buds, results in petals developing as sepals and stamens as carpels. Excision of the transposon restores *GLO* function, as shown by the petaloid sectors in the uppermost flower. Such unstable alleles are also available for the second B-class gene, *DEFICIENS* (*DEF*), with phenotypes that are indistinguishable from that shown here for the *globosa* (*glo*) mutant[18,44].

lymphocytes[16], which now seems likely to reflect a transposon origin of the system. Transposon activity was also exploited to generate periclinal and mericlinal chimaeras (BOXES 1,2), which can be used to study cell-to-cell communication that is governed by developmentally relevant genes[17,18].

The *Antirrhinum* genome contains at least 11 different 'cut and paste' transposons the mobility of which provides an excellent opportunity to obtain stable or unstable mutants in many different genes. Rosemary Carpenter and Enrico Coen recognized the potential of transposons in 'reverse genetic screens' during the late 1980s; they used their transposon-mutagenized seed collection to establish DNA pools for large-scale PCR screening for transposon insertions. DNA from several hundred mutants from the classical collection was also included in the pools, prompted by the observation that, despite their origin from different mutagenesis programmes, most of the mutants characterized so far contain mobile or stabilized transposon insertions.

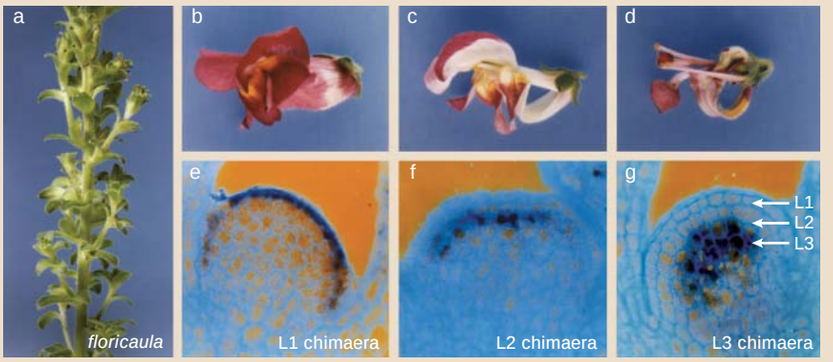
From simple models to complex circuits

The availability of a transposon-tagging system by the mid 1980s independently prompted researchers at the JIC and the MPIZ to use unstable mutants to identify genes that control flower development, floral-organ identity and inflorescence architecture. However, each group chose a different strategy. Rosemary Carpenter and Enrico Coen used large-scale transposon-mutagenesis programmes to isolate unstable mutants, whereas Hans Sommer and Heinz Saedler selected interesting mutants from the classical collection with the aim of either detecting instability or targeting stable mutants to obtain new unstable alleles. Both strategies were successful and the genes that were isolated became important pioneers in plant developmental genetics. Their characterization supported experimental approaches towards unveiling the mysteries of flower development in other species, including *Arabidopsis*. Although many important developmental genes were first isolated in *Antirrhinum*, they are now more familiar by the names of their *Arabidopsis* orthologues (shown in brackets), these include: the floral-organ identity genes *DEFICIENS*[19] (*APETALA3*) and *GLOBOSA*[20] (*PISTILLATA*); the floral-meristem identity genes *FLORICAULA*[21] (*LEAFY*) and *SQUAMOSA*[22] (*APETALA1*); *FIMBRIATA*[23] (*UNUSUAL FLORAL ORGANS*), which controls floral homeotic gene expression; and *CENTRORADIALIS*[24] (*TERMINAL FLOWER*), which regulates inflorescence architecture.

DEFICIENS (*DEF*) was the first floral plant homeotic gene to be cloned[19]. It is a member of the *def* allelic series that was originally described in 1924 by Baur[25] as a mutant in which sepals replace petals, and carpels replace stamens (identical to the phenotype of *globosa* shown in BOX 1). *DEF* became the founder member of a well-known gene family with a common DNA-binding domain, called the MADS box[26]. This domain is also present in transcription factors from other eukaryotes. Ironically, although *DEF* was tagged by a transposon, it was eventually isolated by a *tour de force* of molecular biology by Hans Sommer and colleagues, through the differential screening of a subtracted cDNA library. Instability of the *def* mutant was caused by insertion of a previously unknown transposon (Tam7) in the *def-gli* mutant described by Baur, which helped to confirm the identity of the *DEF* gene. During the following years, several important features of MADS-box proteins were discovered in *Antirrhinum*. These include the ability to dimerize and form higher order complexes[27,28] and the cross regulation among family members[20,29]. These results were confirmed subsequently in *Arabidopsis* and other plants (reviewed in REF. 30).

The classical collection contained several recessive mutants with homeotic defects in flower development. These mutants, together with the *Arabidopsis* homeotic mutants, provided the basis for the 1991 ABC model[31]. This combinatorial model describes the genetic basis for patterning the radial axis of the flower. The letters *A*, *B* and *C* represent three developmental functions controlled by class A, B or C homeotic genes, respectively. These genes are expressed in two adjacent floral whorls and control, either alone or in combination, the development of the four organ types of the flower. Expression of *A* alone specifies sepals, *A* and *B* together specify petals, *B* and *C* specify stamens, and *C* alone specifies carpels (BOX 3). Crucial to the model is the exclusion of the *C* function from the two outer whorls by *A*, which manifests in the expansion of the *C* domain into the *A* domain in recessive *Arabidopsis A* mutants.

Box 2 | The usefulness of genetic mosaics to study cell communication



The vegetative and floral meristems of *Antirrhinum* that give rise to the future lateral organs (leaves or floral organs) form three layers — L1, L2 and L3 (indicated by arrows in panel **g**). Cells in a layer are clonally related and there is little exchange between cells from neighbouring layers during development. Excision events that occur in one layer can eventually overtake an entire side branch during growth of the plant, which results in a PERICLINAL CHIMAERA. In contrast to the variegated pattern of mericlinal chimaeras (BOX 1), mosaic structures in periclinal chimaeras are uniform and can be maintained, provided that no further excisions occur during vegetative propagation. The advantage of *Antirrhinum* is the availability of transposon-induced unstable mutations combined with the ability to maintain chimaeras by propagating individuals as cuttings for several years. Periclinal chimaeras are useful tools to study the developmental consequences of communication between layers, for example in the layer-dependent influence of *FLORICAULA* (*FLO*) on flower development.

floricaula (*flo*) mutants have axial inflorescences instead of flowers, because the control of floral meristem identity is impaired (**a**). Panels **b**, **c** and **d** show the phenotype of periclinal chimaeras of an unstable *flo* mutant. Development of nearly wild-type flowers in an L1 *flo* chimaera (**b**) indicates that the restored wild-type *FLO* gene product in L1 is sufficient to non-autonomously control *FLO* target genes in the underlying *flo* mutant layers. When *FLO* is expressed either in the L2 (**c**) or L3 (**d**) layers, the level of restoration is much reduced. In the wild-type flower, *FLO* is expressed in all layers (not shown). Expression of the restored wild-type gene in the individual layers of young flower buds of the periclinal chimaeras is confirmed by *in situ* hybridization (**e**–**g**). Images reproduced with permission from REFS 17,61.

Notice that the mericlinal or sectorial chimaeras shown in BOX 1 are also informative in terms of cell communication. In this case, the structure of the boundary between wild type and mutant sectors is indicative for lateral communication (or the absence thereof) between cells. The lack of exchange of substances or signals between cells — as in the instances shown for *pal* and *glo* in BOX 1 — result in sharp boundaries.

Furthermore, some *A* mutants in *Arabidopsis* develop leaf-like organs, rather than floral organs, in their perianth, which indicates a role of class A genes in sepal and petal organ specification.

The overwhelming success of the model is based on its simplicity and applicability to the control of floral-organ identity in many different species (reviewed in REF. 30). Delving into the molecular and mechanistic details of this control in *Antirrhinum*, however, has shown interesting species-specific differences that might contribute to the diversity of floral structures[32]. The example of differences in the involvement of class B and class C genes in *Antirrhinum* and *Arabidopsis* in the control of floral determinacy (BOX 3) shows the importance of comparative approaches for learning about the complexity of control mechanisms.

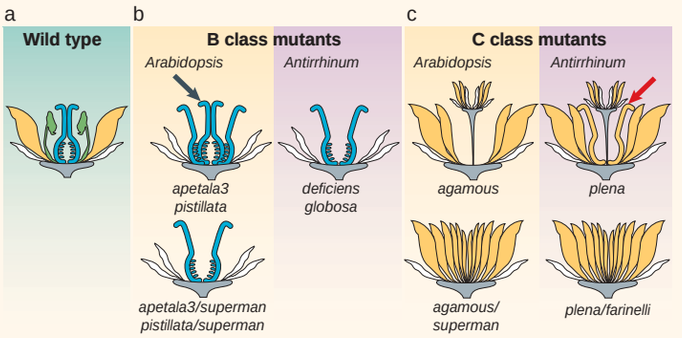
Although generally overlooked in favour of the ABC model, the AB model (which refers to the B and C functions in the ABC model), which was formulated in 1990 (REF. 26), accounted for the lack of recessive class A mutants in *Antirrhinum*[33] and correctly reflected the overall similarities of the *B* and *C* functions (BOX 3). Indeed, the *Antirrhinum* orthologues of the *Arabidopsis A*-function genes seem to have no role in the spatial restriction of the *C* function[34] and organ specification defects are either absent[22] or relatively minor[34] in their mutants. Because this aspect of the ABC model differs so greatly between *Arabidopsis* and other species it is not surprising that recessive *A*-function mutants of the *Arabidopsis* type have been difficult, if not impossible, to find in other plants[30]. Therefore, the exact contribution of the *A* function to floral-organ

Figure 3 | **Mutants of *Antirrhinum majus*.** The collection shows heritable traits in floral colour and shape, as well as transposon-induced colour variegation (indicated by asterisks). Reproduced with permission from REF. 62.

specification remains enigmatic. Again, this shows the importance of comparative studies and the dangers of extrapolating from a single species.

The dependence of cell identity on signalling from neighbouring cells is an intriguing aspect in developmental genetics that can be elegantly accessed in *Antirrhinum* by exploiting transposons to obtain periclinal chimaeras (BOX 2). Chimaeras of this type have also been produced, albeit by different means, in *Arabidopsis*. Comparisons of chimaeras have shown that the degree of control by cell communication exerted by three pairs of orthologous transcription factors (*FLORICAULA/LEAFY*, *DEFICIENS/APETALA3* and *GLOBOSA/PISTILLATA*) differs considerably between species, being far more pronounced in *Arabidopsis* than in *Antirrhinum* (see REF. 35 and references therein).

Box 3 | The control of floral determinacy in *Antirrhinum* and *Arabidopsis*



In the wild-type flower of both *Arabidopsis* and *Antirrhinum*, four distinct organ types are arranged in four WHORLS, as shown in panel **a** (sepals are shown in white, petals in yellow, stamens in green and carpels in blue). The yellow and blue colours correspond to the domains of *B* and *C* gene expression, respectively, which overlap in the stamens in whorl three (green)[26,31].

The *Antirrhinum* and *Arabidopsis B* and *C* mutants are shown schematically in panels **b** and **c**. For reasons discussed in the text, *A* mutants are not considered here. Initiation of a new flower, which is a feature of *C* mutants in both species, is exaggerated. The homeotic organ identity changes in the *Arabidopsis* and *Antirrhinum B*-function mutants and *C*-function mutants are comparable (for instance, in *B* mutants the petals are sepaloid and the stamens are carpelloid), which can be taken as evidence for the generality of the ABC model.

However, the number of whorls differs between the mutants in the two species. *Antirrhinum B* mutants terminate organ initiation after three whorls, but *Arabidopsis B* mutants form four whorls (black arrow). Similarly, in both species there is a *C*-function mutant in which the reproductive organs are replaced by PERIANTH organs. In *Antirrhinum*, a new mutant flower initiates after the production of four whorls (red arrow), whereas in *Arabidopsis* this happens after just three.

These differences can be resolved by a model that involves similar genes in similar processes in both species, but with altered regulatory interactions[32]. The model postulates that, although the number of whorls in *Arabidopsis* and *Antirrhinum* wild-type flowers is identical, the mechanism of termination of organ initiation (the control of determinacy) differs as a result of differences in regulatory interactions between conserved genes. This has been corroborated by the analysis of certain double-mutant phenotypes. First, a combination of either of the *Arabidopsis B* mutants with *superman* (in which the boundary control between whorl three and four is defective and so *B* is ectopically expressed) results in phenotypes that are identical to *Antirrhinum B* single mutants. Second, the initiation of a new mutant flower in *agamous C* mutants can be prevented by combination with the *superman* mutant. Such flowers produce extra petals in the centre of the flower, which indicates that a reduction in *B* expression might be required for initiation of a new flower. Third, a comparable phenotype to that of the *Arabidopsis agamous superman* double mutants is found when the *Antirrhinum C* mutant *plena* is combined with *farinelli*. Surprisingly, *FARINELLI* (*FAR*) does not encode a SUPERMAN-like protein, but rather another C-class MADS-BOX factor, which is not present in the *Arabidopsis* genome. In a wild-type background, *farinelli* mutants are partially male sterile, but when combined with the *C* mutant *plena*, they produce a flower that consists only of internal petals, with no central initiation of a new flower.

These analyses indicate that in both species the *B* and *C* functions control organ identity and floral determinacy: the *C* function promotes termination of organ initiation, whereas the *B* function antagonises *C*. *Antirrhinum* and *Arabidopsis* differ, however, in the regulatory interactions between the homeotic functions and *SUPERMAN* (*SUP*) or its *Antirrhinum* orthologue *OCTANDRA* (*OCT*), respectively. As a consequence, wild-type flowers (as well as *superman* and *octandra* single mutants) have comparable phenotypes, but differences are observed between the *B* and *C* single mutants in the two species. Figure modified from REFS 30,32.

Floral colour, scent and cell shape

The most eye-catching features of *Antirrhinum* are its large colourful petals (FIG. 2). Their function — as well as to enchant gardeners — is to attract pollinators[36]. Elucidating the mechanisms that underlie this attraction is important for the understanding of pollination biology. As mentioned earlier, obtaining and studying mutants in flower-colour pattern and pigment formation has a long tradition in *Antirrhinum* genetics (FIG. 3). This tradition was built on by deciphering structural and regulatory components of the anthocyanin biosynthesis pathway that contributed to it becoming the best biochemically characterized biosynthetic pathway in plants[37].

Emitting scent is another way to appeal to pollinators, although bumblebees seem to appreciate colour more than scent[38]. Nevertheless, studies in *Antirrhinum* have shown that the circadian rhythm of scent emission follows the peak of activity of bumblebees[39].

The specialized conical-shaped cells of the petal epidermis have an important role in intensifying colour. Cathie Martin and her co-workers discovered that the dull-coloured petals of *Antirrhinum mixta* mutants produce flattened petal epidermal cells, which shows that the *MIXTA* gene is required for the production of conical cells[40] (see Cathie Martin's web site in online links box). Intriguingly, ectopic expression of *MIXTA* in transgenic *Antirrhinum* and tobacco plants showed that *MIXTA* could promote either a conical cell or a multicellular TRICHOME fate and suppress the formation of STOMATA, depending on the developmental stage at which it was expressed[41]. This shows that the formation of multicellular trichomes and conical cells share a common mechanism and raises questions about the relationship between the mechanisms that control unicellular trichomes, which are found in *Arabidopsis*, and the multicellular trichomes that are found in many other species.

Asymmetry and growth control

Although cell movements are important in animal development, they do not occur in plants. The final form of a plant therefore results from asymmetric growth. Studies in *Antirrhinum* have provided early insights into how axes of symmetry are elaborated and asymmetric growth is controlled.

Antirrhinum presented an opportunity to analyse control of an asymmetric character that it does not share with *Arabidopsis*. In common with many eudicot families, the wild-type flower of *Antirrhinum* shows strong

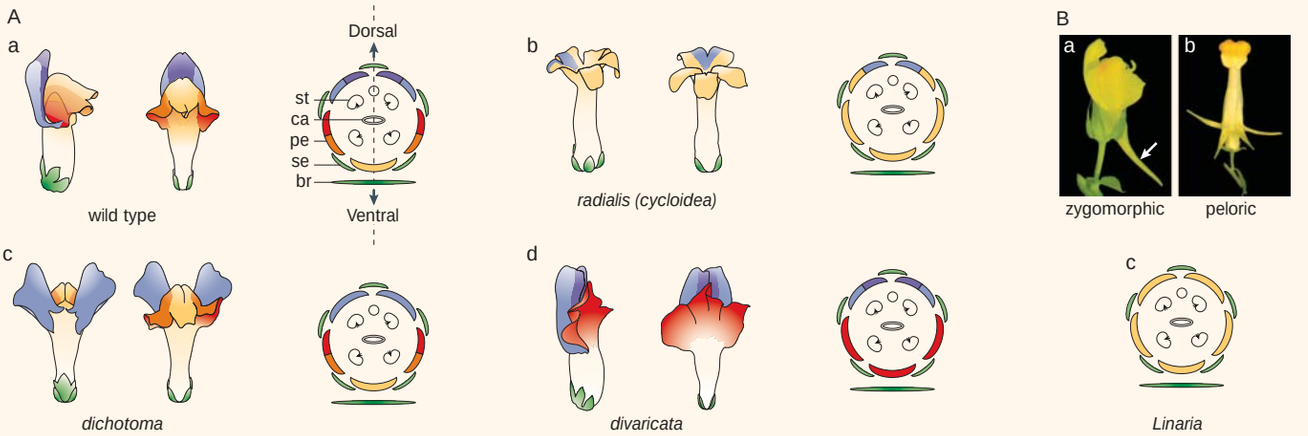


Figure 4 | **Floral asymmetry**. **A** | Wild type and mutant *Antirrhinum* flowers are shown in lateral (left) and ventral (centre) views (except for *dichotoma*, which is shown in dorsal and ventral views). The floral diagrams (right) represent the organization of the floral organs: bract (br), carpel (ca), petals (pe), sepals (se) and stamens (st). The petals are colour coded as follows: ventral petal identity (yellow), lateral petal identity (red) and dorsal petal identity (blue). For simplicity, change in the dorsal or ventral identity of stamens is not considered. The COROLLA of wild-type *Antirrhinum* flowers is composed of five petals and has dorsoventral asymmetry (**Aa**); the two halves are mirror images (the axis of symmetry is indicated by the dotted line). In the wild type, the ventral petal is symmetric (yellow), but the two lateral (orange/red) and two dorsal organs (light blue/dark blue) are asymmetric. This is schematically shown in the floral diagrams, in which the green bract identifies the ventral (lower or abaxial) side of the flower. Several mutations affect the dorso–ventral axis of the flower. *radialis* (and *cycloidea*) mutants have enhanced ventral identity of lateral and dorsal petals (**Ab**). In *dichotoma* mutants, asymmetry of the dorsal petals is reduced (**Ac**). By contrast, in *divaricata* — a semi-dominant mutant — the ventral organs are dorsalized (**Ad**). **B** | The organization of the petals of wild-type *Linaria* flowers is similar to that of *Antirrhinum*, except that the ventral organ has a spur-shaped nectary (white arrow) at its base (**Ba**). Naturally-occurring peloric *Linaria* mutants produce radially symmetric flowers that are composed of five identical ventral petals with spurs (**Bb,c**). This phenotype is similar to *Antirrhinum cycloidea dichotoma* double mutants, which produce symmetrical peloric flowers (not shown).

dorsoventral asymmetry (or ZYGOMORPHY) (BOX 1; FIG. 4A). Analysis of asymmetry mutants showed that floral asymmetry depends on interaction of the dorsally expressed genes *CYCLOIDEA* (*CYC*)[42], *DICHOTOMA* (*DICH*)[43] and *RADIALIS* (*RAD*)[44], and the ventral-identity promoting gene *DIVARICATA* (*DIV*)[45,46]. The *Antirrhinum* asymmetry genes can now be used to address the question of how floral asymmetry evolved. *Arabidopsis*, for example, has radially symmetrical flowers, yet has asymmetric *CYC*-like gene expression[47]. In evolutionary terms, this indicates that an ancestral plant might have possessed an incipient asymmetry that was recruited to control asymmetric floral morphology in the *Antirrhinum* lineage. Floral asymmetry evolved independently in different lineages. It is now possible to test whether *CYC*-like gene expression has been recruited to control asymmetry on more than one occasion. A mechanism by which floral asymmetry could subsequently be lost was found by analysing Linnaeus's peloric and non-peloric flowers of *Linaria*[48], which is a close relative of *Antirrhinum* (FIG. 4B). In this case, loss of asymmetry is the result of a heritable epigenetic mutation that silences the *CYC* orthologue in *Linaria* by methylation[49].

In *Antirrhinum*, the dorsal and lateral petals are themselves asymmetric (FIG. 4A). In a collaboration between developmental geneticists and computer scientists, a new method of clonal analysis was used to infer the growth pattern responsible for this asymmetry[50]. This study indicated that asymmetric petal shape might result from a rotation of the petal lobe relative to the principle direction of growth, if growth direction was maintained parallel to the proximodistal axis of the flower, presumably by a long-range signal.

Asymmetric growth can be caused by gain-of-function mutations in two paralogous homeobox genes, *HIRZINA* (*HIRZ*) and *INVAGINATA* (*INA*)[51]. Ectopic expression of either *HIRZ* or *INA* in developing petals results in the duplication of the petal tube as an outgrowth from the existing tube, which produces a structure that resembles the spurs of *Linaria* (FIG. 4B). Spurs might, therefore, have evolved by the redeployment of the mechanism that controls the development of the petal tube, possibly through change in expression of genes such as *HIRZ* and *INA*.

Leaves, like petals, are dorsoventrally asymmetric in their morphology and anatomy. Analysis of the classical *Antirrhinum* mutant *phantastica* (*phan*) indicated that interaction between cells in the dorsal and ventral parts of each developing organ might be needed to establish lateral growth of the leaf blade or petal lobe[52]. Loss of PHAN activity resulted in leaves and petals in which cells in dorsal positions had gained ventral identity and lateral growth had been lost. Although this indicated a role for *PHAN* in regulating two fundamental aspects of leaf development — asymmetry and, therefore, growth — it does not seem to share this role with its *Arabidopsis* orthologue *ASYMMETRIC LEAVES1* (*AS1*), because *as1*-mutant leaves retain dorsoventral polarity and a flattened leaf blade[53]. However, both orthologues are involved in the negative regulation of *KNOX* genes, which is necessary for the development of a normally shaped leaf.

Once growth of the leaf blade has been initiated, it must be coordinated between cell layers and in different regions to result in a flat leaf with a characteristic shape. This coordination is lost in *cincinnata* (*cin*) mutants of *Antirrhinum*, which show increased leaf growth, particularly towards the margins, which are therefore curled. This is consistent with *CIN* acting to promote sensitivity to a growth-arrest signal[54]. It will be interesting, if not amusing, to learn to what extent curling of the leaves of other plants — lettuce, for instance — relates to the control of growth by *CIN*-like genes.

Present and future resources

The collection of classical *Antirrhinum* mutants has weathered the dramatic events of twentieth century Europe largely intact. More than 450 mutants remain available from the IPK-Gatersleben, in the former East Germany, where they have survived the descent and rise of the iron curtain. There is also a second collection of more than 300 mutants, generated, collected and curated by Rosemary Carpenter and colleagues at the JIC. The mutant phenotypes from Germany and the United Kingdom are described at DragonDB, and Enrico Coen and Rosemary Carpenter's web site, respectively. *Antirrhinum* research already benefits from this collection of mutants, as well as proven forward and reverse genetics based on transposons and the ability to genetically transform plants[55]. Standard tools of molecular biology established by Hans Sommer and his co-workers at the MPIZ, including cDNA libraries, genomic libraries and various yeast two-hybrid libraries, further support research and are freely available to the academic community on request.

More recently, genomic resources have been developed to increase the usefulness of *Antirrhinum*. A molecular linkage map has been constructed mainly on the basis of transcribed genes[56]. This has an average interval between markers of 2.5 cM at present. However, most of the protein-coding loci are aggregated into clusters, which reduces the effective distance between genes, and further markers continue to be added. BAC and TAC LIBRARIES representing the *Antirrhinum* genome are also available (see University of Leeds Centre for Plant Sciences in the online links box). These libraries are being used in the analysis of SYNTENY and, together with molecular maps and the relatively small genome size of *Antirrhinum* (which is three times larger than that of *Arabidopsis*), they make positional cloning feasible[57]. To facilitate gene identification and expression analysis, an expressed sequence tag (EST) database has been created containing ~12,000 unique sequences. The EST Collection has already been successfully used for testing functional accordance between *Antirrhinum* and *Arabidopsis* genes and to provide evidence for the separation of function between members of a gene family in *Arabidopsis*[58]. The first ~2,500 EST sequences have been submitted to the European Molecular Biology Laboratory (EMBL) database and can be searched at DragonDB. Perhaps, in the future, the availability of a map, libraries and a large EST data set, combined with a small haploid genome size, will make sequencing the *Antirrhinum* genome a realistic prospect.

Glossary

ANTHOCYANIN
A soluble flavonoid pigment that is responsible for the blue-to-red colours in the flowers and other tissues of many angiosperm species.

AUTONOMOUS TRANSPOSON
Encodes a transposase protein that catalyses its excision and reintegration in the genome. An autonomous transposon can therefore direct its own transposition.

CHIASMA
The cytological manifestation of genetic exchange between chromosomes, which indicates that a crossover has occurred between homologous chromosomes.

COROLLA
A collective term for petals.

HOMEOTIC
A mutation that causes one member of a repetitive series to assume the identity of another member, for example, the transformation of sepals into petals.

MADS BOX
An acronym for the DNA-binding domain of a gene family that is derived from the initials of the founding members *MCM1*, *AGAMOUS*, *DEFICIENS* and *SRF*, in yeast, *Arabidopsis*, *Antirrhinum* and humans, respectively.

MERICLINAL CHIMAERA
A plant shoot in which only part of a cell layer is genetically distinct.

PELORIC
A term coined by Darwin to describe a mutant flower that has many planes of reflectional symmetry.

PERIANTH
A collective term for the sepals and petals.

PERICLINAL CHIMAERA
A shoot that is formed from an apical meristem in which at least one of the clonally distinct cell layers is genetically different.

STOMATA
Natural openings in the epidermis of the stem or leaf of a plant, which are surrounded by specialized guard cells and allow gaseous exchange with the air.

SYNTENY
The conservation of the relative order of genes in the chromosomes of different species.

TAC LIBRARY
A library consisting of large fragments of plant genomic DNA in a transformation-competent bacterial artificial chromosome (TAC) vector. This allows rapid transfer of genomic DNA to plant hosts through *Agrobacterium*-mediated transformation.

TRICHOMES
Epidermal hairs, which in *Antirrhinum* are multicellular.

WHORL
Organs of the same structure and function that are arranged in a concentric ring. In the flower, the outermost whorl (whorl one) develops first and contains the sepals, followed by the petals, stamens and carpels in whorls two, three and four, respectively.

ZYGOMORPHY
A zygomorphic flower has only one plane of reflectional symmetry and is often insect pollinated.

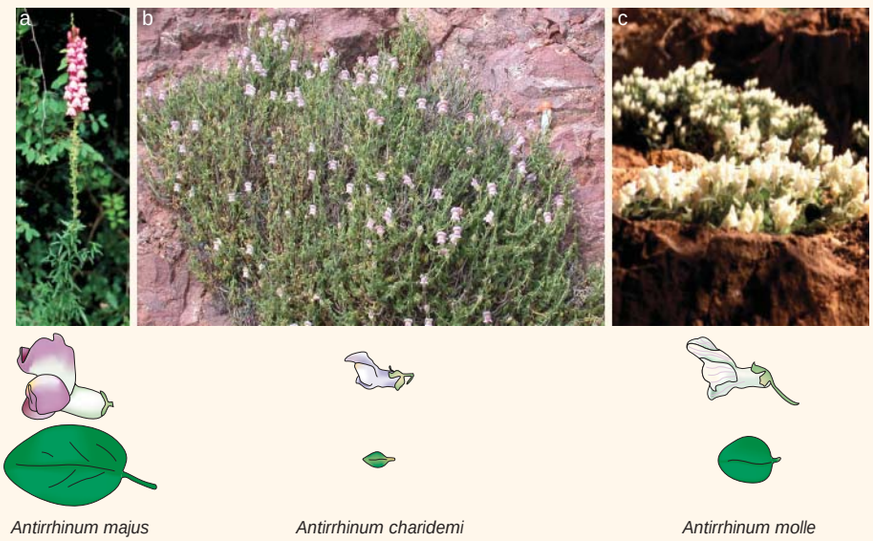


Figure 5 | **Natural variation in the genus *Antirrhinum*. a** | *Antirrhinum majus* is widely distributed around the Mediterranean coast of Spain and France; it has an upright growth habit, little lateral branching, large leaves and magenta flowers. **b** | *Antirrhinum charidemi* is endemic to Cabo de Gata, south eastern Spain, which is the driest place in mainland Europe; it has many lateral branches, small leaves and pink flowers. **c** | *Antirrinum molle* is found on cliffs and screes in the Pyrenees; it has highly branched, trailing stems and organs of intermediate size that are covered with many hairs, and ivory flowers with a magenta venation pattern. Photographs courtesy of Thomas Gübitz and Nicolas Langdale.

The organisms themselves, however, represent the main untapped resource of *Antirrhinum* genetics[1]. The genus *Antirrhinum* consists of ~18 species as well as the model *Antirrhinum majus* from south western Europe and northern Africa. It is sister to a clade containing 11 species that are endemic to mid-California, which have been mostly placed in the genus *Sairocarpus* but are loosely termed antirrhinums[59]. The New World species are less well characterized than those from Europe, which are morphologically and physiologically diverse — from trailing hairy alpines of the Pyrenees to a drought-adapted sub-shrub of south eastern Spain (FIG. 5) — but share the same chromosome number (2n = 16) and form fertile hybrids when artificially cross pollinated[59].

Research perspectives

Looking back over the past 150 years of *Antirrhinum* research we can see that *Antirrhinum* studies have made important contributions to the fields of plant genetics and development. So, what can we expect from the continuation of research with *Antirrhinum* in the future?

Antirrhinum majus can act as a model system for investigations that are impossible with some other model species, such as perennial behaviour or zygomorphy. The large and elaborate flower is easy to dissect and so is particularly well suited to biochemical and proteomic studies of flower shape, organ identity, colour and scent.

Also, species hybrids, together with recombinant inbred and near-isogenic lines derived from them, make it feasible to use the resources from *Antirrhinum majus* to identify and isolate the genes that underlie species differences, and to test their adaptive importance. *Antirrhinum* species also differ in their breeding systems, ranging from complete self-fertility in *Antirrhinum majus* to obligate out-breeders, and have been used to compare the effects of breeding systems on genetic diversity[60]. Several *Antirrhinum* species coexist with at least one other species but rarely form natural hybrids, providing a model to investigate the mechanisms of species isolation and the genetic consequences of their breakdown. Of particular interest in the context of isolation is the role of flower colour, which differs between species and is known to influence pollinator choice in *Antirrhinum majus*[36].

These, and many other aspects of *Antirrhinum* biology, are likely to result in the genus being used more widely in ecological and evolutionary studies in the twenty-first century.

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1. Stubbe, H. *Genetik und Zytologie von Antirrhinum L. sect. Antirrhinum* (Gustav Fischer, Jena, 1966).
2. Darwin, C. R. *Variation of Animals and Plants Under Domestication* (John Murray, London, 1868).
3. Stubbe, H. Neue Mutanten von Antirrhinum majus L. *Kulturpflanze* **22**, 189–213 (1974).
4. McClintock, B. The origin and behaviour of mutable loci in maize. *Proc. Natl Acad. Sci.* **36**, 344–355 (1950).
5. Stickland, R. G. & Harrison, B. J. Precursors and genetic control of pigmentation. I. Induced biosynthesis of pelargonidin, cyanidin and delphidin in *Antirrhinum majus*. *Heredity* **33**, 108–112 (1974).
6. Harrison, B. J. & Carpenter, R. A comparison of the instabilities at the *nivea* and *pallida* loci in *Antirrhinum majus*. *Heredity* **31**, 309–323 (1973).
7. Harrison, B. & Carpenter, R. Resurgence of genetic instability in *Antirrhinum majus*. *Mutat. Res.* **63**, 47–66 (1979).
8. Wienand, U. *et al.* A general method to identify plant structural genes among genomic DNA clones using transposable element induced mutations. *Mol. Gen. Genet.* **187**, 195–201 (1982).
9. Bonas, U., Sommer, H. & Saedler, H. The 17-Kb Tam-1 element of *Antirrhinum majus* induces a 3-bp duplication upon integration into the chalcone synthase gene. *EMBO J.* **3**, 1015–1019 (1984).
10. Martin, C., Carpenter, R., Sommer, H., Saedler, H. & Coen, E. S. Molecular analysis of instability in flower pigmentation of *Antirrhinum majus*, following isolation of the *Pallida* locus by transposon tagging. *EMBO J.* **4**, 1625–1630 (1985).
11. Sommer, H., Carpenter, R., Harrison, B. J. & Saedler, H. The transposable element Tam3 of *Antirrhinum majus* generates a novel type of sequence alteration upon excision. *Mol. Gen. Genet.* **199**, 225–231 (1985).
12. Gierl, A. & Saedler, H. in *Nucleic Acids and Molecular Biology* Vol. 3 (eds. Eckstein, F. & Lilley, D. M. J.) 251–259 (Springer, Berlin, Heidelberg, 1989).
13. Schwarz-Sommer, Z. & Saedler, H. Plant transposable elements 1984. *Oxford Surv. Plant Mol. Cell Biol.* **2**, 353–360 (1985).
14. Coen, E. S., Carpenter, R. & Martin, C. Transposable elements generate novel spatial patterns of gene expression in *Antirrhinum majus*. *Cell* **47**, 285–296 (1986).
15. Sommer, H., Bonas, U. & Saedler, H. Transposon-induced alterations in the promoter region affect transcription of the chalcone synthase gene of *Antirrhinum majus*. *Mol. Gen. Genet.* **211**, 49–55 (1988).
16. Agrawal, A., Eastman, Q. M. & Schatz, D. G. Transposition mediated by RAG1 and RAG2 and its implications for the evolution of the immune system. *Nature* **394**, 744–751 (1998).
17. Carpenter, R. & Coen, E. S. Transposon induced chimeras show that *floricaula*, a meristem identity gene, acts non-autonomously between cell layers. *Development* **121**, 19–26 (1995).
18. Perbal, M.-C., Haughn, G., Saedler, H. & Schwarz-Sommer, Z. Non-cell-autonomous function of the *Antirrhinum* floral homeotic proteins DEFICIENS and GLOBOSA is exerted by their polar cell-to-cell trafficking. *Development* **122**, 3433–3441 (1996).
19. Sommer, H. *et al. Deficiens*, a homeotic gene involved in the control of flower morphogenesis in *Antirrhinum majus*: the protein shows homology to transcription factors. *EMBO J.* **9**, 605–613 (1990).
20. Tröbner, W. *et al. GLOBOSA*: a homeotic gene which interacts with *DEFICIENS* in the control of *Antirrhinum* floral organogenesis. *EMBO J.* **11**, 4693–4704 (1992).
21. Coen, E. S. *et al. floricaula*: a homeotic gene required for flower development in *Antirrhinum majus*. *Cell* **63**, 1311–1322 (1990).
22. Huijser, P. *et al.* Bractomania, an inflorescence anomaly, is caused by the loss of function of the MADS-box gene *squamosa* in *Antirrhinum majus*. *EMBO J.* **11**, 1239–1249 (1992).
23. Simon, R., Carpenter, R., Doyle, S. & Coen, E. Fimbriata controls flower development by mediating between meristem and organ identity genes. *Cell* **78**, 99–107 (1994).
24. Bradley, D. *et al.* Control of inflorescence architecture in *Antirrhinum*. *Nature* **379**, 791–797 (1996).
25. Baur, E. Untersuchungen über das wesen, die entstehung und die vererbung von rassenunterschieden bei *Antirrhinum majus*. *Bibl. Genetica* **4**, 101–103 (1924).
26. Schwarz-Sommer, Z., Huijser, P., Nacken, W., Saedler, H. & Sommer, H. Genetic control of flower development by homeotic genes in *Antirrhinum majus*. *Science* **250**, 931–936 (1990).
27. Davies, B., Egea-Cortines, M., de Andrade Silva, E., Saedler, H. & Sommer, H. Multiple interactions amongst floral homeotic MADS-box proteins. *EMBO J.* **15**, 4330–4343 (1996).
28. Egea-Cortines, M., Saedler, H. & Sommer, H. Ternary complex formation between the MADS-box proteins SQUAMOSA, DEFICIENS and GLOBOSA is involved in the control of floral architecture in *Antirrhinum majus*. *EMBO J.* **18**, 5370–5379 (1999).
29. Zachgo, S. *et al.* Functional analysis of the *Antirrhinum* floral homeotic *DEFICIENS* gene *in vivo* and *in vitro* by using a temperature-sensitive mutant. *Development* **121**, 2861–2875 (1995).
30. Davies, B., Sommer, H. & Schwarz-Sommer, Z. in *Development: Genetics, Epigenetics and Environmental Regulation* (eds. Russo, V. A. E., Cove, D. J., Edgar, L. G. & Salamini, F.) 167–183 (Springer, Berlin, Heidelberg, New York, Tokyo, 1999).
31. Coen, E. S. & Meyerowitz, E. M. The war of the whorls: genetic interactions controlling flower development. *Nature* **353**, 31–37 (1991).
32. Davies, B. *et al.* PLENA and FARINELLI: redundancy and regulatory interactions between two *Antirrhinum* MADS-box factors controlling flower development. *EMBO J.* **18**, 4023–4034 (1999).
33. Motte, P., Saedler, H. & Schwarz-Sommer, Z. STYLOSA and FISTULATA: regulatory components of the homeotic control of *Antirrhinum* floral organogenesis. *Development* **125**, 71–84 (1998).
34. Keck, E., McSteen, P., Carpenter, R. & Coen, E. Separation of genetic functions controlling organ identity in flowers. *EMBO J.* **22**, 1058–1066 (2003).
35. Efremova, N. *et al.* Epidermal control of floral organ identity by class B homeotic genes in *Antirrhinum* and *Arabidopsis*. *Development* **128**, 2661–2671 (2001).
36. Glover, B. J. & Martin, C. The role of petal cell shape and pigmentation in pollination success in *Antirrhinum majus*. *Heredity* **80**, 778–784 (1998).
37. Martin, C. & Gerats, T. Control of pigment biosynthesis genes during petal development. *Plant Cell* **5**, 1253–1264 (1993).
38. Odell, E., Raguso, R. A. & Jones, K. N. Bumblebee foraging responses to variation in floral scent and color in snapdragons (*Antirrhinum*: Scrophulariaceae). *Am. Midland Nat.* **142**, 257–265 (1999).
39. Dudareva, N. *et al.* Developmental regulation of methyl benzoate biosynthesis and emission in snapdragon flowers. *Plant Cell* **12**, 949–961 (2000).
40. Noda, K., Glover, B. J., Linstead, P. & Martin, C. Flower colour intensity depends on specialized cell shape controlled by a Myb-related transcription factor. *Nature* **369**, 661–664 (1994).
41. Martin, C. *et al.* The mechanics of cell fate determination in petals. *Philos. Trans. R. Soc. Lond. B* **357**, 809–813 (2002).
42. Luo, D., Carpenter, R., Vincent, C., Copsey, L. & Coen, E. Origin of floral asymmetry in *Antirrhinum*. *Nature* **383**, 794–799 (1996).
43. Luo, D. *et al.* Control of organ asymmetry in flowers of *Antirrhinum*. Cell **99**, 367–376 (1999).
44. Carpenter, R. & Coen, E. S. Floral homeotic mutations produced by transposon-mutagenesis in *Antirrhinum majus*. *Genes Dev.* **4**, 1483–1493 (1990).
45. Almeida, J., Rocheta, M. & Galego, L. Genetic control of flower shape in *Antirrhinum majus*. **124**, 1387–1392 (1997).
46. Galego, L. & Almeida, J. Role of DIVARICATA in the control of dorsoventral asymmetry in *Antirrhinum* flowers. *Genes Dev.* **16**, 880–891 (2002).
47. Cubas, P., Coen, E. & Zapater, J. M. M. Ancient asymmetries in the evolution of flowers. *Curr. Biol.* **11**, 1050–1052 (2001).

48. Gustafson, A. Linnaeus' peloria: the history of a monster. *Theor. Appl. Genet.* **54**, 241–248 (1979).
49. Cubas, P., Vincent, C. & Coen, E. An epigenetic mutation responsible for natural variation in floral symmetry. *Nature* **401**, 157–161 (1999).
50. Rolland, A.-G., Bangham, J. A. & Coen, E. Growth dynamics underlying petal shape and asymmetry. *Nature* **422**, 161–163 (2003).
51. Golz, J. F., Keck, E. J. & Hudson, A. Spontaneous mutations in KNOX genes give rise to a novel floral structure in *Antirrhinum*. *Curr. Biol.* **12**, 515–522 (2002).
52. Waites, R. & Hudson, A. *Phantastica*: a gene required for dorsoventrality of leaves in *Antirrhinum majus*. *Development* **121**, 2143–2154 (1995).
53. Byrne, M. E. *et al.* Asymmetric leaves1 mediates leaf patterning and stem cell function in *Arabidopsis*. *Nature* **408**, 967–971 (2000).
54. Nath, U., Crawford, B. C. W., Carpenter, R. & Coen, E. Genetic control of surface curvature. *Science* **299**, 1404–1407 (2003).
55. Heidmann, I., Efremova, N., Saedler, H. & Schwarz-Sommer, Z. A protocol for transformation and regeneration of *Antirrhinum majus*. *Plant J.* **13**, 723–728 (1998).
56. Schwarz-Sommer, Z. *et al.* A linkage map of an F2 hybrid population of *Antirrhinum majus* and *A. molle*. *Genetics* **163**, 699–710 (2003).
57. Lai, Z. *et al.* An F-box gene linked to the self-incompatibility (S) locus of *Antirrhinum* is expressed specifically in pollen and tapetum. *Plant Mol. Biol.* **50**, 29–42 (2002).
58. Müller, I. *et al.* Syntaxin specificity in *Arabidopsis* cytokinesis. *Nature Cell Biol.* **5**, 531–534 (2003).
59. Sutton, D. A. *A Revision of the Tribe Antirrhineae* (British Museum Natural History, London, 1988).
60. Zwettler, D., Vieira, C. P. & Schlotterer, C. Polymorphic microsatellites in *Antirrhinum* (Scrophulariaceae), a genus with low levels of nuclear sequence variability. *J. Hered.* **93**, 217–221 (2002).
61. Hantke, S. S., Carpenter, R. & Coen, E. S. Expression of *floricaula* in single cell layers of periclinal chimeras activates downstream homeotic genes in all layers of floral meristems. *Development* **121**, 27–35 (1995).
62. Baur, E. *Einführung in die Experimentelle Vererbungslehre* (Gebr. Borntraeger, Berlin, 1914).
63. Paxton, J. *Paxton's Magazine of Botany, and Register of Flowering Plants* Vol. 5 55–56 (Periodical Publications, London, 1938).
64. Penzig, O. *Pflanzen-Teratologie, Systematisch Geordnet* Vol. 3 (Gebr. Borntraeger, Berlin, 1890).
65. Masters, M. T. *Vegetable Teratology: An Account of the Principal Deviations from the Usual Construction of Plants* (Ray Society, London,1869).
66. de Vries, H. *Die Mutationstheorie 1* (von Veit u. Co, Leipzig, 1901).
67. de Vries, H. *Die Mutationstheorie 2* (von Veit u. Co, Leipzig, 1903).
68. Schwarz-Sommer *et al.* Characterization of the *Antirrhinum* floral homeotic MADS-box gene *deficiens*: evidence for DNA binding and autoregulation of its persistent expression throughout flower development. *EMBO J.* **11**, 251–263 (1992).
69. Waites *et al.* The *PHANTASTICA* gene encodes a MYB transcription factor involved in growth and dorsoventrality of lateral organs in *Antirrhinum*. *Cell* **5**, 779–789 (1998).
70. Gutierrez-Cortines, M. E. & Davies, B. Beyond the ABCs: ternary complex formation in the control of floral organ identity. *Trends Plant Sci.* **5**, 471–476 (2000).

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