

African genomes illuminate the early history and transition to selfing in *Arabidopsis thaliana*

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Over the past 20 y, many studies have examined the history of the plant ecological and molecular model, *Arabidopsis thaliana*, in Europe and North America. Although these studies informed us about the recent history of the species, the early history has remained elusive. In a large-scale genomic analysis of African *A. thaliana*, we sequenced the genomes of 78 modern and herbarium samples from Africa and analyzed these together with over 1,000 previously sequenced Eurasian samples. In striking contrast to expectations, we find that all African individuals sampled are native to this continent, including those from sub-Saharan Africa. Moreover, we show that Africa harbors the greatest variation and represents the deepest history in the *A. thaliana* lineage. Our results also reveal evidence that selfing, a major defining characteristic of the species, evolved in a single geographic region, best represented today within Africa. Demographic inference supports a model in which the ancestral *A. thaliana* population began to split by 120–90 kya, during the last interglacial and Abbassia pluvial, and Eurasian populations subsequently separated from one another at around 40 kya. This bears striking similarities to the patterns observed for diverse species, including humans, implying a key role for climatic events during interglacial and pluvial periods in shaping the histories and current distributions of a wide range of species.

evolution | population history | self-compatibility | climate | migration

The plant *Arabidopsis thaliana* is the principal plant model species, and as such has been useful not only to examine basic biological mechanisms but also to elucidate evolutionary processes. The exceptional resources available in this species, including seed stocks collected from throughout Eurasia for over 75 y, have been a valuable tool for learning about the natural history of *A. thaliana* on this continent (1, 2). Previous studies have shown that current variation in Eurasia is mainly a result of expansions and mixing from refugia in Iberia, Central Asia, and Italy/Balkans after the end of the last glacial period ~10 kya (3–8). The main finding of the recent analysis of 1,135 sequenced genomes was that a few Eurasian samples represent divergent relict lineages, whereas the vast majority derived from the recent expansion of a single clade (4). Given the large number of studies that examine the natural history of *A. thaliana*, one would expect that this history would by now be described rather completely and there would be no major surprises left to uncover. However, there are still many open questions about the ancient history of the species.

Several features differentiate *A. thaliana* from its closest relatives. Although most members of the *Arabidopsis* genus are obligate outcrossing perennials with large flowers and genome sizes of over 230 Mb and 8 chromosomes, *A. thaliana* is a predominantly selfing annual with reduced floral morphology and a reduced genome size of ~150 Mb and 5 chromosomes. The transition to predominant selfing in *A. thaliana* was likely the catalyst for these derived morphological and genomic features (9–13). These changes, in particular the rearranged and shrunken genome, created a strong reproductive barrier between *A. thaliana* and its closest relatives (14).

Although the genetic basis of self-compatibility in *A. thaliana* is known, the specific events that occurred during the transition to predominant selfing are still unclear. In obligate outcrossing *Arabidopsis* species, many highly divergent S-locus haplogroups (S-haplogroups) are maintained by balancing selection, providing a mechanism for inbreeding avoidance. In *A. thaliana*, three S-haplogroups are found, and each contains mutations that obliterate function of the S-locus genes (15–17). Loss-of-function occurred independently in each S-haplogroup (18–21), but because these three S-haplogroups were never found together in the same geographic region, self-compatibility is inferred to have evolved separately in multiple locations (16, 21, 22). However, the hypothesis of geographically distinct origins is difficult to reconcile with the major genomic and phenotypic changes that render *A. thaliana* incompatible with its outcrossing congeners (9–13). Shifts from outcrossing to predominant selfing are common and have been considered the most prevalent evolutionary transitions in flowering plants (23). Reconstructing the evolutionary history of the transition to selfing in *A. thaliana* could provide general insights into this common evolutionary

Significance

The principal plant model species, *Arabidopsis thaliana*, is central to our understanding of how molecular variants lead to phenotypic change. In this genome-sequencing effort focused on accessions from Africa, we show that African populations represent the most ancient lineages and provide new clues about the origin of selfing and the species itself. Population history in Africa contrasts sharply with the pattern in Eurasia, where the vast majority of samples result from the recent expansion of a single clade. This previously unexplored reservoir of variation is remarkable given the large number of genomic studies conducted previously in this well-studied species and implies that assaying variation in Africa may often be necessary for understanding population history in diverse species.

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Data deposition: The sequences reported in this paper has been deposited in the European Nucleotide Archive/Sequence Read Archive database, study PRJEB19780 (accession nos. ERS1575066–ERS1575147). Analysis scripts are available at https://github.com/HancockLab/African_A.thaliana.

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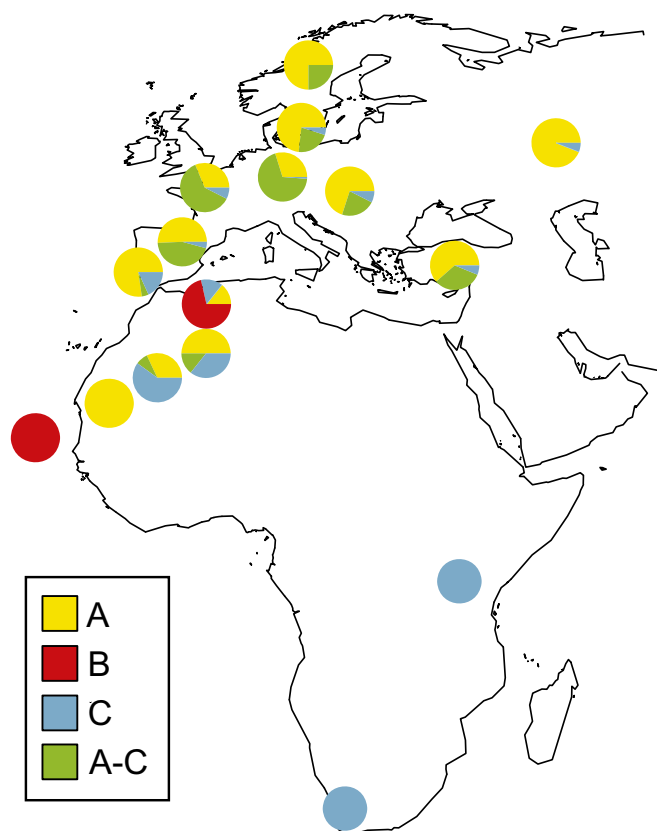


Fig. 4. Map of S-locus haplogroup diversity.

size changes over time, maxima and minima are informative but the slope should be interpreted with caution (33). In addition, the precise timing associated with inferred population size changes and splits is dependent on parameters that are difficult to measure and may vary over space and time, including mutation rate, degree of purifying selection, and the possible input from a seed bank. We used the best available data for mutation rate [based on mutation accumulation experiments (40)] and made the usual simplifying assumptions for other parameters (one generation per year), but

the timing we infer would need to be revised if these assumptions turned out to be incorrect.

Discussion

Genomic studies thus far have amassed data for nearly 2,000 Eurasian *A. thaliana* accessions but were unable to provide insight into the early history of the species. Here, in a genome-scale sequencing effort focused on African accessions, we find clear evidence for a deep history of African *A. thaliana* populations, which harbor variation that was either lost or never present in Eurasia. Several specific results were unexpected based on current knowledge in this well-studied species. First, we discovered surprising and clear evidence that *A. thaliana* is native not only to North Africa but also to Afro-alpine regions of sub-Saharan Africa. Second, our results revealed that the deepest splits species-wide separate the African lineages from one another and that in ancient times, the effective population size was largest in Africa. Finally, we learned that variation at the S-locus is highest in Africa and that all three S-haplogroups are present there.

Based on our results, we can outline a model for the early history and transition to selfing in *A. thaliana* (detailed in *SI Appendix*, Fig. S12). In the first step, we infer that the population ancestral to *A. thaliana* became geographically separated from its parental out-crossing population. Our results suggest that this separation involved migration of the ancestral subpopulation into Africa by 1.2–0.8 Mya. This timing corresponds to the Middle Pleistocene Transition, a shift to drier more variable climate and more open habitats in Africa (i.e., grasslands versus woodlands), as evidenced by soil carbon analysis showing an increase in the ratio of C4 to C3 plants (41, 42).

Although the estimated divergence times between *A. thaliana* and *Arabidopsis lyrata* center around 5–7 Mya (9, 43), the origin of *A. thaliana* itself appears to be much younger. Our model predicts that there was an initial bottleneck as the subpopulation that led to *A. thaliana* split from a *A. lyrata*-like ancestral population [similar to that observed in *Mimulus nasutus* (44) and *Capsella rubella* (45–47)], followed by an expansion in N_e as the selfing population began to spread. In this case, we could interpret the MSMC results to suggest that the transition to selfing occurred between 1 Mya and 500 kya, before the most ancient maximum in N_e . This finding is in line with an estimate based on the depth of the *A. thaliana* genealogy (0.84% maximum divergence among individuals sampled here) under a simple model ($T \sim D/2\mu \sim 598$ kya). Our estimated timing is also consistent

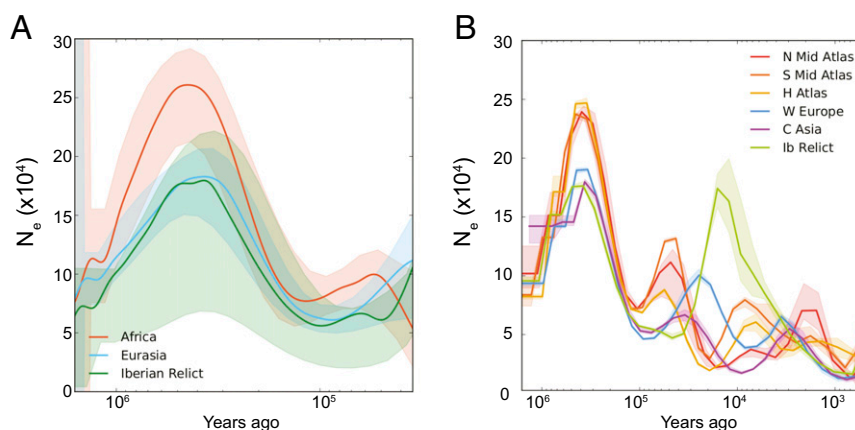


Fig. 5. Historical effective population size of *A. thaliana* inferred using MSMC. Although two-haplotype analysis provides more resolution in the distant past, eight-haplotype analysis provides better resolution in the recent past. (A) Inference using pairs of haplotypes, with lines representing medians and shading representing ± 1 SD calculated across pairs. This analysis is expected to produce unbiased estimates between 40 kya and 1.6 Mya (*SI Appendix*). (B) Inference based on sets of eight haplotypes with lines representing medians. This analysis is expected to produce unbiased estimates as recently as 1.6 kya.

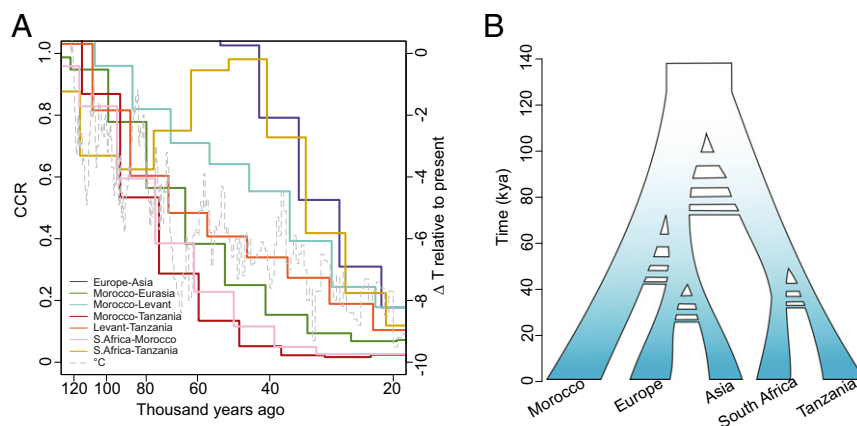


Fig. 6. Inferred timing of population splits. (A) Relative CCR between populations. Decreasing values from 1.0 indicate population separation. The dashed line represents historical temperature (63). (B) A schematic model for the demographic history of *A. thaliana* based on CCR results, with hashes to represent uncertainty regarding possible timing of gene flow events.

with previous estimates for the loss of self-incompatibility and origin of selfing (24–26).

Once selfing was established, traits associated with the “selfing syndrome” would have been favored, including reduced pollen number and petal size (48). Such phenotypic shifts are common in predominantly selfing species and have occurred in *A. thaliana* compared with its closest relatives (26). At the genomic level, *A. thaliana* exhibits major chromosomal rearrangements and a reduction in genome size and number of chromosomes (49). This genomic reduction is also likely a by-product of the shift to predominant selfing in *A. thaliana* (9–11), consistent with an observed link between reduced genome size and selfing in other plant species (11–13). These changes introduce a strong reproductive barrier as found in hybrids of *A. thaliana* and *A. lyrata*, which are infertile because of the chromosomal rearrangements that occurred in *A. thaliana* (14).

Given that all three S-haplogroups co-occur in Morocco, we hypothesize that the transition to predominant selfing occurred in a single region, best represented today in Morocco. This finding differs from previous assertions that these events likely happened separately in geographically distinct populations (15, 16). Moreover, it allows for the possibility that the transition to selfing was aided by a shared precursor mutation, a shared climate, and the bottleneck that occurred during the migration away from the ancestral population (22). Our proposed model parallels observations in partially selfing populations of *A. lyrata* (50). Here, self-compatibility is associated with two different S-haplogroups in Great Lakes populations and self-compatibility may have been favored because of the bottleneck that initially limited S-haplogroup diversity and thus mate availability.

After the origin and initial population size increase of *A. thaliana*, we infer several demographic changes that are congruent with known climatic shifts. At 120–90 kya, we find evidence from MSMC and *δaδi* for splitting among the major clades: Morocco, Levant and sub-Saharan Africa. This split corresponds to the Abbassia pluvial, which produced migration corridors within Africa (120–90 kya) (35, 39) as well as Marine Isotope Stage 5e (130–116 kya), the last interglacial period, when worldwide temperatures were 1–2° warmer than they are currently (51, 52). This is consistent with a model in which *A. thaliana* spread widely throughout Africa and into Eurasia when conditions were favorable (~120 kya), with isolation as gene flow was reduced (*SI Appendix*, Fig. S12). More recent major demographic events include the split between European and Asian populations at around 40 kya and the increase in N_e within Africa during the most recent pluvial.

The patterns we observe and their concordance with climatic events suggest that the transition to selfing and speciation occurred within Africa, with subsequent migration out of Africa into Eurasia. However, it is also possible that the initial transition to selfing occurred within Eurasia followed by migration into Africa and concomitant loss of variation in Eurasia. This alternative would require that the ancient variation in the *A. thaliana* lineage was either lost or has not been sampled in Eurasia and the bottleneck into Africa was mild enough to preserve high levels of genetic variation.

Overall, the patterns in *A. thaliana* bear striking similarities to those observed for human populations, particularly in the larger effective population size in Africa (34), the exodus from Africa approximately 120 kya (39, 53–55), and the splitting of major human populations in Europe and Asia (approximately 45–35 kya) (53, 54). Analogous to what we propose here, demographic events in human populations have been attributed to major climate transitions (35, 39, 56).

Moreover, the timing and types of demographic events we infer during the history of *A. thaliana* are consistent with previous observations in a broad range of other plant species. Specifically, the shift to predominance of C4 plants across Africa at 1.2–0.8 Mya and the intensification of glacial cycles worldwide (57) correspond with our estimated timing of the evolution of selfing in *A. thaliana* and a clustering of speciation events more generally (58). The geographic expansion approximately 120 kya corresponds to an African pluvial and worldwide interglacial, which resulted in expansion of forests across Africa (59) and Eurasia (51, 52). Finally, we see evidence of an increase in effective population size overlapping with the most recent and well-described African pluvial at 11–5 kya, when the Sahara was heavily vegetated and filled with lakes (38, 60, 61). The concordance between inferred population size changes, climate, and reports for other species implies that the patterns we observe in *A. thaliana* may be representative of climate-mediated population dynamics across diverse taxa.

Materials and Methods

For full materials and methods, please see [SI Appendix, Supplementary Text](#).

We sequenced the genomes of 79 *A. thaliana* individuals, including 70 fresh samples and 9 herbarium samples (SI Appendix, Table S1). For fresh leaf samples, sequencing libraries were prepared using Illumina TruSeq DNA sample prep kits (Illumina) and sequenced on Illumina Hi-Seq instruments. DNA from herbarium specimens was extracted, authenticated, and treated with uracil glycosylase to remove damaged nucleotides in a clean room facility at the University of Tübingen. To align the sequences to the TAIR10 reference genome and to call variants, we used two different pipelines: the MPI-SHORE pipeline (62) and a more conservative pipeline designed to reduce false positives resulting from indels.

For population structure analyses, we subsampled the complete dataset to match sample sizes across clusters as some Eurasian geographic regions are heavily oversampled, which could cause biases in some analyses, and we pruned SNPs based on LD to select a representative set. For ADMIXTURE, the number of clusters (K) was determined based on the outcome of cross-validation analyses.

To infer patterns of effective population size and population separations over historical time, we used a MSMC v2 (33). Because *A. thaliana* accessions are inbred, we created pseudodiploids by combining chromosomes from pairs of individuals from the same populations and ran MSMC in the two- and eight-haplotype configurations (Fig. 5). We assumed a mutation rate of 7.1×10^{-9} based on results of mutation accumulation experiments (40) and a generation time of 1 y. We confirmed inferences using $\delta a \delta i$ (37) on joint site frequency spectra from pairs of populations.

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