Precise timing and location of sugar signals can alter the development of plant reproductive tissues. In this issue, Nuccio et al. exploit the control of both the timing and locale of sugar signals to promote the development of newly forming maize ears under drought conditions. The right time turns out to be the maximally stress-sensitive period just before and after pollination, and the right place is a system of vascular and nonvascular cells that deliver sugars into maize ovaries, which become kernels if pollinated (Fig. 1a). The result is a long-sought increase in yield for drought-stressed maize that is consistent over several years and across a broad range of field conditions.

Nuccio et al. alter sugar signals using the well-known strategy of trehalose-6-phosphate phosphatase (TPP) overexpression. Constitutive TPP expression, resulting in altered trehalose metabolism, has been used to improve drought tolerance in a range of species, including potato, tomato and rice. However, constitutive TPP expression in transgenic plants commonly causes pleiotropic effects. Nuccio et al. overcome this problem by fusing TPP to the promoter of a rice transcriptional regulator, OsMads6, that is essential for floral organ identity and endosperm nutrient accumulation. This promoter targets transcription to young florets before pollination and in newly forming kernels immediately after pollination. The authors chose this promoter because it is active when maize is most vulnerable to stress. Using this strategy Nuccio et al. succeed in engineering maize in which TPP is expressed at the right time, and in the right place, which is in tissues that are crucial for sucrose import, metabolism and sensing (Fig. 1a). Importantly, grains of other species are also drought sensitive during the same period.

The duration, geographic breadth and diversity of genetic backgrounds included in the rigorous field analyses of Nuccio et al. provide an unusually thorough appraisal of the performance of transgenic lines. Results from drought-stressed plants were effectively compared along a gradient of water availability. Positive responses to the transgene were most prominent when conditions were severe, and notably, yield of those plants was not lower than that of controls grown in well-watered conditions. Too often, strategies that prevent yield reduction under stress also prevent maximal yield when conditions are good. Results were also noteworthy in the extent of what was achieved by a single-gene alteration.

The TPP transgenic may contribute to yield increases, as well as the observed increase in floret sucrose levels and positive effects on development, by improved sucrose delivery to very young kernels as the authors propose (Fig. 1b). However, other explanations for the improved yield are possible. To fully appreciate the intriguing issues raised by the authors' findings, we need to view them in the context of sugar signaling in maize.

Yield is determined by how newly forming kernels fare because kernel number at harvest depends on how many ovaries (kernels-to-be) remain viable at pollination and how many kernels survive abortion-sensitive early growth. Growth of ovaries and kernels requires sugars (delivered by the vascular system) and the capacity to import, metabolize and sense sugars (Fig. 1a). For example, the expression of important developmental genes in ovaries and kernels is modulated by signals of sucrose and hexose abundance rather than by the sugars' actual concentrations. When sugar availability and use are altered, as happens during drought stress, widespread changes in gene expression occur. Sugar-responsive genes include those for ear and kernel

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**Figure 1** Targeted overexpression of TPP in maize. (a) In florets TPP is targeted to vascular and nonvascular tissues (brown) that deliver sucrose into stress-sensitive ovaries. Upon pollination, ovaries develop into kernels. The more florets that remain viable, the more kernels there are likely to be at harvest. (b) The overexpression of TPP (purple dot) increases sucrose levels (gray), and decreases T6P, both leading to changes in sugar signals (pink). Changes in sugar signals (pink) can affect metabolism (gray arrows) and developmental programs (pink arrow), including those contributing to enhanced yield.
development\textsuperscript{6}, as well as those that mediate the cell cycle, cell expansion, metabolism and sucrose import\textsuperscript{3}. Feast and famine signals are pivotal to adjustment of reproductive load by a mother plant through regulation of kernel abortion and ovary viability under stress. This mechanism provides a vital means for increasing collective sink strength (import capacity) of sucrose-using structures when sugars are plentiful, and decreasing import capacity when resources are limited\textsuperscript{3,4}. If signals of sugar abundance are artificially enhanced for even a short period at crucial stages of development, yield could increase.

The TPP transgenic plant produced by Nuccio et al.\textsuperscript{1} poses some puzzles because although sucrose levels increase slightly—“up to 20%,” according to the authors—the sucrose signal (mediated by trehalose-6-phosphate (T6P)) should decrease due to depletion of T6P by TPP. This could seemingly lead to mixed messages if signals for sucrose itself are reduced whereas those for its metabolism to hexoses are not. This balance in itself may be the key to the observed results\textsuperscript{6,8}. Alternatively, the extent of the impact for starvation signals from depleted T6P could be attenuated in some other way. How then does the TPP transgenic increase yield under stress? There are several possible explanations, including the specificity of targeted sites and T6P-related signaling.

Developmental context might be crucial. For example, expression of a subset of famine-responsive genes is thought to confer import priority to cells and tissues, which enables post-stress recovery of plant organs\textsuperscript{8}. Developing maize kernels do not achieve this ‘essential-sink’ status until one-third of the way through development, after which time they are no longer aborted\textsuperscript{4,5}. Conceivably, localized TPP overexpression might reduce kernel abortion by promoting an early transition to essential-sink status. Early phases of post-pollination development might also be affected because the rice promoter used in the TPP transgenics targets sites involved later in grain growth. Also, increased sucrose levels in florets of the transgenics could exert a developmental influence owing to changes in sucrose/T6P ratios\textsuperscript{10} and probable shifts in sucrose/hexose ratios\textsuperscript{8}. Finally, other outcomes of T6P signaling that are not yet defined may have altered development or perception of development.

Questions about the mechanisms underlying TPP-mediated yield increases in maize have broader relevance for the impacts of altered T6P signaling in transgenics. What happens when adjacent cells have constitutively different ratios of sucrose and T6P? Work thus far indicates that such an outcome is likely, as ratios change with transgenic perturbation, but otherwise remain tightly coupled during responses to diverse conditions\textsuperscript{10}. This is important for development of targeted TPP transgenics, because it is not yet known what effect neighboring cells will have on each other when their sucrose levels, sensing and metabolism are different. Another question is the effect in TPP transgenics of the interplay between T6P signaling and other sugar signals that respond to hexose and glycolytic flux (mediated by hexokinase and TOR systems). The significance of this lies in the extreme sensitivity of plants to sugar signals mediated by T6P. The ratio of sucrose signals to hexose signals may underlie the long-observed correlations between sucrose and hexose “sugar states,” and cell maturation and division\textsuperscript{8}. Finally, we need to understand the extent and impact of the sucrose cycling that occurs in transgenics that reduce T6P levels and relieve inhibition of sucrose resynthesis. Such cycling may seem futile, but could increase classic sugar signals by raising flux through hexokinase reactions. Effects could be prominent in and near vascular tissues, such as those targeted in the present study.\textsuperscript{1}

This work could hold implications for global food supplies. Even food production in mesic areas is increasingly threatened by drought stress, so advances in protecting maize and other grains from such stress will be invaluable.

\section*{Research Highlights}

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\textbf{Vireaemia suppressed in HIV-1-infected humans by broadly neutralizing antibody 3BNC117}

\textbf{Directional dominance on stature and cognition in diverse human populations}

\section*{COMPETING FINANCIAL INTERESTS}

The authors declare no competing financial interests.