

Exploring regulatory networks in plants: transcription factors of starch metabolism

Cristal López-González¹, Sheila Juárez-Colunga¹,
Norma Cecilia Morales-Elías¹ and Axel Tiessen^{1,2}

¹ Departamento de Ingeniería Genética, CINVESTAV Unidad Irapuato, Irapuato, México

² Laboratorio Nacional PlanTECC, Irapuato, México

ABSTRACT

Biological networks are complex (non-linear), redundant (cyclic) and compartmentalized at the subcellular level. Rational manipulation of plant metabolism may have failed due to inherent difficulties of a comprehensive understanding of regulatory loops. We first need to identify key factors controlling the regulatory loops of primary metabolism. The paradigms of plant networks are revised in order to highlight the differences between metabolic and transcriptional networks. Comparison between animal and plant transcription factors (TFs) reveal some important differences. Plant transcriptional networks function at a lower hierarchy compared to animal regulatory networks. Plant genomes contain more TFs than animal genomes, but plant proteins are smaller and have less domains as animal proteins which are often multifunctional. We briefly summarize mutant analysis and co-expression results pinpointing some TFs regulating starch enzymes in plants. Detailed information is provided about biochemical reactions, TFs and cis regulatory motifs involved in sucrose-starch metabolism, in both source and sink tissues. Examples about coordinated responses to hormones and environmental cues in different tissues and species are listed. Further advancements require combined data from single-cell transcriptomic and metabolomic approaches. Cell fractionation and subcellular inspection may provide valuable insights. We propose that shuffling of promoter elements might be a promising strategy to improve in the near future starch content, crop yield or food quality.

Subjects Agricultural Science, Biochemistry, Molecular Biology, Plant Science

Keywords Transcriptional regulation, Sucrose-starch, Biological networks, Regulatory loops, Network hierarchies, Sink-source, Subcellular

INTRODUCTION

Plant cells are autotrophic organisms fully exposed to many environmental signals. While plants must cope with a wide range of conditions (e.g., light, temperature, water availability, etc.), animals enjoy more stable environments since they are able to escape from danger and to migrate searching for food. Plants are totipotent while animal cells are non-totipotent due to regulatory restrictions by cytosolic and nuclear factors. Photosynthesis in plants leads to sucrose and starch providing food for heterotrophic organisms. This review summarizes what we know about transcriptional regulation of starch metabolism in flowering plants. Most genes of starch synthesis and degradation

Submitted 18 January 2019

Accepted 25 March 2019

Published 9 July 2019

Corresponding author

Axel Tiessen,
atiessen@ira.cinvestav.mx

Academic editor

Renate Scheibe

Additional Information and
Declarations can be found on
page 17

DOI [10.7717/peerj.6841](https://doi.org/10.7717/peerj.6841)

© Copyright
2019 López-González et al.

Distributed under
Creative Commons CC-BY 4.0

OPEN ACCESS

have been widely studied due to their importance for plant physiology and growth (Zhang *et al.*, 2012). The expression of key enzymes and their regulatory mechanism at different levels have been investigated (Sakulsingharoj *et al.*, 2004; Li *et al.*, 2011c; Gámez-Arjona *et al.*, 2011). However, their regulation at transcriptional level is still unclear (Kötting *et al.*, 2010; Geigenberger, 2011). The difficulty may arise by the great number of genes (isozymes) that catalyze the main key biochemical reactions in autotrophic organisms (Tiessen & Padilla-Chacon, 2013; Huang, Hennen-Bierwagen & Myers, 2014). This review starts by listing relevant enzymes and then proceeds to clarify some paradigms of biological networks. It continues with examples of gene co-expression analysis that have pinpointed some transcription factors (TFs) in plant cells. It concludes by stating the need of more molecular information by performing single cell transcription analysis combined with metabolic profiling at the subcellular level. The systematic characterization of all TFs and cis regulatory elements of starch metabolism might provide a promising avenue for rational crop improvement.

Survey methodology

The review started with an electronic literature survey that was expanded iteratively. Scientific articles were searched in PubMed, ISI Web of Science, Google Scholar and other databases such as EndNote and Mendeley. The first search terms included following key words: starch metabolism, TFs, regulation and plants. The abbreviated names of genes and the enzyme commission (EC) numbers of key reactions of starch metabolism were also included in the literature survey. The search also included the names of the first and senior authors of publications in high impact journals during the last 20 years about starch metabolism. The pathway of sucrose to starch conversion has been intensively investigated mainly in Arabidopsis and in potato ((Stitt & Zeeman, 2012) and references therein).

Comprehensive list of starch enzymes

Starch metabolism is a network of reversible biochemical reactions that is orchestrated by more than 20 proteins annotated with an EC number as depicted in Fig. 1. For some of those enzymes there are both cytosolic and plastidial isoforms. Some cytosolic isoforms are bound to the outer plastidial membrane allowing for metabolic channeling (Satoh *et al.*, 2008; Hejazi, Steup & Fettke, 2012; Kunz *et al.*, 2014; Fettke & Fernie, 2015; Malinova *et al.*, 2017; Nakamura *et al.*, 2017). Isoform expression and sugar signaling depend on the subcellular compartment, cell type, tissue and stage of development (Tiessen & Padilla-Chacon, 2013).

Starch synthesis in leaves and in storage organs

Green leaves synthesize starch inside the chloroplast using ATP and F6P provided directly by the Calvin Cycle (Fig. 1). Reproductive organs like growing tubers, seeds and fruits depend on the supply of sucrose imported via the phloem by mass flow (Rockwell, Gersony & Holbrook, 2018). Incoming sucrose is then used for growth, cell wall deposition, respiration and storage processes such as starch biosynthesis in the plastid.

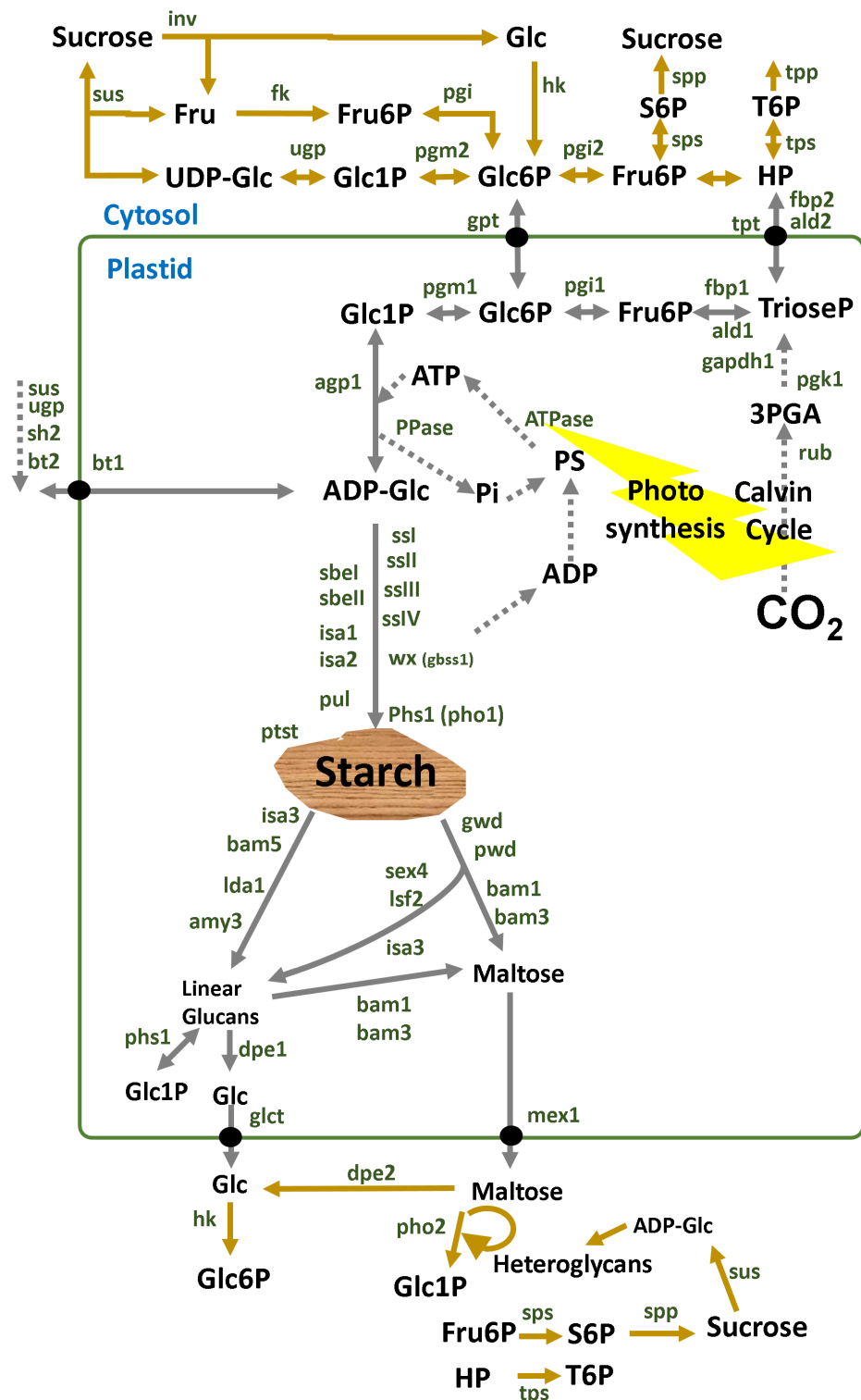


Figure 1 Overview of starch enzymes. Starch metabolism is a network of biochemical reactions that is orchestrated by some key enzymes such as ADP-glucose pyrophosphorylase (AGPase, EC:2.7.7.27), starch synthase (SS, EC:2.4.1.21), granule bound starch synthase (GBSS, EC:2.4.1.242), starch branching enzyme (SBE, EC:2.4.1.18), starch debranching enzyme (DBE, EC:3.2.1.196), α -amylase (AMY,

Figure 1 (continued)

EC:3.2.1.1), β -amylase (BAM, EC:3.2.1.2) and many other enzymes and factors (Lloyd, Kossmann & Ritte, 2005; Comparot-Moss & Denyer, 2009; Tetlow & Emes, 2011; Stitt & Zeeman, 2012). Alkaline pyrophosphatase (PPase, E.C. 3.6.1.1) catalyzes the cleavage of pyrophosphate (PPi) to orthophosphate (Pi) inside the plastid shifting the equilibrium of the AGPase reaction towards starch synthesis (Gross & Ap-Rees, 1986). Additional enzymes such as the alpha-glucan water dikinase (GWD, EC:2.7.9.4), the phospho-glucan water dikinase (PWD, EC:2.7.9.5), disproportionating enzyme (DPE, EC:2.4.1.25), isoamylase (ISA, EC:3.2.1.68), and α -glucan phosphorylase (PHS, EC:2.4.1.1) are also involved in the breakdown of starch (Streb & Zeeman, 2012). Membrane transporters participate in the metabolic network connecting several subcellular compartments such as the ATP transporter (ATT), hexose-phosphate translocator (HPT), glucose translocator (GLT) and maltose exporter (MEX1) (Purdy et al., 2013; Ryoo et al., 2013; Stritzler et al., 2017; Liang et al., 2018). Cytosolic enzymes are involved such as invertase (INV, EC:3.2.1.26), sucrose synthase (SUS, EC:2.4.1.13), hexokinase (HK, EC:2.7.1.1), fructokinase (FK, EC:2.7.1.4), glucose-6-phosphate isomerase (PGI, EC:5.3.1.9) and phosphoglucomutase (PGM, EC:5.4.2.2) (Bahaji et al., 2015; Stitt & Zeeman, 2012; Tetlow & Emes, 2011). In potato tubers, the adenylate-translocator imports ATP from the cytosol in counter exchange with ADP and AMP and thus provides the energy equivalents for starch synthesis (Tjaden et al., 1998). In sink organs, cytosolic sucrose is converted to fructose and UDP-glucose (UDPglc) through SUS in a reversible reaction (Morell & Ap-Rees, 1986; Geigenberger & Stitt, 1993; Zrenner et al., 1995). Using inorganic pyrophosphate (PPi) in the cytosol, fructose and UDPglc are finally processed to hexose-phosphates that can be partitioned to maintain both respiration and starch synthesis. Thereby UDP is regenerated for the SUS reaction. In potato tubers, G6P is imported to the amyloplast by an hexose phosphate translocator (HPT) (Schott et al., 1995; Kammerer et al., 1998) and converted to glucose-1-phosphate (G1P) by plastidic phosphoglucomutase (Fernie et al., 2001). Abbreviations: Fru, fructose; Glc, glucose; Fru6P, fructose-6P; UDP-Glc, UDP-glucose; Glc1P, glucose-1P; Glc6P, glucose-6P; ADP-Glc, ADP-glucose. Enzymes are in dark green: sus1, sus2 and sus3, sucrose synthase isoform 1, 2 and 3; fk, fructokinase; pgi, glucose-6-phosphate isomerase; pgm, phosphoglucomutase; agp, ADP-glucose pyrophosphorylase; agpS, agp small subunit; agpL, agp large subunit; ssI, ssII, ssIII and ssIV, starch synthase type I, II, III and IV; pho, phosphorylase; sbeI, sbeII, starch branching enzyme I, II; isa1, isa2, isa3, isoamylase isoform 1, 2, 3; pul, pullulanase; wx (gbss1), granule bound starch synthase 1; Ida1, limit dextrinase 1; amy3, alpha-amylase 3; bam1, bam2, bam3, bam5, beta-amylase isoform 1, 2, 3, 5; sex4, starch excess 4; lsf2, like sex four 2; gwd, glucan water dikinase; pwd, phosphoglucan water dikinase; phs1, plastidial starch phosphorylase 1; dpe1, dpe2, disproportionating enzyme 1, 2; glct, glucose transporter; mex1, maltose exporter.

Full-size  DOI: 10.7717/peerj.6841/fig-1

ADP-glucose pyrophosphorylase is a key player

ADP-glucose pyrophosphorylase is the first committed step in the starch synthesis pathway (Smith, Denyer & Martin, 1997). The plant enzyme is a heterotetramer, consisting of two subunits of similar size (AGPL ~51 kD, AGPS ~50 kD) (Okita et al., 1990). AGPase is a key enzyme exerting major control on the pathway of starch synthesis in storage as well as in photosynthetic tissue (Tiessen et al., 2002). The enzyme catalyzes an ATP consuming reaction, making it an exquisite candidate for regulation according to metabolic control theory (Fig. 1). Thus, the regulatory properties of this enzyme have been subject of many investigations in the past decades (Tiessen et al., 2002, 2003; Kolbe et al., 2005; Stitt & Zeeman, 2012). In the cereal endosperm, a cytosolic isoform of AGPase (Shrunken2 and Brittle2) and the Brittle1 transporter are the main providers of ADPglc for starch synthesis in the amyloplast (Emes et al., 2003; James, Denyer & Myers, 2003; Tiessen et al., 2012). Some TFs regulate the expression of several AGPase isogenes (*agpS1-2*, *agpL1-3*) (Table 1; Figs. 2–3).

Table 1 Transcription factors regulating starch enzymes.

TF	ID	TF family	Species	Reference
MeERF72	manes.15g009900	AP2/EREB	<i>Manihot esculenta</i>	<i>Liu et al. (2018b)</i>
PBMY1	Pavirv 00046166	AP/EREB	<i>Panicum virgatum</i>	<i>Ambavaram et al. (2018)</i>
PBMY3	Pavirv 00029298	NY-F	<i>Panicum virgatum</i>	<i>Ambavaram et al. (2018)</i>
ZmEREB156	GRMZM2G421033	AP2/EREB	<i>Zea mays</i>	<i>Huang et al. (2016)</i>
ZmbZIP91	GRMZM2G043600	bZIP	<i>Zea mays</i>	<i>Chen et al. (2016)</i>
CRCT	LOC_Os02G15350	bZIP	<i>Oryza sativa</i>	<i>Morita et al. (2015)</i>
ZmNAC36	GRMZM2G154182	NAC (CUC)	<i>Zea mays</i>	<i>Zhang et al. (2014)</i>
OsSERF1	LOC_Os05G34730	DREB	<i>Oryza sativa</i>	<i>Schmidt et al. (2014)</i>
RPBF	LOC_Os05g15350	DOF	<i>Oryza sativa</i>	<i>Schmidt et al. (2014)</i>
OsZIP58	LOC_Os07g08420	bZIP	<i>Oryza sativa</i>	<i>Wang et al. (2013)</i>
NAC96	At5g46590	CUC	<i>Arabidopsis thaliana</i>	<i>Bumee et al. (2013)</i>
WRKY75	At5g13080	WRKY	<i>Arabidopsis thaliana</i>	<i>Bumee et al. (2013)</i>
ZmDOF1	AC155434.2_FG006	DOF	<i>Zea mays</i>	<i>Noguero et al. (2013), Yanagisawa (2000)</i>
ZmDOF2	GRMZM2G009406	DOF	<i>Zea mays</i>	<i>Noguero et al. (2013), Yanagisawa (2000)</i>
LEC2	At1g28300	B3	<i>Arabidopsis thaliana</i>	<i>Angeles-Núñez & Tiessen (2012)</i>
AtIDD5	At2g02070	IDD	<i>Arabidopsis thaliana</i>	<i>Ingkasuwan et al. (2012)</i>
COL	At2g21320	COL	<i>Arabidopsis thaliana</i>	<i>Ingkasuwan et al. (2012)</i>
RSR1	LOC_Os5g03040	AP2/EREB	<i>Oryza sativa</i>	<i>Fu & Xue (2010)</i>
AtIDD8	At5g44160	IDD	<i>Arabidopsis thaliana</i>	<i>Seo et al. (2011)</i>
SRF1	AB469355	DOF	<i>Ipomoea batatas</i>	<i>Tanaka et al. (2009)</i>
ETR2	AF420319	ETR	<i>Oryza sativa</i>	<i>Wuriyanghan et al. (2009)</i>
OsBP-5		MYC-like	<i>Oryza sativa</i>	<i>Zhu et al. (2003)</i>
OsBP-89		AP2/EREB	<i>Oryza sativa</i>	<i>Zhu et al. (2003)</i>
SUSIBA2	AY323206	WRKY	<i>Hordeum vulgare</i>	<i>Sun (2003)</i>

Starch enzymes and plastidial proteins build metabolic complexes

Some starch biosynthetic enzymes assemble in high molecular weight complexes (*Hennen-Bierwagen et al., 2009; Crofts et al., 2015*). One consequence of enzyme clustering in space and time is metabolite-channeling through the formation of multienzyme assemblies known as metabolons (*Sweetlove & Fernie, 2013*). Proteins that copurified with SSIII, SSIIa, SBEIIa and SBEIIb included AGPase and SUS-SH1 forming a ~670-kD complex that may regulate carbon partitioning in developing seeds of cereals (*Hennen-Bierwagen et al., 2009*). In *Arabidopsis* leaves, coiled-coil proteins and PROTEIN TARGETING TO STARCH form complexes with starch synthases (SS) during granule initiation (*Seung et al., 2015, 2017, 2018*). Therefore, transcriptional regulation of one protein might affect the abundance of other proteins. This may be the case, for example, in the rice mutant FLOURY ENDOSPERM2 (FLO2), which pleiotropically altered the expression of many starch genes (*She et al., 2010*).

Numerous families and multiple isoforms of starch genes

Several starch synthase isoforms use ADPglc to add its glucose moiety to amylose and amylopectin molecules in the ordered and crystalline structure of the starch granule

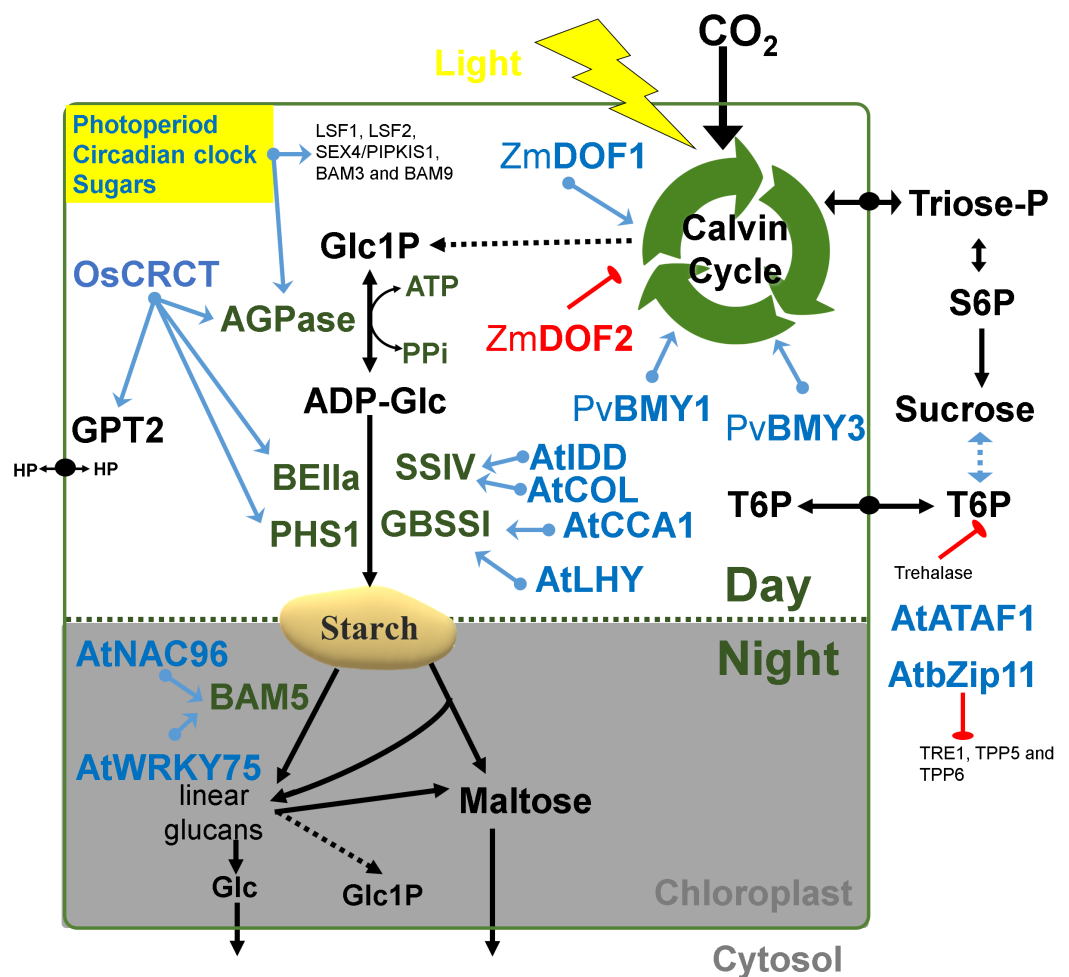
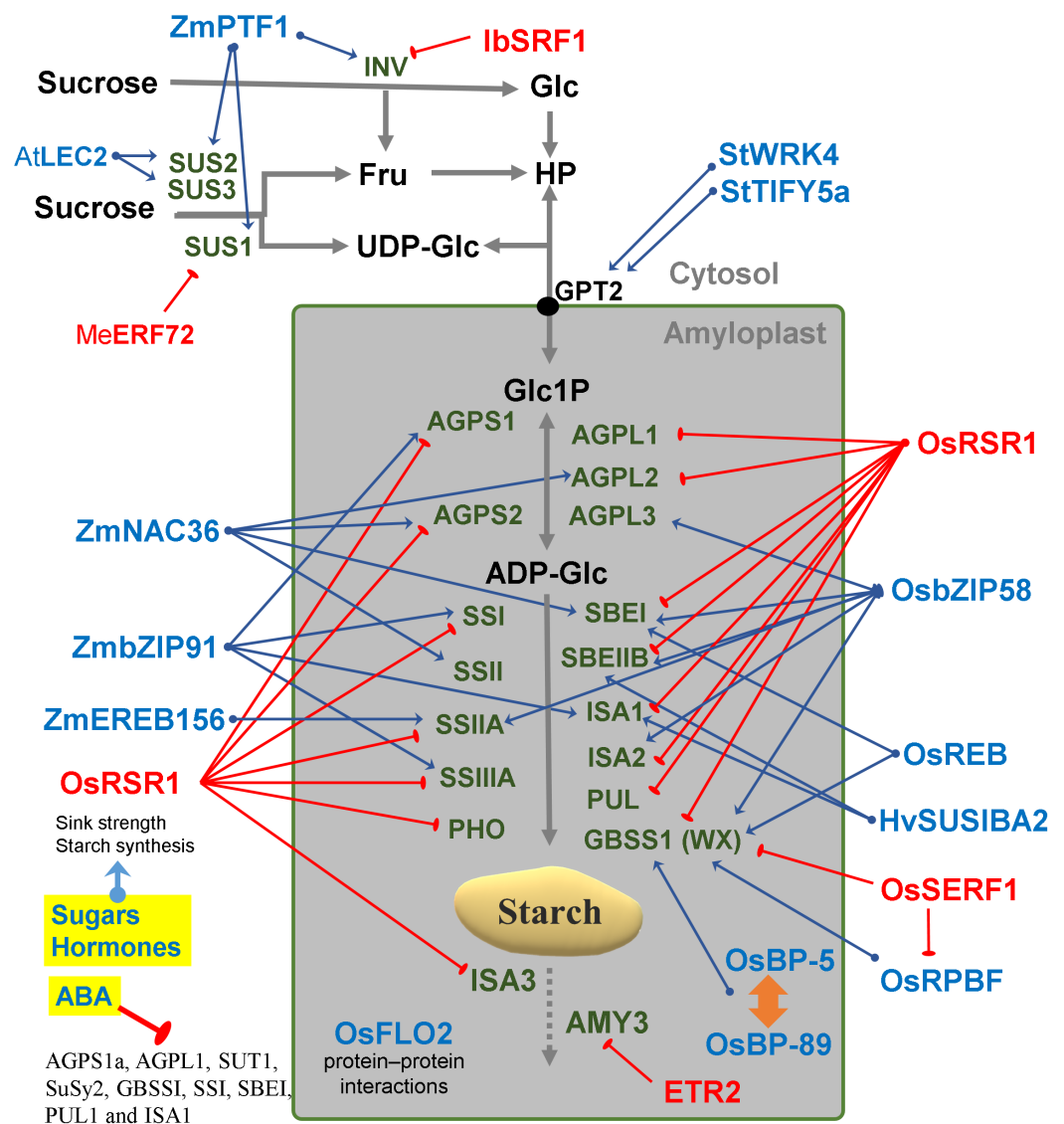


Figure 2 Regulatory factors of starch metabolism in leaves. Metabolites are in black letters while TFs are in blue or red color indicating activation or repression. Abbreviations: AGPase, ADP-glucose pyrophosphorylase; AtATAF1, *Arabidopsis thaliana* Transcription Activation Factor; AtCCA1, *Arabidopsis thaliana* CCA1; AtCOL, *Arabidopsis thaliana* Constant-like; AtIDD, *Arabidopsis thaliana* Indeterminate domain; AtLHY, *Arabidopsis thaliana* LATE ELONGATED HYPOCOTYL; ATP, Adenosine triphosphate; BAM, beta-amylase; BE, Branching enzyme; bZIP11, basic leucine zipper TF 11; CRCT, CO₂ Responsive CCT protein; GBSS, Granule bound starch synthase; Glc, Glucose; GPT2, Glucose-phosphate translocator 2; HP, Hexose-phosphates; LSF, LIKE SEX FOUR; NAC96, NAC domain TF 96; PHS1, α -glucan phosphorylase 1; PPi, Pyrophosphate inorganic; PvBMY, *Pisum sativum* BiomassYield TF; S6P, Sucrose-6P; SEX, Starch excess; SS, Starch synthase; T6P, Trehalose-6P; TPP, Trehalose phosphatase; TRE1, Trehalase 1; WRKY75, WRKY domain TF; ZmDOF, *Zea mays* DNA binding with one finger TF.
Full-size DOI: 10.7717/peerj.6841/fig-2

(Martin & Smith, 1995; Marshall et al., 1996; Smith, Denyer & Martin, 1997; Smith, 1999). Different isoforms of branching enzyme and debranching enzyme are involved in the synthesis of glucans (Ball et al., 1991; Zeeman et al., 1998) (Fig. 1).

Starch synthases are divided into four subfamilies of soluble Ss (SSI, SSII, SSIII and SSIV) and one subfamily of granule-bound starch synthases (GBSS) (Patron & Keeling, 2005; Leterrier et al., 2008). Starch phosphorylase plays also an important role for starch synthesis (Satoh et al., 2008; Tetlow & Emes, 2011). Each of these enzymes are encoded by



Full-size DOI: 10.7717/peerj.6841/fig-3

many different isogenes, forming large enzyme families in plants. In maize, more than 30 genes participate in starch synthesis (Yan et al., 2009); while in rice are around 21 genes in total (Hirose et al., 2006). These isozymes have been classified by their tissue-specific expression patterns in maize and rice: type I starch genes were preferentially expressed in

endosperm (reproductive organs, sink), whereas type II starch genes were preferentially expressed in vegetative tissues (leaves, source) (Hirose *et al.*, 2006; Fu & Xue, 2010; Huang, Hennen-Bierwagen & Myers, 2014).

Starch synthesis in leaves has been said to be largely similar to that in storage organs (Santelia & Zeeman, 2011; Smith, 2012; Stitt & Zeeman, 2012). Table 2 list some key genes in several plant species.

Differences between metabolic and transcription networks

Metabolic and transcriptional regulation are commonly thought to be equivalent in both plant and animal systems. According to Tom Ap Rees and Mark Stitt, central metabolism of pea is like the subway map of London (Stitt & Ap Rees, 1978, 1980). Certainly, compared to animal and bacterial metabolism, plant metabolism is more complex, flexible, redundant and compartmentalized (Sweetlove & Fernie, 2013). Even though the subcellular compartmentation of plant metabolism is thought to be well understood, unexpected results are continuously revealed by detailed gene-by-gene studies (Lunn, 2006). Usually, metabolic pathways are not as linear as depicted in most textbooks (Kruger, Hill & Ratcliffe, 1999; Berg, Tymoczko & Stryer, 2006). Instead of metabolic pathways, it is more accurate to speak of metabolic networks.

There are some important differences between metabolic and transcriptional networks that must be taken into account when trying to explore them by correlation analysis. Plant cells may produce a larger number of chemically distinct metabolites (~10,000) than the number of enzymes encoded by their DNA (~5,000). In metabolic networks, connections (chemical reactions) are theoretically reversible, bidirectional and may have certain stoichiometry (Fig. 4A). Metabolites can be chemically interconverted between each other, while genes are fixed entities. In transcriptional networks, some genes are more important than others; some proteins are regulatory while others are structural. Therefore, in gene networks, connections are one-directional arrows that have a certain hierarchy (Fig. 4B). From a biochemical perspective, metabolites are structurally much more diverse than genes that are all built from the same four letters (nucleotides). But from the functional and regulatory point of view, the opposite is true: Metabolites can be interconverted and are therefore more or less “equal.” Genes on the contrary are “non-equal”; some have a higher hierarchy than others (Fig. 4). One transcription factor may regulate a gene coding for an enzyme but not vice versa. Many genes do the metabolic work but itself do not regulate DNA transcription or RNA translation. Thus, in transcriptional networks there are different types of genes: regulator genes and endpoint genes (Fig. 4B). Among the regulator genes, some have higher authority, since they may command many genes (both structural and regulatory genes) and are thus considered higher level factors (master switches). Connections in metabolic networks should be represented by bi-directional arrows that have a certain stoichiometry and mass action ratio but no hierarchy (Fig. 4A). In metabolic networks, in addition to standard connections (chemical reactions with an EC number), there may be regulatory connections related to allosteric regulation of enzymes, most frequently positive feed forward loops or negative feedback inhibition loops (Fig. 4A).

Table 2 IDs of the main starch metabolic enzymes.

Gene name	Protein product (Enzyme)	Maize	Rice	Arabidopsis
<i>SUS1</i>	Sucrose synthase 1	GRMZM2G152908		At5g20830
<i>SUS2</i>	Sucrose synthase 2	GRMZM2G318780		At5g49190
<i>SUS3</i>	Sucrose synthase 3			At4g02280
<i>PGM</i>	Phosphoglucomutase	GRMZM2G023289		
<i>AGPL1</i>	ADP-glucose pyrophosphorylase large subunit 1	GRMZM2G429899	LOC_Os05g50380	At5g19220
<i>AGPL2</i>	ADP-glucose pyrophosphorylase large subunit 2	GRMZM2G027955	LOC_Os01g44220	
<i>AGPL3</i>	ADP-glucose pyrophosphorylase large subunit 3	GRMZM2G144002	LOC_Os03g52460	
<i>AGPL4</i>	ADP-glucose pyrophosphorylase large subunit 4	GRMZM2G391936	LOC_Os07g13980	
<i>AGPS1</i>	ADP-glucose pyrophosphorylase small subunit 1	GRMZM2G068506	LOC_Os09g12660	At5g48300
<i>AGPS2</i>	ADP-glucose pyrophosphorylase small subunit 2	GRMZM2G163437	LOC_Os08g25734	
<i>SSI</i>	Starch synthase I	GRMZM2G129451	LOC_Os06g06560	At5g24300
<i>SSII</i>	Starch synthase II	GRMZM2G141399		At3g01180
<i>SSIIa</i>	Starch synthase IIa	GRMZM2G348551	LOC_Os06g12450	At2g36390
<i>SSIIb</i>	Starch synthase IIb	GRMZM2G032628	LOC_Os02g51070	
<i>SSIIc</i>	Starch synthase IIc		LOC_Os10g30156	
<i>SSIII</i>	Starch synthase III			At1g11720
<i>SSIIIa</i>	Starch synthase IIIa	GRMZM2G141399	LOC_Os08g09230	
<i>SSIIIb</i>	Starch synthase IIIb		LOC_Os04g53310	
<i>SSIV</i>	Starch synthase IV	GRMZM2G044744	LOC_Os01g52260	At4g18240
<i>SSIVb</i>	Starch synthase IVb		LOC_Os05g45720	
<i>GBSSI</i>	Granule-bound starch synthase I	GRMZM2G024993	LOC_Os06g04200	
<i>GBSSII</i>	Granule-bound starch synthase II		LOC_Os07g22930	At1g32900
<i>BEI</i>	Starch branching enzyme I	GRMZM2G088753	LOC_Os06g51084	
<i>BEII</i>	Starch branching enzyme II	GRMZM2G032628		At5g03650
<i>BEIIa</i>	Starch branching enzyme IIa		LOC_Os04g33460	At2g36390
<i>BEIIb</i>	Starch branching enzyme IIb		LOC_Os02g32660	
<i>ISA1</i>	Starch debranching enzyme: Isoamylase I	GRMZM2G138060	LOC_Os08g40930	At2g39930
<i>ISA2</i>	Starch debranching enzyme: Isoamylase II		LOC_Os05g32710	At1g03310
<i>ISA3</i>	Starch debranching enzyme: Isoamylase III	GRMZM2G150796	LOC_Os09g29404	At4g09020
<i>PUL</i>	Starch debranching enzyme: Pullulanase	GRMZM2G158043	LOC_Os04g08270	
<i>PHOH</i>	Starch phosphorylase H		LOC_Os01g63270	
<i>PHOL</i>	Starch phosphorylase L		LOC_Os03g55090	
<i>DPE1</i>	Disproportionating enzyme I		LOC_Os07g43390	At5g64860
<i>DPE2</i>	Disproportionating enzyme II		LOC_Os07g46790	At2g40840
<i>GWD1</i>	Glucan water dikinase			At1g10760
<i>PHS1</i>	Plastidial starch phosphorylase 1			At3g29320
<i>PHS2</i>	Plastidial starch phosphorylase 1			At3g46970
<i>PTST2</i>	Protein targeting to starch 2		OS03G0686900	At1g27070
<i>AMY3</i>	α -Amylase 3	GRMZM2G138468		At1g69830
<i>BAM5</i>	β -Amylase 5	GRMZM2G058310		At4g15210

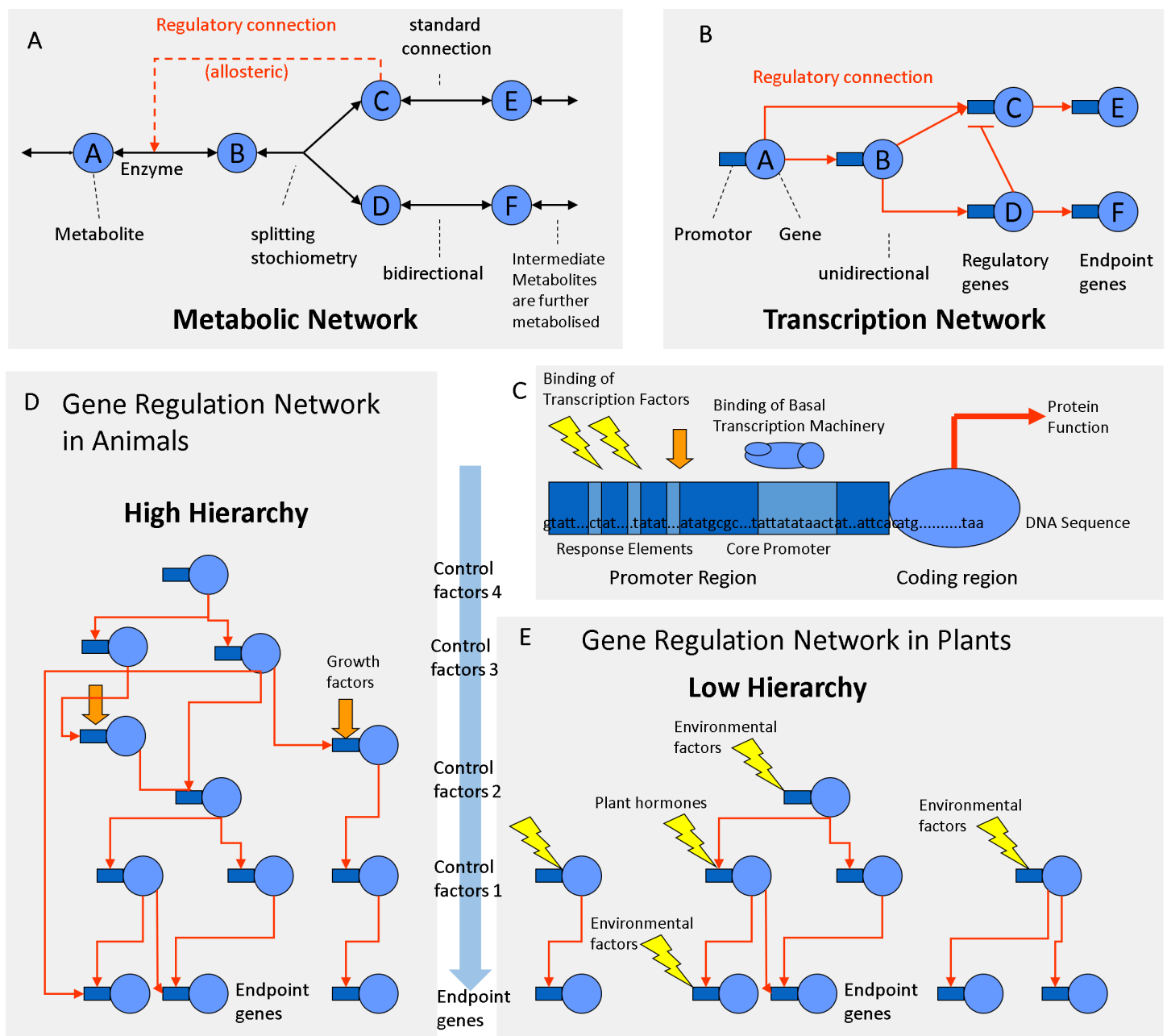


Figure 4 Regulation networks in plants. (A) Metabolic network. (B) Transcriptional network. (C) Gene composed of coding determining sequence (CDS) and promoter region containing transcription factor binding elements. (D) Gene regulation network with high hierarchy (animals). (E) Gene regulation network with low hierarchy (plants). [Full-size !\[\]\(1663bb69f307a960345edb0e712f8c02_img.jpg\) DOI: 10.7717/peerj.6841/fig-4](https://doi.org/10.7717/peerj.6841/fig-4)

Differences between animal and plant protein networks

According to the classifications of gene ontology (GO) ~4–8% of the genes are involved in DNA transcription and regulation, whereas 10–20% of the genes are involved in metabolism (*Gene Ontology Consortium, 2004; Maere, Heymans & Kuiper, 2005*). In plants, 5–7% of all protein-coding genes correspond to TFs (*Riaño-Pachón et al., 2007; Yilmaz et al., 2009*). In animal genomes, TFs make up 5–8% of the genes (*Wang & Nishida,*

2015). Plant genomes contain 34% more proteins than animal genomes (Ramírez-Sánchez *et al.*, 2016). On average, an animal genome contains 25,189 proteins, whereas a plant genomes contain 36,795 proteins on average (Ramírez-Sánchez *et al.*, 2016). Consequently, plant genomes code for more TFs (~1,839) than animal genomes (~1,259) (Fig. 4). The fact that plants possess more TFs is relevant for the topology of the regulatory network.

Across species there is a negative correlation between protein size and protein number in eukaryotic genomes (Tiessen, Pérez-Rodríguez & Delaye-Arredondo, 2012). Plant proteins are smaller and have less domains as animal proteins which are often multifunctional (Ramírez-Sánchez *et al.*, 2016). Compared to the average of eukaryotic species, plants have ~34% more but ~20% smaller proteins (Ramírez-Sánchez *et al.*, 2016). Compared to animal genes, plant genes have longer exons but are encoded by half the number of exons and introns (Ramírez-Sánchez *et al.*, 2016). Consequently, plant proteins are simpler and have less domains and perform less complex functions (Ramírez-Sánchez *et al.*, 2016). Plant transcriptional networks need to respond to a wide range of environmental inputs. Therefore, plant transcriptional networks may have more TFs that regulate gene expression with a lower hierarchy (Fig. 4E) compared to animal networks that work at a higher hierarchy (Fig. 4D). The regulatory hierarchy of plants is similar to that of one celled bacteria in that respect: flat. The consequences of the differences in the network topology can be observed at the whole organism level. Regulatory complexity becomes most evident at the tissue culture level: plant cloning can be simply done with almost any pre-differentiated vegetative cell with a mixture of auxins (roots) and cytokinin's (shoots), while regeneration and cloning of animals is harder because it requires a protected environment and a precise mixture of epigenetic, cytosolic, nuclear and membranal factors (Zuo *et al.*, 2017). Co-expression analysis identified several barriers of animal cloning during somatic cell nuclear transfer (Zuo *et al.*, 2017). TFs and epigenetic regulators hampered the embryo reprogramming process (Zuo *et al.*, 2017). In comparison, plant cells have less barriers of transcriptional reprogramming. Therefore, plant cells are totipotent and respond to many external environmental signals, similar to bacterial cells (Fig. 4E). Animal cells are flexible and can create their own internal environment because they build tissue layers and are able to migrate between the endo-, meso- or ecto-derm in order to accommodate to better conditions. Animals make burrows, nests and lairs; the blood circulatory system regulates glucose levels, oxygen, pH and temperatures in a narrow range, while plant cells are exposed to a much greater range of environmental variation. For example, desert plants adapt to diurnal variations of temperature from 5 °C in the morning to 55 °C at noon, while mammalian cells stop working if temperatures drop or rise a few degrees from 37 °C. Animals form complex organs through multiple cell layers that have a predefined cell lineage (fixed transcriptional fate). They are non-totipotent due to hierarchical restrictions by cytosolic and nuclear factors (Zuo *et al.*, 2017). Animal transcription networks are more hierarchical because they react strongly to cell lineage, growth factors and cell-to-cell communication (Fig. 4D). In comparison, plant organs are less complex; the transcription networks of plant cells work less hierarchical because they respond much more directly to hormones and abiotic factors (Fig. 4E).

The number of TFs in the human genome ranges from 1,391 ([Vaquerizas et al., 2009](#)) to 1,639 ([Lambert et al., 2018](#)) while more than 2017 TFs have been reported in maize ([Burdo et al., 2014](#)). The Arabidopsis genome encodes >1,533 TFs, this number was 1.3 times that of *Drosophila* and 1.7 times that of *Caenorhabditis elegans* and *Saccharomyces* ([Riechmann et al., 2000](#)). There are many TF families that are found only in plants, such as the APETALA2/ethylene responsive element binding protein (AP2/EREBP), NAC and WRKY families; the trihelix DNA binding proteins and the auxin response factors ([Riechmann et al., 2000](#)). The DNA-binding with One Finger (DOF) is a group of plant-specific TFs that are implicated in stress responses, photosynthesis and flowering induction ([Noguero et al., 2013](#)).

Starch transcription networks

The regulatory network involved in starch metabolism was summarized in [Figs. 2–3](#). References of TFs and genes were listed in [Tables 1](#) and [2](#). As can be seen in [Figs. 2–3](#), the hierarchy of the regulatory network is flat, with most genes responding to hormones and environmental cues. Currently, we have limited knowledge of master TFs that with a high hierarchy regulate other TFs of starch metabolism. This contrasts with several examples of gene regulatory networks in animals that have multiple layers of hierarchical transcriptional regulation ([Cvekl & Zhang, 2017](#)).

The identification of TFs directly involved in the regulation of starch enzymes have been made through different strategies (mutant characterization & co-expression networks) ([Tables 1](#) and [2](#)). Genome-wide analysis of starch genes in potato leaves and potato tubers revealed tissue-specific expression of isoenzymes ([Van Harsselaar et al., 2017](#)). Therefore, we need to build regulatory schemes separately for photosynthetic and storage organs ([Figs. 2](#) and [3](#)).

Transcriptional control of transitory starch in leaves

There are several interesting examples of transcriptional correlation between photosynthesis and starch biosynthesis. In maize, ZmDOF1 enhances transcription from the C4 phosphoenol pyruvate carboxylase (PEPC) promoter and ZmDOF2 blocks this transactivation and represses PEPC expression ([Yanagisawa, 2000](#)) ([Fig. 2](#)). In sweet potato, a DOF protein called SRF1 was found to have an indirect positive effect on starch synthesis ([Tanaka et al., 2009](#)) ([Fig. 2](#)). In switchgrass, PvBMY1 (BioMass Yield 1) and PvBMY3 (BioMass Yield 3) regulate photosynthesis and starch synthesis ([Ambavaram et al., 2018](#)). In Arabidopsis, *BAM5* is regulated by two TFs, WRKY DNA-binding domain 75 (WRKY75, At5g13080) and NAC domain-containing protein 96 (NAC096, At5g46590) ([Bumee et al., 2013](#)) ([Fig. 2](#)). In the *Atidd5* and *col* mutants, the reduction of *SS4* expression led to a significant increase in the number of starch granules ([Ingkasuwan et al., 2012](#)). In rice, CRCT was shown to positively control the expression of *BEIIa*, *OsAGPL1*, *OsAGPS1* and *GPT2*, all of which are classified as vegetative organ isoforms ([Morita et al., 2015](#)) ([Fig. 2](#)).

Microbial volatiles promote the accumulation of starch in leaves via a photoreceptor-mediated control ([Li et al., 2011a](#)). The transcriptional and post-translational regulation

network may involve NTRC-mediated changes in the redox status of plastidial enzymes (Li et al., 2011a).

Transitory starch is highly responsive to the external environment

Transcripts of many starch genes are regulated by both an endogenous clock and by the diurnal cycle (i.e., light/dark cycle) (Lu, 2005; Ral, 2006) and also by sugar availability and different hormones (Blasing et al., 2005; Graf & Smith, 2011). The plant clock regulates developmental transitions like flowering, dormancy and the onset of senescence and bud break to ensure that they occur at an appropriate season or time of the day (Flis et al., 2016). For example, the rice GBSSII is regulated by a circadian rhythm (Dian et al., 2003). In Arabidopsis leaves, expression of the GBSS1 gene is controlled by two clock TFs, namely the LATE ELONGATED HYPOCOTYL (LHY) and the Myb-related CIRCADIAN CLOCK ASSOCIATED 1 (CCA1) (Tenorio et al., 2003) (Fig. 2).

Also, some SS isoforms are affected by photoperiods (Lu, 2005; Ral, 2006). Even though regulation of starch genes at the transcriptional level has been reported, much less is known about translational control of protein synthesis (Kötting et al., 2010). Diurnal changes in the transcriptome of Arabidopsis leaves revealed both transcriptional and posttranscriptional regulation of starch enzymes (Smith, 2004). Strong transcriptional control of starch genes occurs toward the end of the light (Zeeman, Smith & Smith, 2007; Tsai et al., 2009; Streb & Zeeman, 2012). Different AGPase isoforms respond differently to photoperiod, circadian clock or sugar (Geigenberger, 2011; Seferoglu et al., 2013). The Arabidopsis genes APL3 and APL4 are induced by both Suc and hexoses in leaves (Li et al., 2002; Thellin et al., 2009; Michalska et al., 2009). In lentil leaves, some AGPase isoforms are differentially regulated during short and long days (Seferoglu et al., 2013). Overall, it can be said that the expression of isogenes is certainly tissue-dependent, such as in the case of AGPase (Huang, Hennen-Bierwagen & Myers, 2014).

The duration of the photoperiod has two major consequences for plant growth and metabolism. Firstly, a longer night requires alterations in the timing of growth and the diurnal allocation of carbon (Sulpice et al., 2009, 2014). Secondly, shorter light periods decrease growth because less light energy is available to sustain carbon fixation by photosynthesis. The transient reserves of carbon are used as a energy buffer during darkness (Smith & Stitt, 2007; Stitt & Zeeman, 2012). In Arabidopsis, expression of LSF1, LSF2, SEX4/PIPKIS1, BAM3 and BAM9 were regulated by the clock-, C- and light-signaling (Flis et al., 2016) (Fig. 2). At dawn, while starch biosynthesis was transcriptionally down-regulated, β -amylase was strongly up-regulated (Flis et al., 2016). The activity of β -amylase is associated with starch grains normally during late grain filling and also during germination (Radchuk et al., 2017). The rate of starch synthesis in the green leaves is increased during short photoperiods because a higher amount of carbon is required for sucrose synthesis during the long night (Pokhilko et al., 2014; Sulpice et al., 2014; Mugford et al., 2014). Overall, it can be said that the expression of many starch genes in photosynthetic tissues is light and time-regulated (Fig. 2), while in sink organs, transcriptional regulation might depend more upon the levels of sugars and/or phytohormones (Fig. 3).

Plant transcription networks are highly responsive to hormones

The coordinated regulation of gene expression in sink and source sink tissues is orchestrated by light, sugars and energy status (*Geigenberger, 2011*). In addition to light and sugars, hormones and volatiles also play a key role. Ethylene and other hormones such as abscisic acid (ABA), salicylic acid and jasmonic acid are major players in coordinating signaling networks involved in the response to biotic and abiotic factors (*Foyer, Kerchev & Hancock, 2012*). The highly expressed GBSS gene was strongly repressed during ethylene-induced ripening in the banana pulp (*Zhu et al., 2011*). Also, the rice DNA-binding protein OsBP-5 forms a heterodimer with OsEBP-89, an ethylene-responsive element-binding protein that negatively regulates GBSSI expression (*Zhu et al., 2003*).

Abscisic acid treatment can promote AGPase and SS activity and decrease α -amylase and β -amylase (*Liu et al., 2018b*). ABA regulates sucrose import into the developing endosperm leading to a repression of *AGPS1a*, *AGPL1*, *SUT1*, *SuSy2*, *GBSSI*, *SSI*, *SBE1*, *PUL1* and *ISA1* genes (*Mukherjee et al., 2015*) (Fig. 3). An ethylene-responsive factor, ZmEREB156 is involved in the regulation of *ZmSSIIIa* in response to the synergistic effect between Suc and ABA (*Huang et al., 2016*). An ethylene receptor, ETR2, increases starch accumulation in the internodes of rice (*Wuriyanghan et al., 2009*). Overall, it can be said that the expression of many starch genes is strongly hormone- and sugar-regulated (Fig. 3).

Transcriptional control of storage starch in tubers and seeds

In barley, SUSIBA2, a sugar-inducible TF belonging to the WRKY class, bound to the *ISA1* promoter and exhibited a similar expression pattern as *ISA1* (*Sun, 2003*) (Fig. 3). Furthermore, WRKY4 and TIFY5a (a plant-specific TF) were co-expressed with starch synthesis genes in potato tubers (*Van Harsseelaar et al., 2017*) (Fig. 3). In rice it has been reported that OsSERF1 influences grain filling and starch synthesis. It binds directly to the *GBSSI* promoter and regulates *RPBF* which in turn also directly binds to *pGBSSI* (*Schmidt et al., 2014*). OsSERF1 can also negatively regulate the expression of *AGPL2*, *SSI*, *SSIIIa* and *GBSSI* (*Schmidt et al., 2014*) (Fig. 3).

Transcriptional regulators of sucrose degradation

In sweet potato, SRF1 negatively regulates the vacuolar invertase gene (*Ibbfruct2*) (*Tanaka et al., 2009*). In cassava, MeERF72 is a negative regulator of *MeSus1* (*Liu et al., 2018a*). In Arabidopsis, *AtSUS2* and *AtSUS3* genes are down regulated by LEC2 (*Angeles-Núñez & Tiessen, 2012*). In maize, ZmPTF1 regulates *sus1*, *sus2*, *sh1B* and two invertase genes (*Li et al., 2011c*). ZmbZIP91 lowers osmotic pressure by consuming sucrose in the maize endosperm, thus increasing sucrose fixation from the source to the sink (*Chen et al., 2016*). Mutant analysis determined that FLO2 altered the expression of *SUS* and other genes of sucrose-starch metabolism in rice seeds (*She et al., 2010*). FLO2 harbors a tetratricopeptide repeat motif mediating protein-protein interactions rather than acting itself as a TF (Fig. 3).

Co-expression networks reveal regulatory modules of starch genes

In addition to mutant studies, co-expression networks have been analyzed in Arabidopsis, rice and maize (*Tsai et al., 2009*; *Fu & Xue, 2010*; *Bumee et al., 2013*; *Chen et al., 2016*).

Genes constrained to a specific tissue and genes that are co-regulated across different samples, have been identified by simple linear correlation of transcript abundances (Aoki, Ogata & Shibata, 2007). Co-expression analysis is a powerful tool to identify genes, that regulate specific metabolic pathways, in a systematic manner. This analysis assumes that genes with similar expression patterns may be functionally associated (Yonekura-Sakakibara et al., 2008). A novel photoperiod regulatory mechanism has been coined as translational coincidence (Seaton et al., 2018). In maize, a co-expression network was constructed using data from 60 different stages/tissues of the inbred genotype B73. This constitutes a “developmental” network that characterizes the gene expression pattern of the organs of that crop plant. One example was the identification of ZmbZIP91 which regulates the expression of other starch genes in maize (Chen et al., 2016). Another example was the identification of Rice Starch Regulator 1 (RSR1) by a co-expression analysis (Fu & Xue, 2010). RSR1 was found to be negatively co-expressed with starch synthesis genes and was experimentally confirmed as a modulator of starch metabolic enzymes in rice (Fig. 3).

Some modules have been classified for starch biosynthesis suggesting a general transcriptional co-regulation (Tsai et al., 2009). Some starch genes were co-expressed with TFs of the bZIP family such as MYB, NAC (for NAM, ATAF and CUC) or AP2/EREBP families (Fu & Xue, 2010). In rice, a gene member of the AP2/EREBP family (RSR1) was the only one that negatively co-expressed with type I starch synthesis genes (Fu & Xue, 2010) (Fig. 3). In Arabidopsis, the Transcription Activation Factor1 (ATAF1) activates the expression of TREHALASE1 and leads to a sugar starvation metabolome through reduced trehalose-6-phosphate levels (Fig. 2). Coordinated transcriptional responses of starch metabolic genes triggered by ATAF1 largely overlap with expression patterns of carbon starved plants (Garapati et al., 2015). Starch levels were elevated in *ataf1* knockout plants and reduced in ATAF1 overexpressors (Garapati et al., 2015). The expression of the *TRE1*, *TPP5* and *TPP6* genes was also induced by bZIP11 (Ma et al., 2011) (Fig. 2).

Cis-regulatory elements of starch metabolism

Isogenes with highly variable promoter sequences show the largest divergence in expression (Lemmon et al., 2014). The prominence of cis elements may indicate that cis regulation is a more effective evolutionary mechanism than *trans* regulation for adapting isogene expression to increase fitness under a changing environment (Lemmon et al., 2014). Therefore, a rational approach of cis element shuffling and targeted editing of promoter motifs may yield better results for crop improvement than transgenic approaches. Instead of inserting new coding determining sequences from heterologous species with strong viral promoters such as 35S, it may be safer to shuffle promoter elements and edit the untranslated regions of endogenous genes. A cisgenic fine-tuning may have less biosafety regulatory restrictions than the commercial transgenic strategy. In addition to motifs known to be present in C starvation-induced genes (CACGTG/ACGT), motifs associated with the response to hormones, sugars, light and circadian regulation are also enriched in starch genes (Cookson et al., 2016; Li et al., 2018). Bioinformatic analysis revealed regulatory cis-elements putatively responsible for the spatio-temporal pattern of *AtSUS2* expression such as the W-box (ttgact) and SEF3 (aaccca) motifs (Angeles-Núñez & Tiessen, 2012).

An bZIP TF called REB interacts with the ACGT elements in the promoters of both *Wx* and *SBE1* (Cai, 2002). A cis-acting motif with a signature of [ATC][AC][CTG][ATC]AAAGN [AC] [GCA][ATC] was found in 20 out of 24 (~83 %) of group I genes (*ISA*, *GWD1*, *SS3*, *GBS1*, *AMY3*, *AMY2*, *SBE3*, *ISA1*, *DPE2*, *SS2*, *SEX4-LIKE2*, *PHS1*, *PHS2*, *SEX4*, *BAM2*, *ISA3*, *SS4*, *SBE2*, *MEX1*, *SS1*, *GWD3*, *APS1*, *PGM1* Y *DPE1*); mutation of this cis-element induced *APS1* expression in roots, indicating that this cis-element could mediate transcriptional repression (Tsai et al., 2009). A shifted electrophoresis band was only detected when ZmbZIP91 was incubated with the biotin-labelled ACTCAT element, which indicated that ZmbZIP91 is able to bind directly to ACTCAT elements but not TCATT elements (Chen et al., 2016). Some bZIP TFs (bZIP63/At5g28770, bZIP11/At4g34590, bZIP53/At3g62640, bZIP2/At2g18160 and bZIP1/At5g49450) facilitate SnRK1 signaling via their recruitment to G-box motifs (Baena-González et al., 2007). In rice, OsbZIP58 was shown to bind directly to the promoters of six starch-synthesizing genes, *OsAGPL3*, *OsWx*, *OsSSIIa*, *OsSBE1*, *OsBEIIb* and *OsISA2* (Wang et al., 2013) (Fig. 3). OsbZIP20, REB/OsbZIP33, OsbZIP34 and OsbZIP58 can bind to both the C53 and Ha-2 fragments and may regulate the expression of *SBE1* and *Wx* (Wang et al., 2013) (Fig. 3). In maize, ZmbZIP91 only binds to the promoters of *pAGPS1*, *pISA1*, *pSSIIa* and *pSSI* (Chen et al., 2016).

Perspectives to identify TFs related to plant yield

Identification of all TFs and cis-elements would enable a future strategy of rational metabolic design in order to turn on starch synthesis in tissues that lack starch (Tsai et al., 2009). Increasing crop yield has remained one of the main goals of plant breeding. The fine-tuning of CRCT expression in transgenic rice may contribute to the future development of crop varieties optimized for biorefinery purposes (Morita et al., 2015). In the domestication of maize from teosinte, starch metabolism in the grains was highly correlated with yield and harvest index. Many efforts have been made to increase yield by modifying the regulatory properties of key starch enzymes (Smidansky et al., 2002, 2003; Smith, 2008; Li et al., 2011b; Kang et al., 2013). But several first attempts have failed. In order to achieve a substantial increase in the rate of starch synthesis, the expression of a large set of enzymes and transporters need to be activated simultaneously in the pathway. This is not a simplistic one-enzyme strategy as in the first generation of transgenic plants. We need to elucidate all TFs involved in the regulation of starch metabolic enzymes. Master regulators at the post-transcriptional level have been found such as TOR1 and SNRK1 (sucrose and energy signaling). We still need to find master switches at the transcriptional level for starch metabolism. The possible existence of transcriptional “master switches” for starch is an idea not yet widely accepted among colleagues. Currently, it is assumed that starch can be synthesized whenever there is light (energy) and enough CO₂ inside photosynthetic leaves, or whenever enough oxygen (energy), sucrose and hormones are supplied to storage organs. However, microscopy reveals that not all cells make starch, thus we wonder why some differentiated cells are full of it while others completely lack it. With the advantage of new transcriptomic technologies, it will be possible to build regulatory networks that can help to elucidate the TFs behind

the expression patterns of starch metabolic genes. But we must solve the old problem as when studying metabolism, that whole organs and cell mixtures are homogenized and analyzed in bulk. Subcellular analysis of metabolism is needed to pinpoint key regulation sites. For example, detailed subcellular inspection using fluorescent microscopy allowed to distinguish the metabolic source of blue glow in banana leaves, fruit skin and pulp (Tiessen, 2018). When epidermis cells are mixed with stomatal, palisade and mesophyll cells, it will turn impossible to elucidate all TFs reliably that are responsible for the metabolic differences among those cells. Some cells have chlorophyll, sugars and starch while other not. Therefore, single cell transcriptomic data needs to be generated urgently to better understand regulation of starch metabolism in plants. Both metabolites and transcripts should be measured in the same samples always. In addition to co-expression networks, we should also take more advantage of other strategies such as yeast one hybrid and yeast two hybrid to uncover the regulatory network behind of each metabolism. Currently, there are many Arabidopsis mutant reports describing TFs altering flower development or plant morphology, whereas so much remains unknown about similar TFs regulating primary metabolism. In crop plants providing abundant food supply such as maize, there is still hope to find some master TFs controlling the energy pathway.

CONCLUSIONS

This review highlighted the importance of distinguishing different types of biological networks, namely metabolic interconversion networks and transcriptional regulatory networks (Fig. 4). Comparisons between animal and plant transcriptional networks revealed differences in the number of genes, size of the proteins and the regulatory hierarchies. A comprehensive list of enzymes and chemical reactions that are involved in starch metabolism in plants was provided (Tables 1–2). The review focused on TFs and cis-regulatory elements that are relevant for starch synthesis and degradation. Targeted mutations of cis elements may become a breeding tool in the near future. Genetic diversity may be increased by a strategy of “rational shuffling of minimal promoter elements.” Detailed information about all relevant TFs and regulatory motifs may improve plant sink strength, crop yield and food quality.

ACKNOWLEDGEMENTS

We thank Dr. Andres Estrada-Luna for technical support in the lab and the greenhouse. We also thank Dr. Jesus Ruben Torres-Garcia, Dr. Alberto Camas-Reyes, Dr. Luz Edith Casados-Vázquez and Dr. Julio Armando Massange-Sanchez for their help.

ADDITIONAL INFORMATION AND DECLARATIONS

Funding

This work was supported by grants from the Consejo Nacional de Ciencia y Tecnologia (CONACYT Mexico) to CLG, SJC and AT. Support was also provided from the National Laboratory PlanTECC, Problemas Nacionales and Infraestructura. The authors were further supported by initial funding grants by SAGARPA through CIMMYT and the

MasAgro initiative. Funding CONACYT. PN2015-613, LN2018-293362. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Grant Disclosures

The following grant information was disclosed by the authors:
Consejo Nacional de Ciencia y Tecnología (CONACYT Mexico).
National Laboratory PlanTECC, Problemas Nacionales and Infraestructura.
SAGARPA through CIMMYT and the MasAgro initiative.
CONACYT: PN2015-613, LN2018-293362.

Competing Interests

Axel Tiessen is an Academic Editor for PeerJ.

Author Contributions

- Cristal López-González conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the paper, approved the final draft.
- Sheila Juárez-Colunga performed the experiments, approved the final draft.
- Norma Cecilia Morales-Elías performed the experiments, approved the final draft.
- Axel Tiessen conceived and designed the experiments, analyzed the data, contributed reagents/materials/analysis tools, prepared figures and/or tables, authored or reviewed drafts of the paper, approved the final draft.

Data Availability

The following information was supplied regarding data availability:
This is a literature review with no raw data.

REFERENCES

- Ambavaram MMR, Aminat A, Ryan KP, Peoples O, Snell KD, Somleva MN. 2018.** Novel transcription factors PvBMY1 and PvBMY3 increase biomass yield in greenhouse-grown switchgrass (*Panicum virgatum* L.). *Plant Science* **273**:100–109 DOI [10.1016/j.plantsci.2018.04.003](https://doi.org/10.1016/j.plantsci.2018.04.003).
- Angeles-Núñez JG, Tiessen A. 2012.** Regulation of AtSUS2 and AtSUS3 by glucose and the transcription factor LEC2 in different tissues and at different stages of Arabidopsis seed development. *Plant Molecular Biology* **78**(4–5):377–392 DOI [10.1007/s11103-011-9871-0](https://doi.org/10.1007/s11103-011-9871-0).
- Aoki K, Ogata Y, Shibata D. 2007.** Approaches for extracting practical information from gene co-expression networks in plant biology. *Plant and Cell Physiology* **48**(3):381–390 DOI [10.1093/pcp/pcm013](https://doi.org/10.1093/pcp/pcm013).
- Baena-González E, Rolland F, Thevelein JM, Sheen J. 2007.** A central integrator of transcription networks in plant stress and energy signalling. *Nature* **448**(7156):938–942 DOI [10.1038/nature06069](https://doi.org/10.1038/nature06069).
- Bahaji A, Sánchez-López AM, De Diego N, Muñoz FJ, Baroja-Fernández E, Li J, Ricarte-Bermejo A, Baslam M, Aranjuelo I, Almagro G, Humplík JF, Novák O, Spíchal L, Doležal K, Pozueta-Romero J. 2015.** Plastidic phosphoglucose isomerase is an important determinant of starch

- accumulation in mesophyll cells, growth, photosynthetic capacity, and biosynthesis of plastidic cytokinins in Arabidopsis. *PLOS ONE* **10**(3):e0119641 DOI [10.1371/journal.pone.0119641](https://doi.org/10.1371/journal.pone.0119641).
- Ball S, Guan HP, James M, Myers A, Keeling P, Mouille G, Buleon A, Colonna P, Preiss J. 1991.** From glycogen to amylopectin: a model for the biogenesis of the plant starch granule. *Cell* **86**(3):349–352 DOI [10.1016/s0092-8674\(00\)80107-5](https://doi.org/10.1016/s0092-8674(00)80107-5).
- Berg JM, Tymoczko JL, Stryer L. 2006.** *Biochemistry*. Sixth Edition. New York: Freeman.
- Blasing OE, Gibon Y, Gunther M, Hohne M, Morcuende R, Osuna D, Thimm O, Usadel B, Scheible W-R, Stitt M. 2005.** Sugars and circadian regulation make major contributions to the global regulation of diurnal gene expression in Arabidopsis. *Plant Cell Online* **17**(12):3257–3281 DOI [10.1105/tpc.105.035261](https://doi.org/10.1105/tpc.105.035261).
- Bumee S, Ingkasuwan P, Kalapanulak S, Meechai A, Cheevadhanarak S, Saithong T. 2013.** Transcriptional regulatory network of Arabidopsis starch metabolism under extensive light condition: a potential model of transcription-modulated starch metabolism in roots of starchy crops. *Procedia Computer Science* **23**:113–121 DOI [10.1016/j.procs.2013.10.015](https://doi.org/10.1016/j.procs.2013.10.015).
- Burdo B, Gray J, Goetting-Minesky MP, Wittler B, Hunt M, Li T, Velliquette D, Thomas J, Gentzel I, Brito MDS, Mejía-Guerra MK, Connolly LN, Qaisi D, Li W, Casas MI, Doseff AI, Grotewold E. 2014.** The maize TFome—development of a transcription factor open reading frame collection for functional genomics. *Plant Journal* **80**(2):356–366 DOI [10.1111/tpj.12623](https://doi.org/10.1111/tpj.12623).
- Cai Y. 2002.** Interaction of rice bZIP protein REB with the 5'-upstream region of both rice *sbe1* gene and waxy gene. *Chinese Science Bulletin* **47**(4):310 DOI [10.1360/02tb9074](https://doi.org/10.1360/02tb9074).
- Chen J, Yi Q, Cao Y, Wei B, Zheng L, Xiao Q, Xie Y, Gu Y, Li Y, Huang H, Wang Y, Hou X, Long T, Zhang J, Liu H, Liu Y, Yu G, Huang Y. 2016.** ZmbZIP91 regulates expression of starch synthesis-related genes by binding to ACTCAT elements in their promoters. *Journal of Experimental Botany* **67**(5):1327–1338 DOI [10.1093/jxb/erv527](https://doi.org/10.1093/jxb/erv527).
- Comparot-Moss S, Denyer K. 2009.** The evolution of the starch biosynthetic pathway in cereals and other grasses. *Journal of Experimental Botany* **60**(9):2481–2492 DOI [10.1093/jxb/erp141](https://doi.org/10.1093/jxb/erp141).
- Cookson SJ, Yadav UP, Klie S, Morcuende R, Usadel B, Lunn JE, Stitt M. 2016.** Temporal kinetics of the transcriptional response to carbon depletion and sucrose readdition in Arabidopsis seedlings. *Plant, Cell & Environment* **39**(4):768–786 DOI [10.1111/pce.12642](https://doi.org/10.1111/pce.12642).
- Crofts N, Abe N, Oitome NF, Matsushima R, Hayashi M, Tetlow IJ, Emes MJ, Nakamura Y, Fujita N. 2015.** Amylopectin biosynthetic enzymes from developing rice seed form enzymatically active protein complexes. *Journal of Experimental Botany* **66**(15):4469–4482 DOI [10.1093/jxb/erv212](https://doi.org/10.1093/jxb/erv212).
- Cvekl A, Zhang X. 2017.** Signaling and gene regulatory networks in mammalian lens development. *Trends in Genetics* **33**(10):677–702 DOI [10.1016/j.tig.2017.08.001](https://doi.org/10.1016/j.tig.2017.08.001).
- Dian W, Jiang H, Chen Q, Liu F, Wu P. 2003.** Cloning and characterization of the granule-bound starch synthase II gene in rice: gene expression is regulated by the nitrogen level, sugar and circadian rhythm. *Planta* **218**(2):261–268 DOI [10.1007/s00425-003-1101-9](https://doi.org/10.1007/s00425-003-1101-9).
- Emes MJ, Bowsher CG, Hedley C, Burrell MM, Scrase-Field ESF, Tetlow IJ. 2003.** Starch synthesis and carbon partitioning in developing endosperm. *Journal of Experimental Botany* **54**(382):569–575 DOI [10.1093/jxb/erg089](https://doi.org/10.1093/jxb/erg089).
- Fernie AR, Roessner U, Trethewey RN, Willmitzer L. 2001.** The contribution of plastidial phosphoglucomutase to the control of starch synthesis within the potato tuber. *Planta* **213**(3):418–426 DOI [10.1007/s004250100521](https://doi.org/10.1007/s004250100521).
- Fettke J, Fernie AR. 2015.** Intracellular and cell-to-apoplast compartmentation of carbohydrate metabolism. *Trends in Plant Science* **20**(8):490–497 DOI [10.1016/j.tplants.2015.04.012](https://doi.org/10.1016/j.tplants.2015.04.012).

- Flis A, Sulpice R, Seaton DD, Ivakov AA, Liput M, Abel C, Millar AJ, Stitt M. 2016. Photoperiod-dependent changes in the phase of core clock transcripts and global transcriptional outputs at dawn and dusk in Arabidopsis. *Plant, Cell & Environment* **39**(9):1955–1981 DOI [10.1111/pce.12754](https://doi.org/10.1111/pce.12754).
- Foyer CH, Kerchev PI, Hancock RD. 2012. The ABA-INSENSITIVE-4 (ABI4) transcription factor links redox, hormone and sugar signaling pathways. *Plant Signaling & Behavior* **7**(2):276–281 DOI [10.4161/psb.18770](https://doi.org/10.4161/psb.18770).
- Fu F-F, Xue H-W. 2010. Coexpression analysis identifies rice starch regulator1, a rice AP2/EREBP family transcription factor, as a novel rice starch biosynthesis regulator. *Plant Physiology* **154**(2):927–938 DOI [10.1104/pp.110.159517](https://doi.org/10.1104/pp.110.159517).
- Gómez-Arjona FM, Li J, Raynaud S, Baroja-Fernández E, Muñoz FJ, Ovecka M, Ragel P, Bahaji A, Pozueta-Romero J, Mérida Á. 2011. Enhancing the expression of starch synthase class IV results in increased levels of both transitory and long-term storage starch. *Plant Biotechnology Journal* **9**(9):1049–1060 DOI [10.1111/j.1467-7652.2011.00626.x](https://doi.org/10.1111/j.1467-7652.2011.00626.x).
- Garapati P, Feil R, Lunn JE, Van Dijck P, Balazadeh S, Mueller-Roeber B. 2015. Transcription factor Arabidopsis activating factor1 integrates carbon starvation responses with trehalose metabolism. *Plant Physiology* **169**(1):379–390 DOI [10.1104/pp.15.00917](https://doi.org/10.1104/pp.15.00917).
- Geigenberger P. 2011. Regulation of starch biosynthesis in response to a fluctuating environment. *Plant Physiology* **155**(4):1566–1577 DOI [10.1104/pp.110.170399](https://doi.org/10.1104/pp.110.170399).
- Geigenberger P, Stitt M. 1993. Sucrose synthase catalyses a readily reversible reaction in vivo in developing potato tubers and other plant tissues. *Planta* **189**(3):329–339 DOI [10.1007/bf00194429](https://doi.org/10.1007/bf00194429).
- Gene Ontology Consortium. 2004. The gene ontology (GO) database and informatics resource. *Nucleic Acids Research* **32**(90001):258D–261D DOI [10.1093/nar/gkh036](https://doi.org/10.1093/nar/gkh036).
- Graf A, Smith AM. 2011. Starch and the clock: the dark side of plant productivity. *Trends in Plant Science* **16**(3):169–175 DOI [10.1016/j.tplants.2010.12.003](https://doi.org/10.1016/j.tplants.2010.12.003).
- Gross P, Ap-Rees T. 1986. Alkaline inorganic pyrophosphatase and starch synthesis in amyloplasts. *Planta* **167**(1):140–145 DOI [10.1007/bf00446381](https://doi.org/10.1007/bf00446381).
- Hejazi M, Steup M, Fettke J. 2012. The plastidial glucan, water dikinase (GWD) catalyses multiple phosphotransfer reactions. *FEBS Journal* **279**(11):1953–1966 DOI [10.1111/j.1742-4658.2012.08576.x](https://doi.org/10.1111/j.1742-4658.2012.08576.x).
- Hennen-Bierwagen TA, Lin Q, Grimaud F, Planchot V, Keeling PL, James MG, Myers AM. 2009. Proteins from multiple metabolic pathways associate with starch biosynthetic enzymes in high molecular weight complexes: a model for regulation of carbon allocation in maize amyloplasts. *Plant Physiology* **149**(3):1541–1559 DOI [10.1104/pp.109.135293](https://doi.org/10.1104/pp.109.135293).
- Hirose T, Ohdan T, Nakamura Y, Terao T. 2006. Expression profiling of genes related to starch synthesis in rice leaf sheaths during the heading period. *Physiologia Plantarum* **128**(3):425–435 DOI [10.1111/j.1399-3054.2006.00758.x](https://doi.org/10.1111/j.1399-3054.2006.00758.x).
- Huang B, Hennen-Bierwagen TA, Myers AM. 2014. Functions of multiple genes encoding ADP-glucose pyrophosphorylase subunits in maize endosperm, embryo, and leaf. *Plant Physiology* **164**(2):596–611 DOI [10.1104/pp.113.231605](https://doi.org/10.1104/pp.113.231605).
- Huang H, Xie S, Xiao Q, Wei B, Zheng L, Wang Y, Cao Y, Zhang X, Long T, Li Y, Hu Y, Yu G, Liu H, Liu Y, Huang Z, Zhang J, Huang Y. 2016. Sucrose and ABA regulate starch biosynthesis in maize through a novel transcription factor, ZmEREB156. *Scientific Reports* **6**(1):27590 DOI [10.1038/srep27590](https://doi.org/10.1038/srep27590).
- Ingkasuwan P, Netrphan S, Prasitwattanaseree S, Tanticharoen M, Bhumiratana S, Meechai A, Chaijaruwanich J, Takahashi H, Cheevadhanarak S. 2012. Inferring transcriptional gene

- regulation network of starch metabolism in *Arabidopsis thaliana* leaves using graphical Gaussian model. *BMC Systems Biology* **6**(1):100 DOI [10.1186/1752-0509-6-100](https://doi.org/10.1186/1752-0509-6-100).
- James MG, Denyer K, Myers AM. 2003.** Starch synthesis in the cereal endosperm. *Current Opinion in Plant Biology* **6**(3):215–222 DOI [10.1016/s1369-5266\(03\)00042-6](https://doi.org/10.1016/s1369-5266(03)00042-6).
- Kammerer B, Fischer K, Hilpert B, Schubert S, Gutensohn M, Weber A, Flugge UI. 1998.** Molecular characterization of a carbon transporter in plastids from heterotrophic tissues: the glucose 6-phosphate/phosphate antiporter. *Plant Cell* **10**(1):105–117 DOI [10.1105/tpc.10.1.105](https://doi.org/10.1105/tpc.10.1.105).
- Kang G, Liu G, Peng X, Wei L, Wang C, Zhu Y, Ma Y, Jiang Y, Guo T. 2013.** Increasing the starch content and grain weight of common wheat by overexpression of the cytosolic AGPase large subunit gene. *Plant Physiology and Biochemistry* **73**:93–98 DOI [10.1016/j.plaphy.2013.09.003](https://doi.org/10.1016/j.plaphy.2013.09.003).
- Kolbe A, Tiessen A, Schluepmann H, Paul M, Ulrich S, Geigenberger P. 2005.** Trehalose 6-phosphate regulates starch synthesis via posttranslational redox activation of ADP-glucose pyrophosphorylase. *Proceedings of the National Academy of Sciences of the United States of America* **102**(31):11118–11123 DOI [10.1073/pnas.0503410102](https://doi.org/10.1073/pnas.0503410102).
- Kötting O, Kossmann J, Zeeman SC, Lloyd JR. 2010.** Regulation of starch metabolism: the age of enlightenment? *Current Opinion in Plant Biology* **13**:321–329 DOI [10.1016/j.pbi.2010.01.003](https://doi.org/10.1016/j.pbi.2010.01.003).
- Kruger NJ, Hill SA, Ratcliffe RG. 1999.** *Regulation of primary metabolic pathways in plants*. Netherlands: Springer.
- Kunz H-H, Zamani-Nour S, Hausler RE, Ludewig K, Schroeder JI, Malinova I, Fettke J, Flugge U-I, Gierth M. 2014.** Loss of cytosolic phosphoglucose isomerase affects carbohydrate metabolism in leaves and is essential for fertility of *Arabidopsis*. *Plant Physiology* **166**(2):753–765 DOI [10.1104/pp.114.241091](https://doi.org/10.1104/pp.114.241091).
- Lambert SA, Jolma A, Campitelli LF, Das PK, Yin Y, Albu M, Chen X, Taipale J, Hughes TR, Weirauch MT. 2018.** The human transcription factors. *Cell* **172**(4):650–665 DOI [10.1016/j.cell.2018.01.029](https://doi.org/10.1016/j.cell.2018.01.029).
- Lemmon ZH, Bukowski R, Sun Q, Doebley JF. 2014.** The role of cis regulatory evolution in maize domestication. *PLOS Genetics* **10**(11):e1004745 DOI [10.1371/journal.pgen.1004745](https://doi.org/10.1371/journal.pgen.1004745).
- Leterrier M, Holappa LD, Broglie KE, Beckles DM. 2008.** Cloning, characterisation and comparative analysis of a starch synthase IV gene in wheat: Functional and evolutionary implications. *BMC Plant Biology* **8**:1–21 DOI [10.1186/1471-2229-8-98](https://doi.org/10.1186/1471-2229-8-98).
- Li J, Ezquer I, Bahaji A, Montero M, Ovecka M, Baroja-Fernández E, Muñoz FJ, Mérida Á, Almagro G, Hidalgo M, Sesma MT, Pozueta-Romero J. 2011a.** Microbial volatile-induced accumulation of exceptionally high levels of starch in *Arabidopsis* leaves is a process involving NTRC and starch synthase classes III and IV. *Molecular Plant-Microbe Interactions* **24**(10):1165–1178 DOI [10.1094/MPMI-05-11-0112](https://doi.org/10.1094/MPMI-05-11-0112).
- Li Z, Gao Q, Liu Y, He C, Zhang X, Zhang J. 2011c.** Overexpression of transcription factor ZmPTF1 improves low phosphate tolerance of maize by regulating carbon metabolism and root growth. *Planta* **233**(6):1129–1143 DOI [10.1007/s00425-011-1368-1](https://doi.org/10.1007/s00425-011-1368-1).
- Li X, Xing J, Gianfagna TJ, Janes HW. 2002.** Sucrose regulation of ADP-glucose pyrophosphorylase subunit genes transcript levels in leaves and fruits. *Plant Science* **162**(2):239–244 DOI [10.1016/s0168-9452\(01\)00565-9](https://doi.org/10.1016/s0168-9452(01)00565-9).
- Li Y, Yu G, Lv Y, Long T, Li P, Hu Y, Liu H, Zhang J, Liu Y, Li W-C, Huang Y. 2018.** Combinatorial interaction of two adjacent cis-active promoter regions mediates the synergistic induction of Bt2 gene by sucrose and ABA in maize endosperm. *Plant Science* **274**:332–340 DOI [10.1016/j.plantsci.2018.06.003](https://doi.org/10.1016/j.plantsci.2018.06.003).

- Li N, Zhang S, Zhao Y, Li B, Zhang J. 2011b. Over-expression of AGPase genes enhances seed weight and starch content in transgenic maize. *Planta* 233(2):241–250 DOI 10.1007/s00425-010-1296-5.
- Liang H, Mokrani A, Chisomo-Kasiya H, Wilson-Arop O-M, Mi H, Ji K, Ge X, Ren M. 2018. Molecular characterization and identification of facilitative glucose transporter 2 (GLUT2) and its expression and of the related glycometabolism enzymes in response to different starch levels in blunt snout bream (*Megalobrama amblycephala*). *Fish Physiology and Biochemistry* 44(3):869–883 DOI 10.1007/s10695-018-0477-1.
- Liu C, Chen X, Ma P, Zhang S, Zeng C, Jiang X, Wang W. 2018a. Ethylene responsive factor meERF72 negatively regulates sucrose synthase 1 gene in cassava. *International Journal of Molecular Sciences* 19:1281 DOI 10.3390/ijms19051281.
- Liu Y, Chen X, Wang X, Fang Y, Huang M, Guo L, Zhang Y, Zhao H. 2018b. Improving biomass and starch accumulation of bioenergy crop duckweed (*Landoltia punctata*) by abscisic acid application. *Scientific Reports* 8(1):9544 DOI 10.1038/s41598-018-27944-7.
- Lloyd JR, Kossmann J, Ritte G. 2005. Leaf starch degradation comes out of the shadows. *Trends in Plant Science* 10(3):130–137 DOI 10.1016/j.tplants.2005.01.001.
- Lu Y. 2005. Daylength and circadian effects on starch degradation and maltose metabolism. *Plant Physiology* 138(4):2280–2291 DOI 10.1104/pp.105.061903.
- Lunn JE. 2006. Compartmentation in plant metabolism. *Journal of Experimental Botany* 58(1):35–47 DOI 10.1093/jxb/erl134.
- Ma J, Hanssen M, Lundgren K, Hernández L, Delatte T, Ehlert A, Liu CM, Schluempmann H, Dröge-Laser W, Moritz T, Smeekens S, Hanson J. 2011. The sucrose-regulated Arabidopsis transcription factor bZIP11 reprograms metabolism and regulates trehalose metabolism. *New Phytologist* 191(3):733–745 DOI 10.1111/j.1469-8137.2011.03735.x.
- Maere S, Heymans K, Kuiper M. 2005. BiNGO: a Cytoscape plugin to assess overrepresentation of gene ontology categories in biological networks. *Bioinformatics* 21(16):3448–3449 DOI 10.1093/bioinformatics/bti551.
- Malinova I, Alseekh S, Feil R, Fernie AR, Baumann O, Schöttler MA, Lunn JE, Fettke J. 2017. Starch synthase 4 and plastidal phosphorylase differentially affect starch granule number and morphology. *Plant Physiology* 174(1):73–85 DOI 10.1104/pp.16.01859.
- Marshall J, Sidebottom C, Debet M, Martin C, Smith AM, Edwards A. 1996. Identification of the major starch synthase in the soluble fraction of potato tubers. *Plant Cell* 8(7):1121–1135 DOI 10.2307/3870356.
- Martin C, Smith AM. 1995. Starch biosynthesis. *Plant Cell* 7:971–985.
- Michalska J, Zauber H, Buchanan BB, Cejudo FJ, Geigenberger P. 2009. NTRC links built-in thioredoxin to light and sucrose in regulating starch synthesis in chloroplasts and amyloplasts. *Proceedings of the National Academy of Sciences of the United States of America* 106(24):9908–9913 DOI 10.1073/pnas.0903559106.
- Morell S, Ap-Rees T. 1986. Sucrose metabolism in developing tubers of *Solanum tuberosum*. *Phytochemistry* 25(7):1579–1585 DOI 10.1016/s0031-9422(00)81212-1.
- Morita R, Sugino M, Hatanaka T, Misoo S, Fukayama H. 2015. CO₂ Responsive CCT protein, CRCT is a positive regulator of starch synthesis in vegetative organs of rice. *Plant Physiology* 167:1321–1331 DOI 10.1104/pp.15.00021.
- Mugford ST, Fernandez O, Brinton J, Flis A, Krohn N, Encke B, Feil R, Sulpice R, Lunn JE, Stitt M, Smith AM. 2014. Regulatory properties of ADP glucose pyrophosphorylase are required for adjustment of leaf starch synthesis in different photoperiods. *Plant Physiology* 166(4):1733–1747 DOI 10.1104/pp.114.247759.

- Mukherjee S, Liu A, Deol KK, Kulichikhin K, Stasolla C, Brûlé-Babel A, Ayele BT. 2015.** Transcriptional coordination and abscisic acid mediated regulation of sucrose transport and sucrose-to-starch metabolism related genes during grain filling in wheat (*Triticum aestivum* L.). *Plant Science* **240**:143–160 DOI [10.1016/j.plantsci.2015.09.010](https://doi.org/10.1016/j.plantsci.2015.09.010).
- Nakamura Y, Ono M, Sawada T, Crofts N, Fujita N, Steup M. 2017.** Characterization of the functional interactions of plastidial starch phosphorylase and starch branching enzymes from rice endosperm during reserve starch biosynthesis. *Plant Science* **264**:83–95 DOI [10.1016/j.plantsci.2017.09.002](https://doi.org/10.1016/j.plantsci.2017.09.002).
- Noguero M, Atif RM, Ochatt S, Thompson RD. 2013.** The role of the DNA-binding one zinc finger (DOF) transcription factor family in plants. *Plant Science* **209**:32–45 DOI [10.1016/j.plantsci.2013.03.016](https://doi.org/10.1016/j.plantsci.2013.03.016).
- Okita TW, Nakata PA, Anderson JM, Sowokinos J, Morell M, Preiss J. 1990.** The subunit structure of potato tuber ADP-glucose pyrophosphorylase. *Plant Physiology* **93**:785–790.
- Patron NJ, Keeling PJ. 2005.** Common evolutionary origin of starch biosynthetic enzymes in green and red algae. *Journal of Phycology* **41**(6):1131–1141 DOI [10.1111/j.1529-8817.2005.00135.x](https://doi.org/10.1111/j.1529-8817.2005.00135.x).
- Pokhilko A, Flis A, Sulpice R, Stitt M, Ebenhö O, Ebenhö O. 2014.** Adjustment of carbon fluxes to light conditions regulates the daily turnover of starch in plants: a computational model. *Molecular Biosystems* **10**(3):613–627 DOI [10.1039/c3mb70459a](https://doi.org/10.1039/c3mb70459a).
- Purdy SJ, Bussell JD, Nunn CP, Smith SM. 2013.** Leaves of the Arabidopsis maltose exporter1 mutant exhibit a metabolic profile with features of cold acclimation in the warm. *PLOS ONE* **8**(11):e79412 DOI [10.1371/journal.pone.0079412](https://doi.org/10.1371/journal.pone.0079412).
- Radchuk V, Riewe D, Peukert M, Matros A, Strickert M, Radchuk R, Weier D, Steinbiß HH, Sreenivasulu N, Weschke W, Weber H. 2017.** Down-regulation of the sucrose transporters HvSUT1 and HvSUT2 affects sucrose homeostasis along its delivery path in barley grains. *Journal of Experimental Botany* **68**(16):4595–4612 DOI [10.1093/jxb/erx266](https://doi.org/10.1093/jxb/erx266).
- Ral J-P. 2006.** Circadian clock regulation of starch metabolism establishes GBSSI as a major contributor to amylopectin synthesis in *Chlamydomonas reinhardtii*. *Plant Physiology* **142**(1):305–317 DOI [10.1104/pp.106.081885](https://doi.org/10.1104/pp.106.081885).
- Ramírez-Sánchez O, Pérez-Rodríguez P, Delaye L, Tiessen A. 2016.** Plant proteins are smaller because they are encoded by fewer exons than animal proteins. *Genomics, Proteomics & Bioinformatics* **14**(6):357–370 DOI [10.1016/j.gpb.2016.06.003](https://doi.org/10.1016/j.gpb.2016.06.003).
- Riaño-Pachón DM, Ruzicic S, Dreyer I, Mueller-Roeber B. 2007.** PlnTFDB: an integrative plant transcription factor database. **8**(1):42 DOI [10.1186/1471-2105-8-42](https://doi.org/10.1186/1471-2105-8-42).
- Riechmann JL, Heard J, Martin G, Reuber L, Jiang C, Keddie J, Adam L, Pineda O, Ratcliffe OJ, Samaha RR, Creelman R, Pilgrim M, Broun P, Zhang JZ, Ghandehari D, Sherman BK, Yu G. 2000.** Arabidopsis transcription factors: genome-wide comparative analysis among eukaryotes. *Science* **290**(5499):2105–2110 DOI [10.1126/science.290.5499.2105](https://doi.org/10.1126/science.290.5499.2105).
- Rockwell FE, Gersony JT, Holbrook NM. 2018.** Where does Münch flow begin? Sucrose transport in the pre-phloem path. *Current Opinion in Plant Biology* **43**:101–107 DOI [10.1016/j.pbi.2018.04.007](https://doi.org/10.1016/j.pbi.2018.04.007).
- Ryoo N, Eom J-S, Kim H-B, Thuy Vo T, Lee S-W, Hahn T-R, Jeon J-S. 2013.** Expression and functional analysis of rice plastidic maltose transporter, OsMEX1. *Journal of the Korean Society for Applied Biological Chemistry* **56**(2):149–155 DOI [10.1007/s13765-012-3266-z](https://doi.org/10.1007/s13765-012-3266-z).
- Sakulsingharoj C, Choi S-B, Hwang S-K, Edwards GE, Bork J, Meyer CR, Preiss J, Okita TW. 2004.** Engineering starch biosynthesis for increasing rice seed weight: the role of the cytoplasmic

- ADP-glucose pyrophosphorylase. *Plant Science* **167**(6):1323–1333
DOI [10.1016/j.plantsci.2004.06.028](https://doi.org/10.1016/j.plantsci.2004.06.028).
- Santelia D, Zeeman SC. 2011.** Progress in Arabidopsis starch research and potential biotechnological applications. *Current Opinion in Biotechnology* **22**(2):271–280 DOI [10.1016/j.copbio.2010.11.014](https://doi.org/10.1016/j.copbio.2010.11.014).
- Satoh H, Shibahara K, Tokunaga T, Nishi A, Tasaki M, Hwang S-K, Okita TW, Kaneko N, Fujita N, Yoshida M, Hosaka Y, Sato A, Utsumi Y, Ohdan T, Nakamura Y. 2008.** Mutation of the plastidial α -glucan phosphorylase gene in rice affects the synthesis and structure of starch in the endosperm. *Plant Cell* **20**(7):1833–1849 DOI [10.1105/tpc.107.054007](https://doi.org/10.1105/tpc.107.054007).
- Schmidt R, Schippers JHM, Mieulet D, Watanabe M, Hoefgen R, Guiderdoni E, Mueller-Roeber B. 2014.** SALT-RESPONSIVE ERF1 is a negative regulator of grain filling and gibberellin-mediated seedling establishment in rice. *Molecular Plant* **7**(2):404–421 DOI [10.1093/mp/sst131](https://doi.org/10.1093/mp/sst131).
- Schott K, Borchert S, Muller-rober B, Heldt HW. 1995.** Transport of inorganic phosphate and C3- and C6-sugar phosphates across the envelope membranes of potato tuber amyloplasts. *Planta* **196**(4):647–652 DOI [10.1007/bf01106756](https://doi.org/10.1007/bf01106756).
- Seaton DD, Graf A, Baerenfaller K, Stitt M, Millar AJ, Gruijsem W. 2018.** Photoperiodic control of the Arabidopsis proteome reveals a translational coincidence mechanism. *Molecular Systems Biology* **14**(3):e7962 DOI [10.15252/msb.20177962](https://doi.org/10.15252/msb.20177962).
- Seferoglu AB, Baris I, Morgil H, Tulum I, Ozdas S, Cevahir G, Kavakli IH. 2013.** Transcriptional regulation of the ADP-glucose pyrophosphorylase isoforms in the leaf and the stem under long and short photoperiod in lentil. *Plant Science* **205–206**:29–37 DOI [10.1016/j.plantsci.2013.01.006](https://doi.org/10.1016/j.plantsci.2013.01.006).
- Seo PJ, Ryu J, Kang SK, Park C-M. 2011.** Modulation of sugar metabolism by an INDETERMINATE DOMAIN transcription factor contributes to photoperiodic flowering in Arabidopsis. *Plant Journal* **65**(3):418–429 DOI [10.1111/j.1365-3113.2010.04432.x](https://doi.org/10.1111/j.1365-3113.2010.04432.x).
- Seung D, Boudet J, Monroe J, Schreier TB, David LC, Abt M, Lu K-J, Zanella M, Zeeman SC. 2017.** Homologs of PROTEIN TARGETING TO STARCH control starch granule initiation in Arabidopsis leaves. *Plant Cell* **29**(7):1657–1677 DOI [10.1105/tpc.17.00222](https://doi.org/10.1105/tpc.17.00222).
- Seung D, Schreier TB, Bürgy L, Eicke S, Zeeman SC. 2018.** Two plastidial coiled-coil proteins are essential for normal starch granule initiation in Arabidopsis. *Plant Cell* **30**:1523–1542 DOI [10.1105/tpc.18.00219](https://doi.org/10.1105/tpc.18.00219).
- Seung D, Soyk S, Coiro M, Maier BA, Eicke S, Zeeman SC. 2015.** PROTEIN TARGETING TO STARCH is required for localising GRANULE-BOUND STARCH SYNTHASE to starch granules and for normal amylose synthesis in Arabidopsis. *PLOS Biology* **13**(2):e1002080 DOI [10.1371/journal.pbio.1002080](https://doi.org/10.1371/journal.pbio.1002080).
- She K-C, Kusano H, Koizumi K, Yamakawa H, Hakata M, Imamura T, Fukuda M, Naito N, Tsurumaki Y, Yaeshima M, Tsuge T, Matsumoto K, Kudoh M, Itoh E, Kikuchi S, Kishimoto N, Yazaki J, Ando T, Yano M, Aoyama T, Sasaki T, Satoh H, Shimada H. 2010.** A novel factor FLOURY ENDOSPERM2 is involved in regulation of rice grain size and starch quality. *Plant Cell* **22**(10):3280–3294 DOI [10.1105/tpc.109.070821](https://doi.org/10.1105/tpc.109.070821).
- Smidansky ED, Clancy M, Meyer FD, Lanning SP, Blake NK, Talbert LE, Giroux MJ. 2002.** Enhanced ADP-glucose pyrophosphorylase activity in wheat endosperm increases seed yield. *Proceedings of the National Academy of Sciences of the United States of America* **99**(3):1724–1729 DOI [10.1073/pnas.022635299](https://doi.org/10.1073/pnas.022635299).
- Smidansky ED, Martin JM, Hannah LC, Fischer AM, Giroux MJ. 2003.** Seed yield and plant biomass increases in rice are conferred by deregulation of endosperm ADP-glucose pyrophosphorylase. *Planta* **216**:656–664 DOI [10.1007/s00425-002-0897-z](https://doi.org/10.1007/s00425-002-0897-z).

- Smith AM. 1999.** Making starch. *Current Opinion in Plant Biology* **2**:223–229.
- Smith SM. 2004.** Diurnal changes in the transcriptome encoding enzymes of starch metabolism provide evidence for both transcriptional and posttranscriptional regulation of starch metabolism in Arabidopsis leaves. *Plant Physiology* **136**(1):2687–2699 DOI [10.1104/pp.104.044347](https://doi.org/10.1104/pp.104.044347).
- Smith AM. 2008.** Prospects for increasing starch and sucrose yields for bioethanol production. *Plant Journal* **54**(4):546–558 DOI [10.1111/j.1365-313X.2008.03468.x](https://doi.org/10.1111/j.1365-313X.2008.03468.x).
- Smith AM. 2012.** Starch in the Arabidopsis plant. *Starch/Staerke* **64**(6):421–434 DOI [10.1002/star.201100163](https://doi.org/10.1002/star.201100163).
- Stitt M, Ap Rees T. 1978.** Pathways of carbohydrate oxidation in leaves of *Pisum sativum* and *Triticum aestivum*. *Phytochemistry* **17**(8):1251–1256 DOI [10.1016/S0031-9422\(00\)94566-7](https://doi.org/10.1016/S0031-9422(00)94566-7).
- Stitt M, Ap Rees A. 1980.** Carbohydrate breakdown by chloroplasts of *Pisum sativum*. *Biochimica et Biophysica Acta (BBA)—General Subjects* **627**(2):131–143 DOI [10.1016/0304-4165\(80\)90315-3](https://doi.org/10.1016/0304-4165(80)90315-3).
- Smith AM, Denyer K, Martin C. 1997.** The synthesis of the starch granule. *Annual Review of Plant Physiology and Plant Molecular Biology* **48**:67–87.
- Smith AM, Stitt M. 2007.** Coordination of carbon supply and plant growth. *Plant, Cell & Environment* **30**(9):1126–1149 DOI [10.1111/j.1365-3040.2007.01708.x](https://doi.org/10.1111/j.1365-3040.2007.01708.x).
- Stitt M, Zeeman SC. 2012.** Starch turnover: pathways, regulation and role in growth. *Current Opinion in Plant Biology* **15**(3):282–292 DOI [10.1016/j.pbi.2012.03.016](https://doi.org/10.1016/j.pbi.2012.03.016).
- Streb S, Zeeman SC. 2012.** Starch metabolism in Arabidopsis. *Arabidopsis Book* **10**:e0160 DOI [10.1199/tab.0160](https://doi.org/10.1199/tab.0160).
- Stritzler M, Muñiz García MN, Schlesinger M, Cortelezzi JI, Capiati DA. 2017.** The plasma membrane H⁺-ATPase gene family in *Solanum tuberosum* L. Role of PHA1 in tuberization. *Journal of Experimental Botany* **68**(17):4821–4837 DOI [10.1093/jxb/erx284](https://doi.org/10.1093/jxb/erx284).
- Sulpice R, Flis A, Ivakov AA, Apelt F, Krohn N, Encke B, Abel C, Feil R, Lunn JE, Stitt M. 2014.** Arabidopsis coordinates the diurnal regulation of carbon allocation and growth across a wide range of photoperiods. *Molecular Plant* **7**(1):137–155 DOI [10.1093/mp/sst127](https://doi.org/10.1093/mp/sst127).
- Sulpice R, Pyl E-T, Ishihara H, Trenkamp S, Steinfath M, Witucka-Wall H, Gibon Y, Usadel B, Poree F, Piques MC, Von Korff M, Steinhäuser MC, Keurentjes JJB, Guenther M, Hoehne M, Selbig J, Fernie AR, Altmann T, Stitt M. 2009.** Starch as a major integrator in the regulation of plant growth. *Proceedings of the National Academy of Sciences of the United States of America* **106**(25):10348–10353 DOI [10.1073/pnas.0903478106](https://doi.org/10.1073/pnas.0903478106).
- Sun C. 2003.** A novel WRKY transcription factor, SUSIBA2, participates in sugar signaling in barley by binding to the sugar-responsive elements of the iso1 promoter. *Plant Cell* **15**(9):2076–2092 DOI [10.1105/tpc.014597](https://doi.org/10.1105/tpc.014597).
- Sweetlove LJ, Fernie AR. 2013.** The spatial organization of metabolism within the plant cell. *Annual Review of Plant Biology* **64**(1):723–746 DOI [10.1146/annurev-arplant-050312-120233](https://doi.org/10.1146/annurev-arplant-050312-120233).
- Tanaka M, Takahata Y, Nakayama H, Nakatani M, Tahara M. 2009.** Altered carbohydrate metabolism in the storage roots of sweetpotato plants overexpressing the SRF1 gene, which encodes a Dof zinc finger transcription factor. *Planta* **230**(4):737–746 DOI [10.1007/s00425-009-0979-2](https://doi.org/10.1007/s00425-009-0979-2).
- Tenorio G, Orea A, Romero JM, Mérida Á. 2003.** Oscillation of mRNA level and activity of granule-bound starch synthase I in Arabidopsis leaves during the day/night cycle. *Plant Molecular Biology* **51**(6):949–958 DOI [10.1023/A:1023053420632](https://doi.org/10.1023/A:1023053420632).
- Tetlow IJ, Emes MJ. 2011.** *Starch biosynthesis in higher plants: the enzymes of starch synthesis*. Elsevier DOI [10.1016/B978-0-08-088504-9.00538-9](https://doi.org/10.1016/B978-0-08-088504-9.00538-9).

- Thellin O, ElMoualij B, Heinen E, Zorzi W. 2009.** A decade of improvements in quantification of gene expression and internal standard selection. *Biotechnology Advances* **27**(4):323–333 DOI [10.1016/j.biotechadv.2009.01.010](https://doi.org/10.1016/j.biotechadv.2009.01.010).
- Tiessen A. 2018.** The fluorescent blue glow of banana fruits is not due to symplasmic plastidial catabolism but arises from insoluble phenols esterified to the cell wall. *Plant Science* **275**:75–83 DOI [10.1016/j.plantsci.2018.07.006](https://doi.org/10.1016/j.plantsci.2018.07.006).
- Tiessen A, Hendriks JHM, Stitt M, Branscheid A, Gibon Y, Farre EM, Geigenberger P. 2002.** Starch synthesis in potato tubers is regulated by post-translational redox modification of ADP-glucose pyrophosphorylase: a novel regulatory mechanism linking starch synthesis to the sucrose supply. *Plant Cell* **14**(9):2191–2213 DOI [10.1105/tpc.003640](https://doi.org/10.1105/tpc.003640).
- Tiessen A, Nerlich A, Faix B, Hümmer C, Fox S, Trafford K, Weber H, Weschke W, Geigenberger P. 2012.** Subcellular analysis of starch metabolism in developing barley seeds using a non-aqueous fractionation method. *Journal of Experimental Botany* **63**(5):2071–2087 DOI [10.1093/jxb/err408](https://doi.org/10.1093/jxb/err408).
- Tiessen A, Padilla-Chacon D. 2013.** Subcellular compartmentation of sugar signaling: links among carbon cellular status, route of sucrolysis, sink-source allocation, and metabolic partitioning. *Frontiers in Plant Science* **3**:306 DOI [10.3389/fpls.2012.00306](https://doi.org/10.3389/fpls.2012.00306).
- Tiessen A, Pérez-Rodríguez P, Delaye-Arredondo LJ. 2012.** Mathematical modeling and comparison of protein size distribution in different plant, animal, fungal and microbial species reveals a negative correlation between protein size and protein number, thus providing insight into the evolution of proteomes. *BMC Research Notes* **5**(1):85 DOI [10.1186/1756-0500-5-85](https://doi.org/10.1186/1756-0500-5-85).
- Tiessen A, Prescha K, Branscheid A, Palacios N, McKibbin R, Halford NG, Geigenberger P. 2003.** Evidence that SNF1-related kinase and hexokinase are involved in separate sugar-signalling pathways modulating post-translational redox activation of ADP-glucose pyrophosphorylase in potato tubers. *Plant Journal* **35**(4):490–500 DOI [10.1046/j.1365-313X.2003.01823.x](https://doi.org/10.1046/j.1365-313X.2003.01823.x).
- Tjaden J, Mohlmann T, Kampfenkel K, Henrichs G, Neuhaus HE. 1998.** Altered plastidic ATP/ADP-transporter activity influences potato (*Solanum tuberosum* L.) tuber morphology, yield and composition of tuber starch. *Plant Journal* **16**(5):531–540 DOI [10.1046/j.1365-313x.1998.00317.x](https://doi.org/10.1046/j.1365-313x.1998.00317.x).
- Tsai H-L, Lue W-L, Lu K-J, Hsieh M-H, Wang S-M, Chen J. 2009.** Starch synthesis in Arabidopsis is achieved by spatial cotranscription of core starch metabolism genes. *Plant Physiology* **151**(3):1582–1595 DOI [10.1104/pp.109.144196](https://doi.org/10.1104/pp.109.144196).
- Van Harsselaar JK, Lorenz J, Senning M, Sonnewald U, Sonnewald S. 2017.** Genome-wide analysis of starch metabolism genes in potato (*Solanum tuberosum* L.). *BMC Genomics* **18**(1):37 DOI [10.1186/s12864-016-3381-z](https://doi.org/10.1186/s12864-016-3381-z).
- Vaquerizas JM, Kummerfeld SK, Teichmann SA, Luscombe NM. 2009.** A census of human transcription factors: function, expression and evolution. *Nature Reviews Genetics* **10**(4):252–263 DOI [10.1038/nrg2538](https://doi.org/10.1038/nrg2538).
- Wang K, Nishida H. 2015.** REGULATOR: a database of metazoan transcription factors and maternal factors for developmental studies. *BMC Bioinformatics* **16**(1):114 DOI [10.1186/s12859-015-0552-x](https://doi.org/10.1186/s12859-015-0552-x).
- Wang J-C, Xu H, Zhu Y, Liu Q-Q, Cai X-L. 2013.** OsbZIP58, a basic leucine zipper transcription factor, regulates starch biosynthesis in rice endosperm. *Journal of Experimental Botany* **64**(11):3453–3466 DOI [10.1093/jxb/ert187](https://doi.org/10.1093/jxb/ert187).
- Wuriyangan H, Zhang B, Cao W-H, Ma B, Lei G, Liu Y-F, Wei W, Wu H-J, Chen L-J, Chen H-W, Cao Y-R, He S-J, Zhang W-K, Wang X-J, Chen S-Y, Zhang J-S. 2009.** The ethylene receptor

- ETR2 delays floral transition and affects starch accumulation in rice. *Plant Cell* **21**(5):1473–1494 DOI [10.1105/tpc.108.065391](https://doi.org/10.1105/tpc.108.065391).
- Yan H, Jiang H, Pan X, Li M, Chen Y, Wu G. 2009.** The gene encoding starch synthase IIc exists in maize and wheat. *Plant Science* **176**(1):51–57 DOI [10.1016/j.plantsci.2008.09.003](https://doi.org/10.1016/j.plantsci.2008.09.003).
- Yanagisawa S. 2000.** Dof1 and Dof2 transcription factors are associated with expression of multiple genes involved in carbon metabolism in maize. *Plant Journal* **21**(3):281–288 DOI [10.1046/j.1365-313x.2000.00685.x](https://doi.org/10.1046/j.1365-313x.2000.00685.x).
- Yilmaz A, Nishiyama MY, Fuentes BG, Mendes Souza G, Janies D, Gray J, Grotewold E. 2009.** GRASSIUS: a platform for comparative regulatory genomics across the grasses. *Plant Physiology* **149**(1):171–180 DOI [10.1104/pp.108.128579](https://doi.org/10.1104/pp.108.128579).
- Yonekura-Sakakibara K, Tohge T, Matsuda F, Nakabayashi R, Takayama H, Niida R, Watanabe-Takahashi A, Inoue E, Saito K. 2008.** Comprehensive flavonol profiling and transcriptome coexpression analysis leading to decoding gene-metabolite correlations in Arabidopsis. *Plant Cell* **20**(8):2160–2176 DOI [10.1105/tpc.108.058040](https://doi.org/10.1105/tpc.108.058040).
- Zeeman SC, Smith SM, Smith AM. 2007.** The diurnal metabolism of leaf starch. *Biochemical Journal* **401**(1):13–28 DOI [10.1042/BJ20061393](https://doi.org/10.1042/BJ20061393).
- Zeeman SC, Umemoto T, Lue WL, Au-Yeung P, Martin C, Smith AM, Chen J. 1998.** A mutant of Arabidopsis lacking a chloroplastic isoamylase accumulates both starch and phytylglycogen. *Plant Cell* **10**(10):1699–1711 DOI [10.2307/3870767](https://doi.org/10.2307/3870767).
- Zhang J, Chen J, Yi Q, Hu Y, Liu H, Liu Y, Huang Y. 2014.** Novel role of ZmaNAC36 in co-expression of starch synthetic genes in maize endosperm. *Plant Molecular Biology* **84**(3):359–369 DOI [10.1007/s11103-013-0153-x](https://doi.org/10.1007/s11103-013-0153-x).
- Zhang T-F, Li B, Zhang D-F, Jia G-Q, Li Z-Y, Wang S-C. 2012.** Genome-wide transcriptional analysis of yield and heterosis-associated genes in maize (*Zea mays* L.). *Journal of Integrative Agriculture* **11**(8):1245–1256 DOI [10.1016/S2095-3119\(12\)60121-X](https://doi.org/10.1016/S2095-3119(12)60121-X).
- Zhu T, Budworth P, Chen W, Provart N, Chang H-S, Guimil S, Su W, Estes B, Zou G, Wang X. 2003.** Transcriptional control of nutrient partitioning during rice grain filling. *Plant Biotechnology Journal* **1**(1):59–70 DOI [10.1046/j.1467-7652.2003.00006.x](https://doi.org/10.1046/j.1467-7652.2003.00006.x).
- Zhu G, Ye N, Yang J, Peng X, Zhang J. 2011.** Regulation of expression of starch synthesis genes by ethylene and ABA in relation to the development of rice inferior and superior spikelets. *Journal of Experimental Botany* **62**(11):3907–3916 DOI [10.1093/jxb/err088](https://doi.org/10.1093/jxb/err088).
- Zrenner R, Salanoubat M, Willmitzer L, Sonnewald U. 1995.** Evidence of the crucial role of sucrose synthase for sink strength using transgenic potato plants (*Solanum tuberosum* L.). *Plant Journal* **7**(1):97–107 DOI [10.1046/j.1365-313x.1995.07010097.x](https://doi.org/10.1046/j.1365-313x.1995.07010097.x).
- Zuo Y, Su G, Cheng L, Liu K, Feng Y, Wei Z, Bai C, Cao G, Li G. 2017.** Coexpression analysis identifies nuclear reprogramming barriers of somatic cell nuclear transfer embryos. *Oncotarget* **8**(39):65847–65859 DOI [10.18632/oncotarget.19504](https://doi.org/10.18632/oncotarget.19504).