Molecules and Cells

Minireview

Protein and RNA Quality Control by Autophagy in Plant Cells

Seok Ho Yoon and Taijoon Chung*

Department of Biological Sciences, Pusan National University, Busan 46241, Korea
*Correspondence: taijoon@pusan.ac.kr
http://dx.doi.org/10.14348/molcells.2019.0011
www.molcells.org

Eukaryotic cells use conserved quality control mechanisms to repair or degrade defective proteins, which are synthesized at a high rate during proteotoxic stress. Quality control mechanisms include molecular chaperones, the ubiquitin-proteasome system, and autophagic machinery. Recent research reveals that during autophagy, membrane-bound organelles are selectively sequestered and degraded. Selective autophagy is also critical for the clearance of excess or damaged protein complexes (e.g., proteasomes and ribosomes) and membrane-less compartments (e.g., protein aggregates and ribonucleoprotein granules). As sessile organisms, plants rely on quality control mechanisms for their adaptation to fluctuating environments. In this mini-review, we highlight recent work elucidating the roles of selective autophagy in the quality control of proteins and RNA in plant cells. Emphasis will be placed on selective degradation of membrane-less compartments and protein complexes in the cytoplasm. We also propose possible mechanisms by which defective proteins are selectively recognized by autophagic machinery.

Keywords: aggrephagy, autophagy receptor, granulophagy, NBR1, proteaphagy, ribophagy, ubiquitylation

INTRODUCTION

Quality control (QC) of gene expression is important for protein homeostasis or proteostasis. QC machineries repair or degrade defective proteins to maintain the integrity of cellular proteome (Balchin et al., 2016). The QC process starts in the nucleus where transcription and RNA processing are monitored. As a result, only mature mRNA exits the nucleus. The process continues in the cytoplasm where several QC mechanisms target defective RNAs and proteins. During the first round of translation, aberrant mRNA is recognized and degraded by mRNA surveillance-triggered decay pathways, including the nonsense-mediated decay pathway (Chantarachot and Bailey-Serres, 2018). Upon translational repression, mRNA can be either directly degraded by cytosolic nucleases or sequestered in cytoplasmic compartments containing ribonucleoproteins (RNPs), such as stress granules (SGs) and processing bodies (Chantarachot and Bailey-Serres, 2018)(Fig. 1). SGs contain mRNA, RNA binding proteins, translation factors, and 40S ribosome subunits. SG assembly is induced by stresses, such as heat shock and hypoxia. When cells recover from stress, messenger RNP (mRNP) can be released from SGs and participate in translational re-initiation. Thus, SGs are considered a reservoir of stalled translation initiation complexes that accumulate during global repression of translation induced by stress. Processing bodies contain mRNA decay factors in addition to some SG components. However, mRNAs associated with processing bodies appear stable, and the biological role of processing bodies is still enigmatic (Chantarachot and Bailey-Serres, 2018).

Protein QC requires collaboration of three systems that are conserved in yeast and metazoans - the chaperone network, the ubiquitin-proteasome system (UPS), and autophagy (Balchin et al., 2016; Harper and Bennett, 2016). Molecular

Received 22 January, 2019; revised 3 March, 2019; accepted 19 March, 2019; published online 10 April, 2019

eISSN: 0219-1032
© The Korean Society for Molecular and Cellular Biology. All rights reserved.
This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License. To view a copy of this license, visit http://creativecommons.org/licenses/by-nc-sa/3.0/.

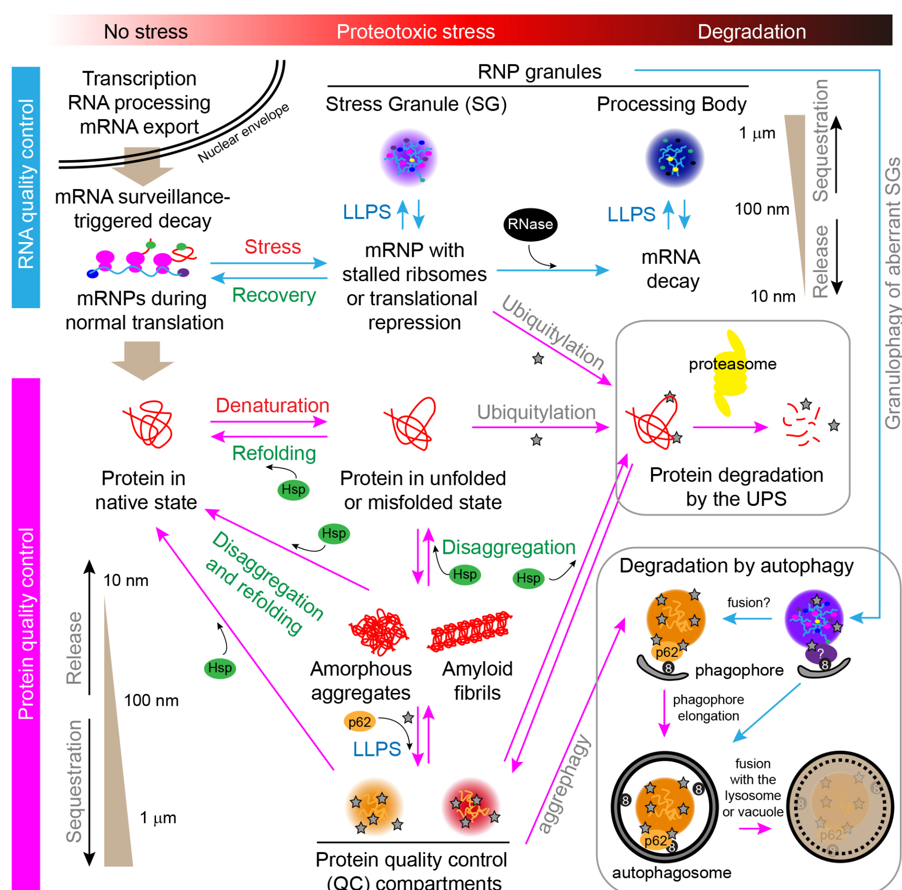

Fig. 1. Diagram of protein and RNA quality control (QC) systems in the cytoplasm. Although the information in the diagram is mostly derived from studies of yeast and mammals, QC systems are largely conserved in plants. After export from the nucleus, QC of messenger ribonucleoproteins (mRNPs) is associated with pioneering and subsequent translation cycles. Decay of mRNA is mostly carried out by cytosolic RNase activities, although bulk RNA degradation in the vacuole can be mediated by multiple types of autophagy. Protein QC systems consist of molecular chaperones (represented by green circles labeled in heat shock proteins [Hsp]), the ubiquitin-proteasome system (UPS), and autophagy. Both the UPS and autophagy (highlighted in two separate boxes) are degradation pathways for terminally misfolded proteins, which are tagged by ubiquitins (grey stars). Circles labeled "8" symbolize ATG8 attached to autophagic membrane. Light blue and magenta arrows indicate the flux of mRNP and proteins, respectively. The approximate size ranges of mRNP, RNP granules, protein aggregates, and protein QC compartments are logarithmically scaled. LLPS, liquid-liquid phase separation.

chaperones assist correct folding of nascent and misfolded proteins. When proteostasis is not maintained because of heat shock and other proteotoxic stresses, misfolded proteins build up and form various types of protein aggregates (Fig. 1). To avoid the potential toxicity of such aggregates, cells may sequester them in compartments specialized for protein QC, such as the aggresome in mammals (Sontag et al., 2017). The chaperone network releases individual polypeptides from protein aggregates and refolds them (Mogk et al., 2018). A portion of misfolded polypeptides is not repaired and can be tagged with ubiquitin for degradation by the UPS. Alternatively, QC compartments sequestering protein aggregates can be enclosed by the autophagosome, which fuses with the vacuole, or lysosome in metazoans, where its contents are degraded (Fig. 1).

Recent studies indicate that plant QC system for cytoplasmic proteins also consists of chaperone network (Wang et al., 2004), UPS, and autophagy (Kim et al., 2017; Shen et al., 2007; Zhou et al., 2014). This review will focus on the role of plant autophagy in the QC of defective proteins and RNPs that may form membrane-less compartments in the cytoplasm. We will consider a mechanism by which these structures are recognized and sequestered by autophagic vesicles. We will not discuss selective autophagy for membranous organelles in plants, as its roles in the QC of proteins targeted to the endoplasmic reticulum (ER)(Strasser, 2018), peroxisomes (Young and Bartel, 2016), plastids (Nakamura and Izumi, 2018; Otegui, 2018), and mitochondria (Broda et al., 2018) have been discussed in previous reviews.

SELECTIVE AUTOPHAGY OF PROTEIN AGGREGATES, RNP GRANULES, PROTEASOMES, AND RIBOSOMES

Autophagy is a membrane trafficking route by which cyto-

plasmic constituents are sequestered by the autophagosome and targeted to the vacuole or lysosome for bulk degradation. In yeast and higher eukaryotes, autophagy is mediated by a conserved set of core Autophagy-related (ATG) proteins (Marshall and Vierstra, 2018a). During starvation, nutrients recycled from autophagic degradation of cytoplasmic materials are important for survival. Starvation-induced autophagy typically sequesters a portion of the cytoplasm without selectivity, although the phagophore, the precursor of the autophagosome, does not seem to be initiated at a random location. Under a nutrient-sufficient condition, cells maintain a basal level of autophagy, enough to eliminate obsolete and defective components. This housekeeping function is often achieved by selective autophagy (Marshall and Vierstra, 2018a), in which the phagophore selectively sequesters its cargo. Generally, autophagic cargo interacts either with core ATG proteins (especially ATG8 covalently attached to autophagic membranes) or with autophagy receptors, which in turn bind to ATG8 (Marshall and Vierstra, 2018a). Cargo is often ubiquitylated and recognized by autophagy receptors that contain one or more domains with affinity for ubiquitin, in addition to the ATG8-interacting motif (AIM). In mammals, Atg8 and ubiquitylated cargo are connected by various autophagy receptors, including p62 and p62-related NBR1. Like many other autophagy receptors, p62 and NBR1 remain associated with cargo and ATG8 until they are finally degraded (Fig. 1). Many plant species have only one homolog for p62 and NBR1 (Svenning et al., 2011; Zientara-Rytter et al., 2011). *Arabidopsis* NBR1 also binds ubiquitin in vitro, interacts with ATG8, and is delivered to the vacuole via an autophagic trafficking pathway (Svenning et al., 2011).

Mammalian p62 and NBR1 mediate the selective autophagy of protein aggregates, termed aggrephagy (Danieli and Martens, 2018; Dikic, 2017). Aggrephagy in plant cells was described in tobacco cells expressing red fluorescent proteins fused to ER-localized proteins (Toyooka et al., 2006). The fusion proteins were mislocalized in the cytosol and detected as small puncta which were delivered to the vacuole via ATG8-positive autophagic vesicles (Toyooka et al., 2006). In heat-exposed *Arabidopsis* plants, mutations in either *NBR1* or core *ATG* genes resulted in the over-accumulation of ubiquitylated insoluble proteins (Zhou et al., 2013). Thus, NBR1 may have a role in aggrephagy during heat stress. Whether plant NBR1 mediates the formation of autophagosomes containing protein aggregates remains to be determined by microscopic analysis using aggregation-prone protein reporters.

RNP compartments are also degraded by selective autophagy. In yeast, SGs and processing bodies are delivered to the vacuole during autophagy, and autophagic clearance of yeast and mammalian SGs requires the AAA-ATPase CDC48/VCP (Buchan et al., 2013). It is unknown whether plant SGs and processing bodies are degraded by autophagy. Selective autophagy of cytoplasmic RNP granules, termed granulophagy, is evident during proteotoxic stress and appears to be linked to other components of the protein QC system (Fig. 1). In yeast, heat-inducible SGs behave like solid, reminiscent of protein aggregates, and chaperones promote SG disassembly. Mammalian SGs normally behave like liquid droplets, but mutations encoding misfolding-prone proteins can result in the formation of aberrant, solidified SGs that accumulate aggregated proteins called defective ribosomal products. The aberrant SGs are targeted to the aggresome and degraded by selective autophagy, although disaggregation and refolding of misfolded SG proteins by chaperones are preferred over autophagic clearance (Ganassi et al., 2016; Mateju et al., 2017).

Some polypeptides are assembled to form large protein complexes with a molecular mass of $>$ 1 MDa, such as ribosomes, spliceosomes, and proteasomes. Chaperones and specific UPS factors are needed when cells repair or selectively degrade defective components of protein complexes (Juszkiewicz and Hegde, 2018). Nevertheless, autophagic degradation of defective ribosomes and proteasomes en bloc can be advantageous. When cells undergo nutrient stress, not all ribosomes and proteasomes are needed and their excess can be recycled to supply amino acids and other breakdown products. In other cases, severe proteome imbalance and proteotoxic stress can result in the accumulation of defective ribosomes and proteasomes, which are toxic unless they are quickly eliminated by selective autophagy.

Selective autophagy of proteasomes, or proteaphagy, is mediated by various receptors, specifically, RPN10 in *Arabidopsis* (Marshall et al., 2015), Cue5 in yeast (Marshall et al., 2016), and p62 in mammals (Cohen-Kaplan et al., 2016). In both *Arabidopsis* and yeast, proteaphagy is activated upon nitrogen starvation and proteasome inhibition. When proteasome is inhibited, proteasome subunits are ubiquitylated and recognized by the proteaphagy receptors (Marshall et al., 2015; 2016). Like p62, Cue5 is also known as aggrephagy receptors (Lu et al., 2014). Hsp42, the oligomeric chaperone found in protein QC compartments in yeast, is required for the aggregation of defective proteasomes (Marshall et al., 2016). These findings imply that proteaphagy and aggrephagy have a common mechanism for cargo recognition. Interestingly, proteaphagy in *Arabidopsis* is not stimulated by carbon starvation, although carbon starvation still induces non-selective autophagy. In this case, functional proteasomes are sequestered in proteasome storage granules that presumably prevent them from becoming autophagic cargo (Marshall and Vierstra, 2018b). Based on this collection of observations, it is suggested that protein QC in plant cells requires compartmentalization and collaboration of chaperones, the UPS, and autophagic machinery.

Nitrogen starvation also induces selective autophagy of ribosomes, or ribophagy, in yeast (Kraft et al., 2008) and mammalian cells (Wyant et al., 2018). Yeast mutants defective in ribophagy had a high level of ubiquitylation of ribosomal proteins, suggesting a role of ubiquitylation in cargo selection during starvation-induced ribophagy (Kraft et al., 2008). Nuclear fragile X mental retardation-interacting protein 1 (NUFIP1) was identified as a mammalian ribophagy receptor that interacts with a mammalian homolog of ATG8 and with the 60S subunit of the ribosome (Wyant et al., 2018), although a ribosome-interacting motif has yet to be mapped in NUFIP1. In plants, the vacuolar ribonuclease RNS2 is responsible for rRNA degradation via constitutive

autophagy (Floyd et al., 2017; Hillwig et al., 2011). *rns2* mutants show defective recycling of rRNA and activate compensatory mechanisms, such as autophagy induction (Floyd et al., 2015) and metabolic change for nucleoside biosynthesis (Morriss et al., 2017). Although direct evidence for ribophagy in plants is lacking, it is notable that *Arabidopsis* NUFIP protein (Rodor et al., 2011) is predicted to have an AIM (http://repeat.biol.ucy.ac.cy/iLIR/).

POSSIBLE MECHANISMS FOR AUTOPHAGIC CARGO RECOGNITION

Two kinds of interactions regulate cargo selection: direct interaction with ATG8 or other core ATG proteins and indirect interactions with autophagy receptors. These interactions are often regulated not only by post-translational modification of interacting interfaces but also by receptor oligomerization.

A few plant autophagic cargo proteins appear to directly interact with ATG8 and other ATG proteins. For example, components of the ATG1 kinase complex in *Arabidopsis* (Li et al., 2014; Suttangkakul et al., 2011) that contain AIMs are degraded in the vacuole during starvation-induced autophagy. Another ATG8-interacting cargo is a virulence factor of *Cotton leaf curl Multan virus* (Haxim et al., 2017). The RNA-dependent RNA polymerase of *Turnip mosaic virus* is autophagic cargo that interacts with tobacco ATG6, one of the core ATG proteins in an autophagy regulatory complex (Li et al., 2018).

Ubiquitylation of cargo for aggrephagy and other types of selective autophagy in yeast and metazoans is common, although ubiquitylation-independent selection is possible (Grumati and Dikic, 2018). In *Arabidopsis*, proteasome subunits were ubiquitylated and degraded by proteaphagy during proteasome inhibition (Marshall et al., 2015). The proteaphagy receptor RPN10 interacts with ubiquitylated proteasome subunits through its ubiquitin-interacting motif. The mammalian proteaphagy receptor p62 also interacts with ubiquitylated proteasome subunits during amino acid starvation (Cohen-Kaplan et al., 2016). Although p62-related *Arabidopsis* NBR1 binds ubiquitin chains (Svenning et al., 2011), it is not required for proteaphagy in *Arabidopsis* (Marshall et al., 2015).

The transcription factor BRI1-EMS Suppressor 1 (BES1), involved in brassinosteroid signaling, was also identified as autophagic cargo that is ubiquitylated (Nolan et al., 2017). Ubiquitylated BES1 interacts with DSK2A, an autophagy adaptor containing a ubiquitin-like domain, two AIMs, and a ubiquitin-associated (UBA) domain. Cytoplasmic BES1 colocalizes with ATG8 and is degraded in the vacuole in a DSK2- and core ATG-dependent manner (Nolan et al., 2017). Eukaryotic DSK2 homologs are encoded by the single gene

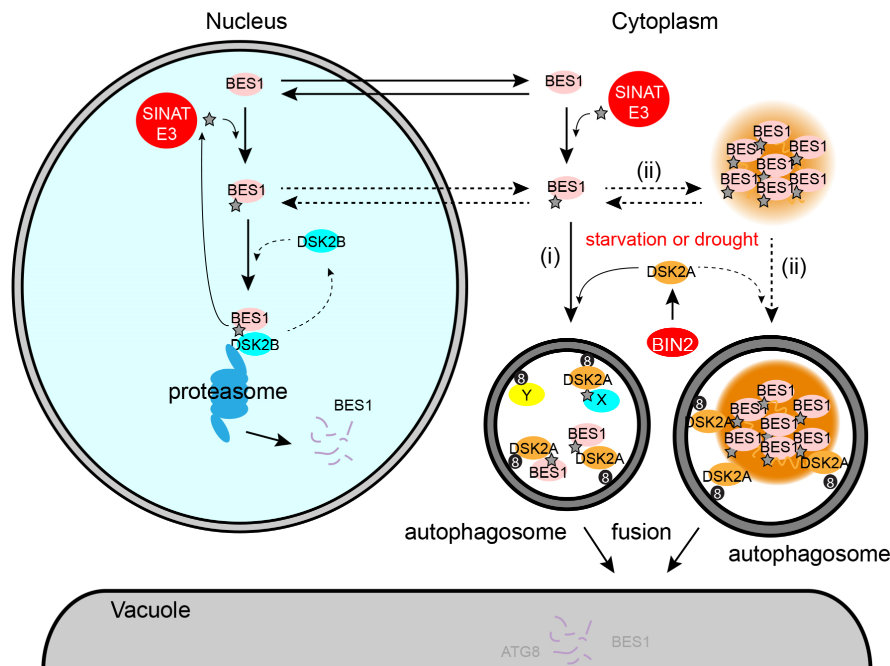

Fig. 2. A model for *Arabidopsis* DSK2 targeting BES1 for degradation. In this model, DSK2B is proposed to serve as a shuttle factor for proteasomal degradation of BES1 in the nucleus. During starvation or drought stress, the autophagy adaptor DSK2A targets ubiquitylated BES1 for vacuolar degradation. Starvation-induced autophagy typically shows little selectivity (i), whereas the possibility of selective autophagy cannot be excluded (ii). For example, ubquitylated BES1 may be concentrated in a cytoplasmic reservoir, which can be selectively delivered to the vacuole. Dashed arrows indicate hypothetical points in nuclear and cytoplasmic pathways, both of which use ubiquitins (grey stars) as a destruction signal. In the cytoplasm, DSK2A/B may mediate the degradation of BES1 by the proteasome (not shown).

Dsk2 in yeast, two genes (*DSK2A* and *DSK2B*) in *Arabidopsis*, and four genes (*Ubiquilin1* to *4*) in humans. Whereas Ubiquilin4 is involved in autophagy (Lee et al., 2013), yeast Dsk2 delivers ubiquitylated proteins to the proteasome (Zhang et al., 2009). Interestingly, Ubiquilin2 is required for the proteasomal degradation of ubiquitylated and misfolded proteins in the nucleus (Hjerpe et al., 2016; Samant et al., 2018). It is unclear whether *Arabidopsis* DSK2B plays a similar role in nuclear protein QC, but DSK2B interacts with RPN10, a proteasome subunit (Lin et al., 2011). Furthermore, bimolecular fluorescence complementation experiments indicated that DSK2B interacts with BES1 in a nucleus-like compartment, whereas DSK2A-BES1 interaction is detected as diffuse and punctate signals in the cytoplasm (Nolan et al., 2017). BES1 stabilization and brassinosteroid response phenotypes are more prominent in *DSK2A/B* double RNAi lines than in autophagy-defective mutants (Nolan et al., 2017). These data are consistent with our proposal that DSK2A and DSK2B function as selective autophagy adaptors and/or UPS shuttle factors (Fig. 2). *Arabidopsis* SINAT family proteins are E3 ligases that ubiquitylate BES1 for its light-dependent degradation (Yang et al., 2017). All five SINAT family proteins were localized in both the nucleus and cytoplasm (Yang et al., 2017), where SINAT-mediated ubiquitylation of BES1 likely takes place. What is the biological significance of autophagic degradation of excess BES1? Autophagy may downregulate the capacity of cytoplasmic BES1 reservoir, thereby preventing re-entry of BES1 into the nucleus and assisting in the termination of brassinosteroid signaling (Fig. 2).

Ubiquitylated proteins sequestered in mammalian QC compartments may be disaggregated and either refolded by chaperones or degraded by the proteasome. Alternatively, the whole QC compartments may be targeted to the vacuole via the autophagy pathway (Fig. 1). The relationship between ubiquitylation of proteasomal substrates and the ubiquitylation of aggrephagy cargo is not fully understood (Kwon and Ciechanover, 2017). However, increasing evidence indicates that ubiquitin-based selection of autophagic cargo can be achieved by multi-valent, weak interactions between polyubiquitin chains on the cargo surface and ubiquitin-binding domains of autophagy receptors. The interactions are enhanced by intermolecular interactions between autophagy receptors. Mammalian p62 self-oligomerizes and forms filamentous structures, which interact with ubiquitylated proteins. It has been proposed that these biochemical properties of p62 promote controlled protein aggregation. More recently, liquid-liquid phase separation (LLPS) has been proposed as a mechanism for concentrating autophagic cargo molecules (Danieli and Martens, 2018). LLPS is responsible for the formation of biomolecular condensates, which include several membrane-less compartments, specifically nucleoli, Cajal bodies, SGs, processing bodies, and protein QC compartments. These condensates rapidly exchange their constituents with surrounding environment and have liquid-like physical properties, analogous to oil droplets separating from surrounding water. Depending on changes in condensate composition and external variables (for example, ionic strength, pH, and temperature), liquid-like condensates can turn into gel-like compartments. Condensates that are p62-positive can grow in vitro to a few micrometers in size when ubiquitin chains are added (Sun et al., 2018; Zaffagnini et al., 2018). In p62 condensates, the p62 filament likely provides a scaffold to which ubiquitylated misfolded proteins can adhere (Danieli and Martens, 2018).

Although the composition of RNP granules such as SGs and processing bodies in plant cells is similar to those in yeast and metazoans (Chantarachot and Bailey-Serres, 2018), their properties as membrane-less condensates have yet to be tested (Cuevas-Velazquez and Dinneny, 2018). Protein QC compartments in plant cells and their relationship to RNP granules are not well understood, partly because amenable models of aggregate-forming proteins are scarce in plants. However, putative protein QC compartments in *Arabidopsis* were induced upon proteasome inhibition and co-localized with chaperones and proteasomes (Oh et al., 2017). It will be interesting to know more about the putative QC compartments, particularly: if they have the liquid-like properties of condensates, what the requirements for their assembly are, and if autophagy is involved in their clearance.

PERSPECTIVES

Important questions remain in the study of selective autophagy for protein QC. Where and how do phagophore nucleation and expansion occur during selective autophagy? What is the source of lipid for phagophore expansion? What is the mechanism for autophagic cargo selection favoring terminally misfolded aggregates that cannot be handled by chaperones and the proteasome?

We also have specific questions for the autophagy of plant QC compartments. What functions are shared by plant NBR1 and mammalian p62 and NBR1? Does DSK2A use a p62-like mechanism to mediate the autophagy of ubiquitylated BES1 and possibly other unknown cargo? Do plants have additional autophagy receptors for protein and RNA QC? A panel of protein QC substrates for plants will be useful to answer these questions.

It has been proposed that the sessile nature of plants demands a high capacity of plant QC systems to confront inevitable environmental stress. Better understanding of RNA and protein QC systems in plants will help plant biotechnologists improve stress tolerance of crops as well as increase yield in molecular farming, which often involves transgenic expression of unstable heterologous proteins.

ACKNOWLEDGMENTS

I apologize to colleagues whose work has not been mentioned because of space limitations. This work is supported by grants NRF-2017R1A2B4002335 to T.C.

REFERENCES

Balchin, D., Hayer-Hartl, M., and Hartl, F.U. (2016). *In vivo* aspects of protein folding and quality control. Science *353*, aac4354.

Broda, M., Millar, A.H., and Van Aken, O. (2018). Mitophagy: a mechanism for plant growth and survival. Trends Plant Sci. *23*, 434-450.

Buchan, J.R., Kolaitis, R.M., Taylor, J.P., and Parker, R. (2013).

Eukaryotic stress granules are cleared by autophagy and Cdc48/VCP function. Cell *153*, 1461-1474.

Chantarachot, T., and Bailey-Serres, J. (2018). Polysomes, stress granules, and processing bodies: a dynamic triumvirate controlling cytoplasmic mRNA fate and function. Plant Physiol. *176*, 254-269.

Cohen-Kaplan, V., Livneh, I., Avni, N., Fabre, B., Ziv, T., Kwon, Y.T., and Ciechanover, A. (2016). p62- and ubiquitin-dependent stress-induced autophagy of the mammalian 26S proteasome. Proc. Natl. Acad. Sci. USA *113*, E7490-E7499.

Cuevas-Velazquez, C.L., and Dinneny, J.R. (2018). Organization out of disorder: liquid-liquid phase separation in plants. Curr. Opin. Plant Biol. *45*, 68-74.

Danieli, A., and Martens, S. (2018). P62-mediated phase separation at the intersection of the ubiquitin-proteasome system and autophagy. J. Cell. Sci. *131*, 10.1242/jcs.214304.

Dikic, I. (2017). Proteasomal and autophagic degradation systems. Annu. Rev. Biochem. *86*, 193-224.

Floyd, B.E., Morriss, S.C., MacIntosh, G.C., and Bassham, D.C. (2015). Evidence for autophagy-dependent pathways of rRNA turnover in *Arabidopsis*. Autophagy *11*, 2199-2212.

Floyd, B.E., Mugume, Y., Morriss, S.C., MacIntosh, G.C., and Bassham, D.C. (2017). Localization of RNS2 ribonuclease to the vacuole is required for its role in cellular homeostasis. Planta *245*, 779-792.

Ganassi, M., Mateju, D., Bigi, I., Mediani, L., Poser, I., Lee, H.O., Seguin, S.J., Morelli, F.F., Vinet, J., Leo, G., et al. (2016). A surveillance function of the HSPB8-BAG3-HSP70 chaperone complex ensures stress granule integrity and dynamism. Mol. Cell *63*, 796-810.

Grumati, P., and Dikic, I. (2018). Ubiquitin signaling and autophagy. J. Biol. Chem. *293*, 5404-5413.

Harper, J.W., and Bennett, E.J. (2016). Proteome complexity and the forces that drive proteome imbalance. Nature *537*, 328-338.

Haxim, Y., Ismayil, A., Jia, Q., Wang, Y., Zheng, X., Chen, T., Qian, L., Liu, N., Wang, Y., Han, S., et al. (2017). Autophagy functions as an antiviral mechanism against geminiviruses in plants. Elife *6*, 10.7554/eLife.23897.

Hillwig, M.S., Contento, A.L., Meyer, A., Ebany, D., Bassham, D.C., and Macintosh, G.C. (2011). RNS2, a conserved member of the RNase T2 family, is necessary for ribosomal RNA decay in plants. Proc. Natl. Acad. Sci. USA *108*, 1093-1098.

Hjerpe, R., Bett, J.S., Keuss, M.J., Solovyova, A., McWilliams, T.G., Johnson, C., Sahu, I., Varghese, J., Wood, N., Wightman, M., et al. (2016). UBQLN2 mediates autophagy-independent protein aggregate clearance by the proteasome. Cell *166*, 935-949.

Juszkiewicz, S., and Hegde, R.S. (2018). Quality control of orphaned proteins. Mol. Cell *71*, 443-457.

Kim, J.H., Cho, S.K., Oh, T.R., Ryu, M.Y., Yang, S.W., and Kim, W.T. (2017). MPSR1 is a cytoplasmic PQC E3 ligase for eliminating emergent misfolded proteins in *Arabidopsis thaliana*. Proc. Natl. Acad. Sci. USA *114*, E10009-E10017.

Kraft, C., Deplazes, A., Sohrmann, M., and Peter, M. (2008). Mature ribosomes are selectively degraded upon starvation by an autophagy pathway requiring the Ubp3p/Bre5p ubiquitin protease. Nat. Cell Biol. *10*, 602-610.

Kwon, Y.T., and Ciechanover, A. (2017). The ubiquitin code in the ubiquitin-proteasome system and autophagy. Trends Biochem. Sci. *42*, 873-886.

Lee, D.Y., Arnott, D., and Brown, E.J. (2013). Ubiquilin4 is an adaptor protein that recruits ubiquilin1 to the autophagy machinery. EMBO Rep. *14*, 373-381.

Li, F., Chung, T., and and Vierstra, R.D. (2014). AUTOPHAGY-RELATED (ATG)11 plays a critical role in general autophagy and senescence-induced mitophagy in *Arabidopsis*. Plant Cell *26*, 788-807.

Li, F., Zhang, C., Li, Y., Wu, G., Hou, X., Zhou, X., and Wang, A. (2018). Beclin1 restricts RNA virus infection in plants through suppression and degradation of the viral polymerase. Nat. Commun. *9*, 1268-018-03658-2.

Lin, Y.L., Sung, S.C., Tsai, H.L., Yu, T.T., Radjacommare, R., Usharani, R., Fatimababy, A.S., Lin, H.Y., Wang, Y.Y., and Fu, H. (2011). The defective proteasome but not substrate recognition function is responsible for the null phenotypes of the *Arabidopsis* proteasome subunit RPN10. Plant Cell *23*, 2754-2773.

Lu, K., Psakhye, I., and Jentsch, S. (2014). Autophagic clearance of polyQ proteins mediated by ubiquitin-Atg8 adaptors of the conserved CUET protein family. Cell *158*, 549-563.

Marshall, R.S., Li, F., Gemperline, D.C., Book, A.J., and Vierstra, R.D. (2015). Autophagic degradation of the 26S proteasome is mediated by the dual ATG8/ubiquitin receptor RPN10 in *Arabidopsis*. Mol. Cell *58*, 1053-1066.

Marshall, R.S., McLoughlin, F., and Vierstra, R.D. (2016). Autophagic turnover of inactive 26S proteasomes in yeast is directed by the ubiquitin receptor Cue5 and the Hsp42 chaperone. Cell. Rep. *16*, 1717-1732.

Marshall, R.S., and Vierstra, R.D. (2018a). Autophagy: the master of bulk and selective recycling. Annu. Rev. Plant. Biol. *69*, 173-208.

Marshall, R.S., and Vierstra, R.D. (2018b). Proteasome storage granules protect proteasomes from autophagic degradation upon carbon starvation. Elife *7*, 10.7554/eLife.34532.

Mateju, D., Franzmann, T.M., Patel, A., Kopach, A., Boczek, E.E., Maharana, S., Lee, H.O., Carra, S., Hyman, A.A., and Alberti, S. (2017). An aberrant phase transition of stress granules triggered by misfolded protein and prevented by chaperone function. Embo J. *36*, 1669-1687.

Mogk, A., Bukau, B., and Kampinga, H.H. (2018). Cellular handling of protein aggregates by disaggregation machines. Mol. Cell *69*, 214-226.

Morriss, S.C., Liu, X., Floyd, B.E., Bassham, D.C., and MacIntosh, G.C. (2017). Cell growth and homeostasis are disrupted in *Arabidopsis* rns2-2 mutants missing the main vacuolar RNase activity. Ann. Bot. *120*, 911-922.

Nakamura, S., and Izumi, M. (2018). Regulation of chlorophagy during photoinhibition and senescence: lessons from mitophagy. Plant Cell Physiol. *59*, 1135-1143.

Nolan, T.M., Brennan, B., Yang, M., Chen, J., Zhang, M., Li, Z., Wang, X., Bassham, D.C., Walley, J., and Yin, Y. (2017). Selective autophagy of BES1 mediated by DSK2 balances plant growth and survival. Dev. Cell. *41*, 33-46.e7.

Oh, T.R., Kim, J.H., Cho, S.K., Ryu, M.Y., Yang, S.W., and Kim, W.T. (2017). AtAIRP2 E3 ligase Affects ABA and High-salinity responses by stimulating its ATP1/SDIRIP1 substrate turnover. Plant Physiol. *174*, 2515-2531.

Otegui, M.S. (2018). Vacuolar degradation of chloroplast components: autophagy and beyond. J. Exp. Bot. *69*, 741-750.

Rodor, J., Jobet, E., Bizarro, J., Vignols, F., Carles, C., Suzuki, T., Nakamura, K., and Echeverria, M. (2011). AtNUFIP, an essential protein for plant development, reveals the impact of snoRNA gene organisation on the assembly of snoRNPs and rRNA methylation in *Arabidopsis thaliana*. Plant J. *65*, 807-819.

Samant, R.S., Livingston, C.M., Sontag, E.M., and Frydman, J. (2018). Distinct proteostasis circuits cooperate in nuclear and cytoplasmic

protein quality control. Nature *563,* 407-411.

Shen, G., Adam, Z., and Zhang, H. (2007). The E3 ligase AtCHIP ubiquitylates FtsH1, a component of the chloroplast FtsH protease, and affects protein degradation in chloroplasts. Plant J. *52,* 309-321.

Sontag, E.M., Samant, R.S., and Frydman, J. (2017). Mechanisms and functions of spatial protein quality control. Annu. Rev. Biochem. *86,* 97-122.

Strasser, R. (2018). Protein quality control in the endoplasmic reticulum of plants. Annu. Rev. Plant. Biol. *69,* 147-172.

Sun, D., Wu, R., Zheng, J., Li, P., and Yu, L. (2018). Polyubiquitin chain-induced p62 phase separation drives autophagic cargo segregation. Cell Res. *28,* 405-415.

Suttangkakul, A., Li, F., Chung, T., and Vierstra, R.D. (2011). The ATG1/ATG13 protein kinase complex is both a regulator and a target of autophagic recycling in *Arabidopsis*. Plant Cell *23,* 3761-3779.

Svenning, S., Lamark, T., Krause, K., and Johansen, T. (2011). Plant NBR1 is a selective autophagy substrate and a functional hybrid of the mammalian autophagic adapters NBR1 and p62/SQSTM1. Autophagy *7,* 993-1010.

Toyooka, K., Moriyasu, Y., Goto, Y., Takeuchi, M., Fukuda, H., and Matsuoka, K. (2006). Protein aggregates are transported to vacuoles by a macroautophagic mechanism in nutrient-starved plant cells. Autophagy *2,* 96-106.

Wang, W., Vinocur, B., Shoseyov, O., and Altman, A. (2004). Role of plant heat-shock proteins and molecular chaperones in the abiotic stress response. Trends Plant Sci. *9,* 244-252.

Wyant, G.A., Abu-Remaileh, M., Frenkel, E.M., Laqtom, N.N., Dharamdasani, V., Lewis, C.A., Chan, S.H., Heinze, I., Ori, A., and Sabatini, D.M. (2018). NUFIP1 is a ribosome receptor for starvation-induced ribophagy. Science *360,* 751-758.

Yang, M., Li, C., Cai, Z., Hu, Y., Nolan, T., Yu, F., Yin, Y., Xie, Q., Tang, G., and Wang, X. (2017). SINAT E3 ligases control the light-mediated stability of the brassinosteroid-activated transcription factor BES1 in *Arabidopsis*. Dev. Cell. *41,* 47-58.e4.

Young, P.G., and Bartel, B. (2016). Pexophagy and peroxisomal protein turnover in plants. Biochim. Biophys. Acta *1863,* 999-1005.

Zaffagnini, G., Savova, A., Danieli, A., Romanov, J., Tremel, S., Ebner, M., Peterbauer, T., Sztacho, M., Trapannone, R., Tarafder, A.K., et al. (2018). P62 filaments capture and present ubiquitinated cargos for autophagy. Embo J. *37,* 10.15252/embj.201798308. Epub 2018 Jan 17.

Zhang, D., Chen, T., Ziv, I., Rosenzweig, R., Matiuhin, Y., Bronner, V., Glickman, M.H., and Fushman, D. (2009). Together, Rpn10 and Dsk2 can serve as a polyubiquitin chain-length sensor. Mol. Cell *36,* 1018-1033.

Zhou, J., Wang, J., Cheng, Y., Chi, Y.J., Fan, B., Yu, J.Q., and Chen, Z. (2013). NBR1-mediated selective autophagy targets insoluble ubiquitinated protein aggregates in plant stress responses. PLoS Genet. *9,* e1003196.

Zhou, J., Zhang, Y., Qi, J., Chi, Y., Fan, B., Yu, J.Q., and Chen, Z. (2014). E3 ubiquitin ligase CHIP and NBR1-mediated selective autophagy protect additively against proteotoxicity in plant stress responses. PLoS Genet. *10,* e1004116.

Zientara-Rytter, K., Lukomska, J., Moniuszko, G., Gwozdecki, R., Surowiecki, P., Lewandowska, M., Liszewska, F., Wawrzynska, A., and Sirko, A. (2011). Identification and functional analysis of Joka2, a tobacco member of the family of selective autophagy cargo receptors. Autophagy *7,* 1145-1158.