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Application of a sunlight-switched sugar signal increases wheat yield in the field

Crop yield improvement has plateaued in the past three decades, owing largely to genetic bottlenecks in the germplasm of staple food crops. We used a chemical intervention method that increases yield in the field, providing a sustainable means to improve yields of wheat and potentially other crops.

The question

The current pace of crop selection is no longer sufficient to achieve the improved yields needed to sustain global populations[1]. Photosynthesis produces glucose and sucrose as a carbon 'source' that 'flows' to various glucose polymers (cell wall cellulose and stored starch) in 'sinks' (seeds, grains) of terrestrial plants, and so effectively determines crop yields. Improving yields requires selection of both source and sink[2], which is difficult using genetic selection or gene editing because they require the identification and manipulation of many genes across many varieties. Chemical intervention, with its alternative temporal control and direct targeting of biomolecules in planta, might circumvent this limit. Trehalose 6-phosphate (T6P) is an indispensable plant sugar signal for sugar utilization[3] that is biosynthesized during the source-to-sink flux. As a metabolic signal for the production of sucrose, which is the end product of photosynthesis and starting point for growth and energy storage, T6P could uniquely link source and sink.

The discovery

To alter T6P levels in wheat, we developed plant-permeable analogs of T6P based on a 'signaling precursor' concept (Fig. 1) for ready uptake into developing plant tissues and sunlight-triggered release[4]. Experiments under controlled conditions suggested possible benefits of this approach (flexible timing, dosing and modulated release), although most agrotechnologies fail field testing[5]. Demonstrating efficacy under typically variable field conditions ideally means increasing starch biosynthesis to alleviate sink limitation during grain filling, thereby increasing yields in periods of drought, without additional nitrogen fertilizer.

A promising candidate is the signaling precursor DMNB-T6P, which in purified powder form is stable in the dark at room temperature for more than 2 years. Scalable synthesis of DMNB-T6P enabled field trials, which were conducted over 4 years in Argentina, where current wheat yields are close to the world average and rainfall was variable, conditions that are typical in global agriculture. DMNB-T6P spray applied 10 days after anthesis increased yields in all 4 years (9.3–12.7%) at an empirically effective dose, with no great difference in percentage increase in yield between wet and dry years. No extra fertilizer was applied and grain protein was not diluted in higher yielding grain. Yield was therefore increased sustainably per unit of fertilizer and water. RNA sequencing of grain (24 h after DNMB-T6P application) showed wholesale upregulation of the sucrose-to-starch pathway. Increases were observed in both source (for example, more CO_2 fixation in flag leaves of treated plants) and sink (for example, increased starchy endosperm volume in grain).

This elevation of both source and sink, timed during early grain filling, overcomes two typically recalcitrant trade-offs: no reduction in percentage protein content in higher yielding treated wheat and increase in both grain number and size.

The implications

DMNB-T6P application breaks the link between increased yield and need for more fertilizer (and the associated greenhouse gas emissions[6]). Non-dilution of protein in higher yielding grain could enable even lower fertilizer inputs. Yield was also increased per unit of water from rainfall, the main uncontrolled factor that limits crop yields.

The precise effects of T6P's chemical modulation on sink–source flux are unknown. Timing of the metabolic intervention might be key and cannot be modulated when using genetic control. As many of the genes for grain number and size are developmental rather than metabolic regulators, they might not link source and sink effectively. Chemical modulation of T6P might control a metabolic switch for source–sink coordination. Extra carbon supply from source could now accompany enhanced sink strength to avoid trade-offs. In this way, the current metabolic balance of yield versus survival that emerged from domestication could be moved towards yield. The target of T6P, SnRK1, is a paralog of mammalian AMPK, which can be modulated by the diabetes drug metformin. Perhaps DMNB-T6P acts as a light-activated plant 'drug' for sugar homeostasis, and further parallels might exist.

The T6P pathway is widespread, and thus T6P modulation could be extended to other crops (such as sorghum and barley). Current T6P signaling precursor synthesis is cost-effective and should scale further. Although this post-translational chemical perturbation cannot yet be reproduced genetically, we identify candidate genes that might be targeted and modulated for yield improvements.

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Griffiths, C. A. et al. Membrane-permeable trehalose 6-phosphate precursor spray increases wheat yields in field trials. *Nat. Biotechnol.* https://doi.org/10.1038/s41587-025-02611-1 (2025).

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EXPERT OPINION

"This paper describes two main breakthroughs in the use of the chemical DMNB-T6P to increase wheat yield: first, the development of a feasible, economic route for the bulk synthesis of DMNB-T6P and, second, data from field trials covering different rainfall conditions and wheat genotypes, which show the exceptional promise of DMNB-T6P to increase wheat yield in the field, with the effects on yield going well beyond those achieved in a year through breeding." **An anonymous reviewer.**

FIGURE

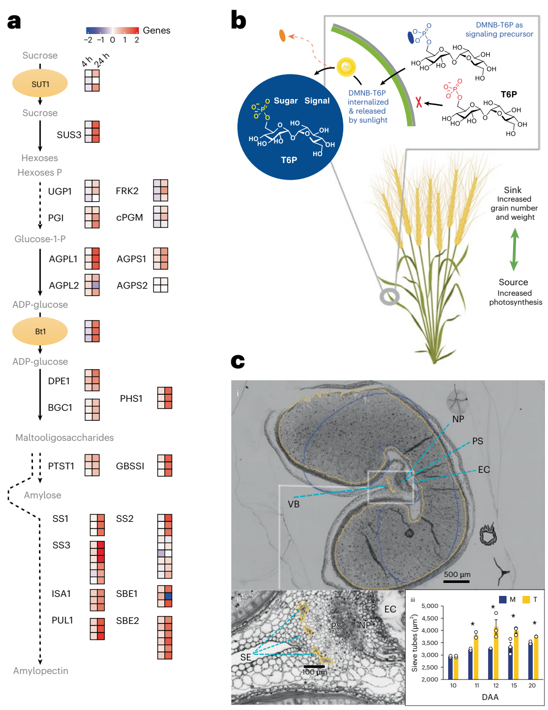

Fig. 1 | Modulation of the T6P pathway and starch synthesis with DMNB-T6P. a, Upregulated starch synthesis in wheat endosperm. Metabolites in gray, enzymes in black. Gene expression for enzymes and transporters at 4 h and 24 h after treatment; $\log_2$(fold) values, capped at ±2. Dashed arrows indicate multiple steps. **b**, DMNB-T6P is released by sunlight for dose-varied control of the T6P pathway. Parts of panel **b** created in BioRender, Davis, B. (2025): https://BioRender.com/p09q308. **c**, i. Transverse section of treated grain. Starchy endosperm and sieve tube area outlined in orange. Overlayed control in blue. VB, vascular bundle; NP, nuclear projection; PS, pigment strand; EC, endosperm cavity; SE, sieve element. ii. SEs in the vascular bundles that supply assimilates to the grain. iii. Sieve tube area increases (in µm^2) with DMNB-T6P treatment. T, treated; M, mock. $^*P < 0.05$.

BEHIND THE PAPER

Almost 20 years ago, M.J.P. and B.G.D. bonded over a common interest in plant glycans and the potential to manipulate these through in vivo chemistries. The initiative "Selective Chemical Intervention in Biological Systems" funded by the UK Research and Innovation (UKRI) – Biotechnology and Biological Sciences Research Council (BBSRC) provided the first opportunity to combine M.J.P.'s insight into sugar signals in plants with B.G.D.'s interest in non-canonical carbohydrate-processing enzymes and carbohydrate-binding proteins. A genetically intractable target seemed ideal for chemical intervention, using an approach based on sunlight-mediated bond-cleavage chemistries that allow correctly timed activation of a compound that is easily absorbed by plants. Progress over the years was only possible by the joint work of numerous loyal partner collaborators, additional funding (primarily from UKRI-BBSRC) and the dedication of colleagues, especially C.A.G., who were willing to translate an initial sketch into something meaningful. **M.J.P. & B.G.D.**

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FROM THE EDITOR

"Here the authors show that microdoses of a scalable, permeable major plant sugar signal and metabolic regulator, T6P, in field trials under natural varying rainfall conditions result in yield gains that are an order of magnitude greater than achieved through any existing wheat breeding program, and could likely be applied to other field crops in addition. This paper is the result of years of international collaboration and field trials." **Editorial Team, *Nature Biotechnology*.**