News & views

Plant genomics

The faba of all genomes

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A high-quality reference genome has been generated for the broad bean (also known as the faba or fava bean). The sequence could be used to identify ways to increase yield, improve pest resistance and more. **See p.652**

Legumes such as broad beans (*Vicia faba*) were called the "slow runners of the Green Revolution"[1], because – unlike staple cereals such as rice, wheat and maize (corn) – legume yields benefited little from changes in breeding and agriculture. Emerging tools for crop breeding, such as genomic selection, are starting to make it possible to unlock the potential of these underused crops, enabling rapid improvement in yields even in the face of climate change and widespread food insecurity[2]. But although whole-genome sequencing and related forms of high-throughput genetic characterization have become routine in crops such as rice, it has been challenging to apply them to species that have big genomes, such as the broad bean. Jayakodi *et al.*[3] report on page 652 the first high-quality, chromosome-scale genome for broad beans.

Broad beans are a key food source in many parts of the world. They are well adapted to a range of climates encompassing considerable precipitation and temperature gradients (from tropical highlands to high latitudes). They can help to fill a need for plant protein in regions where other options are lacking – in the highlands of Ethiopia, for example, where broad beans show greater tolerance for cold than do other cultivated legumes. Even in regions where a variety of legumes thrive, broad beans can enable farmers to lengthen crop rotations, providing people with a rich protein source and the soils with biologically captured nitrogen , which can act as a fertilizer (broad beans being one of the most efficient leguminous crops for such nitrogen fixation[4]). Moreover, lengthening crop rotation reduces the likelihood that diseases and pests will take hold.

A sequence for the broad-bean genome would enhance the potential of this crop (Fig. 1). However, its genome is a whopping 13 gigabases (Gb) long – roughly 4 times the size of the human genome, and bigger than most other crop genomes. As such, its sequencing has lagged nearly a decade behind that of legumes such as the soya bean, chickpea (also called garbanzo) and common bean (*Phaseolus vulgaris*)[5].

Improved algorithms for genome assembly and the declining cost of long-read sequencing technologies were the keys to Jayakodi and colleagues' success. The authors assembled their genome using sequence data from an inbred broad-bean strain. They then used this sequence as a reference, which they compared with sequences from 197 cultivars from a panel chosen for its trait diversity. With these comparison data, the authors analysed the genetic basis of variation in seed size and the colour of a marking called the hilum – traits that are valuable for breeding new broad-bean cultivars of higher market value. They then built tools to harness genetic variation between cultivars – for instance, integrating previous physical and genetic maps made from crosses between differing broad beans into a single online platform (https://pulses.plantinformatics.io).

Jayakodi and colleagues' sequence could be used to reveal the genetic basis of other traits that are important to breeders, facilitating the generation of improved varieties. These traits include resistance to diseases such as chocolate spot, *Ascochyta* blight and *Cercospora* leaf spot, and resistance to insect pests such as broad-bean beetles (*Bruchus rufimanus)* and aphids[6,7].

As well as being a high-protein and nutrient-dense food, legumes fix nitrogen, support pollinators and provide other ecosystem services such as improving the stability of soil aggregates. We hope that Jayakodi and colleagues' work will support efforts to further improve the nitrogen-fixing properties of broad-bean crops, enhancing the rotational value they provide[8].

Much like its genome, the broad bean's domestication has long been mysterious. Seeds distinguishable as broad bean appear in the archaeological record by the tenth

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Figure 1 | The broad bean, *Vicia faba*. Jayakodi *et al.*[3] have generated the first high-quality reference genome sequence for this species.

millennium BC (11,000–12,000 years ago) alongside those of the chickpea[9]. However, the broad bean is one of very few crops for which no sexually compatible wild relative is known. Despite extensive efforts to cross the broad bean with other species of the genus *Vicia*, no successful crosses have been achieved.

It has been speculated that the immediate wild relative of the broad bean might be extinct, lost during approximately 10,000 years of agricultural expansion. It is also possible that the wild relative is not extinct but not yet discovered, perhaps existing in a remote region, such as the Pamir Mountains of Central Asia, from which few geneticists have been able to collect wild relatives of crops. The broad-bean genome will now allow researchers to examine a third hypothesis — that the ancestor of cultivated broad beans underwent major chromosomal rearrangements during domestication, altering it enough to sexually isolate it from its wild relatives.

The broad bean is part of a subgroup of legumes in the genus *Vicia* and the broader tribe Viciaea, whose genome sizes are substantially bigger than those of other legumes. Other members of this subgroup, such as field peas (*Pisum sativum,* 4.45 Gb), lentils (*Lens culinaris,* 4 Gb) and grass peas (*Lathyrus sativus*, 6.3 Gb), harbour many transposable elements that explain this relative increase — these repetitive DNA sequences jump around the genome, propagating as they go[5]. Similarly, Jayakodi *et al.* found that about 79% of the broad-bean genome was derived from transposable elements. Going forward, a better understanding of how transposable elements move might help researchers to understand the part that they play in speciation — not just in the broad bean, but also in groups such as lentils, in which this kind of genetic variation is common.

It is to be hoped that the increasing cost-effectiveness of long-read DNA sequencing will soon support the development of a genus-level pangenome (a collection of sequences that represents the diversity of the genus) for *Vicia*, or even a broader super-pangenome[10] for this genus and other closely related crops. This type of resource will help to illuminate the evolution of this group and its members' genomes. Understanding this variation will help breeders to harness genome regions in distantly related wild species that confer disease resistance and climate resilience, and will facilitate the sharing of genomic information between legumes.

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1. Borlaug, N. E. in *Nutritional Improvement of Food Legumes by Breeding* (ed. Milner, M.) 7–11 (Wiley, 1973).
2. Hickey, J. M., Chiurugwi, T., Mackay, I. & Powell, W. *Nature Genet.* **49**, 1297–1303 (2017).
3. Jayakodi, M. *et al. Nature* **615**, 652–659 (2023).
4. Neugschwandtner, R., Ziegler, K., Kriegner, S., Wagentristl, H. & Kaul, H. P. *Acta Agric. Scand. B* **65**, 658–666 (2015).
5. Bauchet, G. J. *et al. Legum. Sci.* **1**, e16 (2019).
6. Rubiales, D. & Khazaei, H. *Theor. Appl. Genet.* **135**, 3735–3756 (2022).
7. Stoddard, F. L., Nicholas, A. H., Rubiales, D., Thomas, J. & Villegas-Fernández, A. M. *Field Crops Res.* **115**, 308–318 (2010).
8. Marques, E., Kur, A., Bueno, E. & von Wettberg, E. *Crop Sci.* **60**, 2195–2203 (2020).
9. Tanno, K.-I. & Willcox, G. *Veg. Hist. Archaeobot.* **15**, 197–204 (2006).
10. Khan, A. W. *et al. Trends Plant Sci.* **25**, 148–158 (2020).

The authors declare no competing interests.
This article was published online on 8 March 2023.

Alzheimer's disease

Activated immune cells drive neurodegeneration

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An analysis of mice carrying the protein tau — a hallmark of Alzheimer's disease — reveals that immune cells collaborate to drive tau-mediated neurodegeneration, and that drugs already in use in the clinic can combat this decline. **See p.668**

Immune cells called T cells were long discounted as players in brain immunity except in rare circumstances, in part because of dogmatic ideas about their inability to penetrate the blood–brain barrier[1]. However, it has become clear in the past two decades that the adaptive immune system, of which T cells are a major part, does act in the human brain[2]. On page 668, Chen *et al.*[3] describe a role for T cells in neurodegeneration. The authors' work implies the need for a revised view of adaptive immunity in the brain.

Alzheimer's disease is characterized by the accumulation in the brain of extracellular amyloid-β (Aβ) protein and intracellular aggregates of tau protein. But although these proteins are both considered hallmarks of the disease, brain atrophy correlates highly only with tau accumulation, not with Aβ deposition[4]. Might tau trigger a specific response in surrounding cells that drives atrophy? Chen and colleagues address this question directly by using mice that have Aβ deposition or tau aggregation (known as tauopathy), but not both.

There is mounting evidence for an inflammatory immune response in mouse models of neurodegeneration[5] and in people who have Alzheimer's disease[6]. The authors therefore focused on immune cells as possible drivers of tau-specific neurodegeneration. They isolated immune cells from the brains of mice with Aβ deposition and from tauopathy mice, and analysed the cells using single-cell RNA sequencing — an unbiased way to identify cell types on the basis of the genes they express. The analysis revealed 12 immune-cell populations in both models, with many more T cells in the brains of the tauopathy mice than in those of mice with Aβ deposition.

Chen *et al.* validated this finding by examining slices of brain from mice and from people who had died with Alzheimer's disease. Tissue staining revealed that T cells had accumulated in the hippocampus and entorhinal cortex of tauopathy mice and in the superior frontal gyrus in humans. These regions are involved in learning and memory, and are hotspots for tau accumulation. This distribution suggests that T cells respond to tau, and might induce neuronal damage that contributes to the cognitive defects associated with Alzheimer's.

There are many types of T cell, from $CD8^+$ T cells that kill cells flagged by the immune system, to regulatory T cells that suppress immune responses. Knowledge of the subtype and state of T cells is therefore key to determining their potential role in brain atrophy. Examining their sequencing data, the authors discovered that tauopathy mice carried more of a potentially harmful subtype of T cell — activated $CD8^+$ effector T cells — than did mice with Aβ deposition. With increasing amounts of tau in the brain, these cells began to show signs of exhaustion, a dysfunctional condition in which T cells that have been chronically activated lose their normal abilities. The data also revealed that the T cells were clones of a single parent, suggesting that the cell had proliferated (a sign of activation) in response to a specific factor.

T cells are activated when their receptor binds to an antigen (a non-self protein fragment, or a modified self protein fragment)