PLANT SIGNALING & BEHAVIOR
2019, VOL. 14, NO. 7, e1607465 (3 pages)
https://doi.org/10.1080/15592324.2019.1607465

Taylor & Francis
Taylor & Francis Group

REVIEW

Glucose signaling, AtRGS1 and plant autophagy

Yue Jiao, Wenxue Lei, Wan Xu, and Wen-Li Chen

Ministry of Education Key Laboratory of Laser Life Science and Institute of Laser Life Science, College of Biophotonics, South China Normal University, Guangzhou, China

ABSTRACT
Glucose is an important building component in organisms and a central molecule of energy metabolism. It is also a key signaling molecule involved in regulation of many physiologic processes, including organism morphogenesis, anabolism and catabolism, pest and disease stress, environmental stress response. The signal transduction pathway mediated by heterotrimeric G proteins is one of the most important pathways for *Arabidopsis* to recognize, perceive and transduce external stimuli. AtRGS1 (*Arabidopsis thaliana* regulator of G-protein signaling) metabolism is currently thought to be through endosome.This paper introduces relationship between autophagy and RGS1.

ARTICLE HISTORY
Received 21 February 2019
Revised 5 April 2019
Accepted 9 April 2019

KEYWORDS
AtRGS1; autophagy; glucose signaling; G protein; endocytosis; D-glucose

Research progress on autophagy in plants

Autophagy is a procession of orderly degradation and recycling of cellular component, which relies on lysosomes and vacuoles and is highly conserved in eukaryotes. In plant and yeast cells, intracellular materials are entrapped in autophagic vesicles of the bilayer membrane when autophagy occurs, and transported into vacuoles for degradation, resulting in new small molecules for reuse. Over the years, scientists have discovered that autophagy in plants is involved in nutritional hunger, stress, leaf senescence, plant immunity, and coping with environmental stress.[12] In the plant immune system, selective autophagy acts as receptors to mediate degradation of FLAGELLIN-SENSING 2 (FLS2). In *Arabidopsis* plants, overexpression of orosomucoid 1 (ORM1) or ORM2 is undetectable and lack of FLS2 signaling, so that the plants are susceptible to the bacterial pathogen Pseudo Smonas syringae. Yang et al.'s result showed that ORM is a selective autophagy receptor and FLS2 is degraded by autophagy, suggesting that selective autophagy plays a key role in plant immunity.[3] Recent research revealed that Autophagy-related gene MdATG18a plays a key role in plant nutrient deficiencies, drought, pathogens and other stresses. When plants are stressed by pathogens, a large increase in the expression of MdATG18a causes decrease of plant's own active oxygen levels and rise of the SA level, thereby increasing plant resistance.[4,5] Cellular senescence is present in plants, but autophagy plays a key role in cell aging that is a delicate regulation process. Autophagy counteracts the death of transient cells and also participates in degradation of cellular components.[6] Our research indicates that *ATG7*, *NPR3* and *NPR4* are active regulators of plant defense system and aging, while *NPR1* has the opposite function. In addition, *NPR3* and *NPR4* regulate autophagy activity through two ubiquitin-like pathways, which in turn affect the formation of autophagic vacuoles and the degradation of autophagosomes in vacuoles.[7] We found that NPR1 participates in the autophagy metabolic pathway when plants are infected by pathogens (result to be published).

The target of rapamycin (TOR) signaling pathway is a key pathway in cell growth and survival.[8] Studies have shown that TOR enhances insulin sensitivity and reduces hyperinsulinemia in mice having low insulin levels in the pancreas, thus suggesting that the TOR treatment may cause both beneficial and harmful effects dependent insulin level of the pancreas.[9] In plants, TOR protein kinases are able to accept and transmit glucose (15 mM) metabolic signals to promote plant growth. Xiong et al. found that TOR kinase in plants controls genomic expression and activates cell division of apical meristems by positively regulating the transcription factor E2Fa to promote rapid growth of plants.[10] We discovered that the number of autophagysomes in *Arabidopsis* is increased in the presence of glucose.[11] Under 3% glucose treatment, *rgs1* mutants has less autophagisomes and low autophagic flux, indicating that RGS1 promotes the production of autophagosomes (result to be published). However, it is unclear whether AtRGS1 is involved in the initiation and maturation of autophagic membranes under glucose treatment.

Relationship between glucose signaling pathway and autophagy

Sugars are energy and signal substances that play an important role in plant growth and development. Although a variety of sugar signaling pathways plays an important regulatory role in plants from embryonic to senescent death, glucose is the oldest and most conserved regulatory signal that controls gene and protein expression, and nascent and secondary cell cycles. In recent years, studies on the metabolism of glucose, as well

CONTACT Wenli Chen: chenwl@scnu.edu.cn Ministry of Education Key Laboratory of Laser Life Science and Institute of Laser Life Science, College of Biophotonics, South China Normal University, Guangzhou, 510631, China

as the growth and developmental processes of plants, have made great progress on the glucose signal transduction pathway.[12,13] Existing studies have shown that there are mainly three glucose signal transduction pathways in *Arabidopsis*: HEXOKINASE1 (HXK1) glucose signal transduction pathway.[14-18] AtRGS1 related G-protein-coupled glucose signal transduction pathway.[17,19-22] and SUCROSENON-FERMENT-ING1(SNF1)-RELATED KINASE 1/TARGET OF RAPAMYCIN (SnRK1/TOR) pathway that relies on glycolysis.[10,16,23,24] The availability of sugar and the coordination of plant hormone signals are critical for plant growth and development. Recent research indicates that BRI1 (BRASSINOSTEROID INSENSITIVE 1) and BAK1 (BRI1-associated kinase 1) are involved in sugar reactive growth and development. Glucose affects the interaction and phosphorylation of BRI1 and BAK1 in a concentration-dependent manner. BRI1 and BAK1 interact with G proteins and are required for mediating sugar signaling. Biochemical data show that BRI1 phosphorylates G-protein β and γ subunits, and BAK1 phosphorylates G-protein γ subunit. Genetic analysis indicates, and thus BRI1 and BAK1 commonly regulate glycose response via the G-protein subunit, providing a meaningful genetic molecular mechanism for glucose signaling in plants.[25] Studies have shown that AtRGS1 is an important receptor for plant sugar signaling, with high sensitivity to glucose, but poor sensitivity to fructose and sucrose.[17] Endocytosis of AtRGS1 is essential in glucose stress.[26] Its mechanism and pathway is currently not reported in literature. The autophagy pathway plays a very important role in living organisms. We found that our results indicate that AtRGS1 promotes the formation of autophagosomes by regulating the activity of five complexes involved in autophagy, the recovery of AtRGS1 is promoted and endocytosis is inhibited, and AtRGS1 is mainly clustered near the cell membrane, AtRGS1 recovery and endocytosis, autophagy pathways involved in AtRGS1 regulated signaling pathways.[11] Whether selective autophagy is involved in the metabolic regulation of RGS1 remains to be further studied.

Relationship between RGS1 and autophagy

G protein is widely distributed in eukaryotes, binds to guanine nucleotides, has enzymatic activity, and is a class of proteins that act as transducers or molecular switches in cell signaling pathways. G proteins are mainly classified into three groups of a low-molecular-weight small monomer protein, a high-molecular-weight super large protein, and a trimeric protein coupled to a membrane receptor. The heterotrimeric G-protein complex consists of one canonical Gα subunit (GPA1), one Gβ subunit (AGB1), and three Gγ subunits. G-protein-mediated cell signaling is one of the most conserved signal transduction pathways in eukaryotic cell.[27] In animal cells, when G-protein-coupled receptors on the plasma membrane bind to their specific ligands, their conformation will change, and then a series of signal transduction processes will occur, eventually triggering expression of related intracellular genes and physiological/biochemical responses. Modulation of both active and inactive forms of Gα protein is critical for heterotrimeric G-protein complex-mediated signaling processes. Studies have shown that the lipolytic enzyme phospholipase Da1 (PLDa1), a G-protein signaling (RGS1) protein modulator in *Arabidopsis*, acts as G-protein activity accelerating proteins (GAPs) for Gα protein to attenuate its activity. RGS1 and PLDa1 interact with each other, and RGS1 inhibits the activity of PLDa1 during regulation of responses. Phosphatidic acid (PA) is a second messenger that is normally derived from the lipid hydrolyzing activity of PLDa1 and is a molecular target of RGS1, PA binds and inhibits GAP activity of RGS1.[28]

In yeast and animal cells, RGS and GPCR are two proteins with opposite functions in *Arabidopsis*. The N-terminus of RGS1 is a GPCR-like 7-transmembrane domain, and its C-terminal is an RGS domain. Some researchers believe that AtRGS1 is recycled between the plasma membrane and endocytosis, and is possibly a sugar-activated G-protein regulator. It has been found that degradation of Notch 1 (a human gene encoding a single-pass transmembrane receptor) is regulated by autophagy in addition to its traditional endocytic pathway.[29] The mechanism and pathway of AtRGS1 migration into cells has not been reported in the literature. The autophagy pathway plays a very important role in living organisms and participates in a variety of life activities. Our recent findings show that glucose induces autophagy, the production of autophagosomes and also the expression of autophagy-related genes. Real-time Quantitative PCR Detecting System (qPCR) results show that Autophagy-related genes ATG4 and ATG12a are involved in the degradation of RGS1.[11] Our study found that changes in autophagic flux were negatively correlated with RGS1, RGS1-YFP is enveloped by the tonoplast, and autophagosomes have a certain degree of overlap with RGS1 and its truncations. These results indicate that there is a very close relationship between autophagy and RGS1 (result to be published).

Perspective

Autophagy plays an important role in the endocytosis of RGS1 and GPA1 plays a key role in mediation. However, many questions, such as whether the NBR1 selective autophagy receptor is involved in this process and if the RGS1 fragment is involved in the formation of autophagosome membrane, remains unknown. We first proposed that autophagy plays an important role in the endocytosis of RGS1. Our results demonstrate that glucose-induced RGS1 endocytosis is the process of resolution and assembly of RGS1 fragments, GPA1 plays a key role in mediating, and autophagy-related genes are involved in this process. It was found that the RGS1 fragment interacts with the marker gene ATG8a of the autophagosome (result to be published). It is of great significance to further elucidate the mechanism of glucose-mediated RGS1 and autophagy signaling system in plants, in order to improve the plant ability to obtain nutrients growth and enhance plant photosynthetic function.

Acknowledgments

We would like to thank all participants of this study and acknowledge invaluable support of professor Hengming Ke, UNC-Chapel Hill School of Medicine of USA, for proofreading of the manuscript.

Disclosure statement

No potential conflicts of interest were disclosed.

Funding

This work was supported by the National Natural Science Foundation of China [grant number 31570256], [grant number 31170250] and grant from the science and technology project of Guangzhou [grant number 201805010002].

ORCID

Yue Jiao http://orcid.org/0000-0002-1133-9769
Wen-Li Chen http://orcid.org/0000-0002-4768-3844

References

1. Safavi-Rizi V, Franzaring J, Fangmeier A, Kunze R. Divergent N deficiency-dependent senescence and transcriptome response in developmentally old and YoungBrassica napusLeaves:[J]. Front Plant Sci. 2018;9:48.
2. Hafrén A, Hofius D. NBR1-mediated antiviral xenophagy in plant immunity[J]. Autophagy. 2017;13(11):1. doi:10.1080/15548627.2017.1339005.
3. Yang F, Kimberlin AN, Elowsky CG, Liu Y, Gonzalez-Solis A, Cahoon EB, Alfano JR. A plant immune receptor degraded by selective autophagy. Mol Plant. 2019;12(1):113–123. doi:10.1016/j.molp.2018.11.011.
4. Sun X, Wang P, Jia X, Huo L, Che R, Ma F. Improvement of drought tolerance by overexpressing MdATG18a is mediated by modified antioxidant system and activated autophagy in transgenic apple. Plant Biotechnol J. 2018;16:545–557. doi:10.1111/pbi.2018.16.issue-2.
5. Sun X, Huo L, Jia X, Che R, Gong X, Wang P, Ma F. Overexpression of MdATG18a in apple improves resistance to Diplocarpon mali infection by enhancing antioxidant activity and salicylic acid levels[J]. Hortic Res. 2018;5(1). doi:10.1038/s41438-018-0059-5.
6. Wojciechowska N, Marzec-Schmidt K, Kalemba EM, Zarzyńska-Nowak A, Jagodziński AM, Bagniewska-Zadworna A. Autophagy counteracts instantaneous cell death during seasonal senescence of the fine roots and leaves in Populus trichocarpa[J]. BMC Plant Biol. 2018;18(1):260. doi:10.1186/s12870-018-1439-6.
7. Wang X, Gao Y, Yan Q, Chen W. Salicylic acid promotes autophagy via NPR3 and NPR4 in Arabidopsis senescence and innate immune response[J]. Acta Physiologiae Plantarum. 2016;38(10):241. doi:10.1007/s11738-016-2257-9.
8. Dobrenel T, Manceramartínez E, Forzani C, Azzopardi M, Davanture M, Moreau M, Schepetilnikov M, Chicher J, Langella O, Zivy M, et al. The Arabidopsis TOR kinase specifically regulates the expression of nuclear genes coding for plastidic ribosomal proteins and the phosphorylation of the cytosolic ribosomal protein S6:[J]. Front Plant Sci. 2016;7(e70692). doi:10.3389/fpls.2016.01611.
9. Zhuo M, Weizhen Z. Role of mTOR in glucose and lipid metabolism[J]. Int J Mol Sci. 2018;19(7):2043. doi:10.3390/ijms19072043.
10. Xiong Y, McCormack M, Li L, Hall Q, Xiang C, Sheen J. Glc-TOR signalling leads transcriptome reprogramming and meristem activation[J]. Nature. 2013;496(7444):181. doi:10.1038/nature12030.
11. Yan Q, Wang J, Fu ZQ, Chen W. Endocytosis of AtRGS1 is regulated by the autophagy pathway after D-glucose stimulation [J]. Front Plant Sci. 2017;8:1229. doi:10.3389/fpls.2017.01229.
12. Sheen J. Master regulators in plant glucose signaling networks [J]. J Plant Biol. 2014;57(2):67–79. doi:10.1007/s12374-014-0902-7.
13. Ishikawa Y, Miyagi A, Ishikawa T, Nagano M, Yamaguchi M, Hihara Y, Kawai-Yamada M. One of the NAD kinases, sll1415, is required for the glucose metabolism of Synechocystis sp. PCC 6803. Plant J. 2019. doi:10.1111/tpj.14262.
14. Moore B, Zhou L, Rolland F, Hall Q, Cheng W-H, Liu Y-X, Hwang I, Jones T, Sheen J. Role of the Arabidopsis glucose sensor HXK1 in nutrient, light, and hormonal signaling [J]. Science. 2003;300(5617):332–336. doi:10.1126/science.1080585.
15. Jang JC, Leon P, Zhou L, Sheen J. Hexokinase as a sugar sensor in higher plants [J]. Plant Cell. 1997;9(1):5–19. doi:10.1105/tpc.9.1.5.
16. Xiao W, Sheen J, Jang JC. The role of hexokinase in plant sugar signal transduction and growth and development [J]. Plant Mol Biol. 2000;44:451–461.
17. Chen JG, Jones AM. AtRGS1 function in Arabidopsis thaliana [J]. Methods Enzymol. 2004;389:338–350. doi:10.1016/S0076-6879(04)89020-7.
18. Cho YH, Yoo SD, Sheen J. Regulatory functions of nuclear hexokinase-1 complex in glucose signaling [J]. Cell. 2006;127(3):579–589. doi:10.1016/j.cell.2006.09.028.
19. Chen JG, Francis SW, Jirong H. A seven-transmembrane RGS protein that modulates plant cell proliferation. Science. 2003;301(5640):1728–1731. doi:10.1126/science.1087790.
20. Grigston JC, Osuna D, Scheible WR, Liu C, Stitt M, Jones AM. D-glucose sensing by a plasma membrane regulator of G signaling protein, AtRGS1 [J]. FEBS Lett. 2008;582(25–26):3577–3584. doi:10.1016/j.febslet.2008.08.038.
21. Matsuura E, Ishiguro N, Katsumata Y, Urano W, Yamanaka H, Kondo M, Kuwana M, Kaji K, Hamaguchi Y, Fujimoto M, et al. Two young-adult female cases of dermatomyositis with antibodies for transcriptional intermediary factor 1-gamma [J]. Eur J Dermatol. 2012;22(5):668–671. doi:10.1684/ejd.2012.1824.
22. Gambarini G, Carrara M, Tenconi C, Mantaut N, Borroni M, Cutajar D, Petasecca M, Fuduli I, Lerch M, Pignoli E, et al. Online in vivo dosimetry in high dose rate prostate brchytherapy with MOSkin detectors: in phantom feasibility study [J]. Appl Radiat Isot. 2014;83(Pt):C: 222–226. doi:10.1016/j.apradiso.2013.06.001.
23. Lastdrager J, Hanson J, Smeekens S. Sugar signals and the control of plant growth and development[J]. J Exp Bot. 2014;65(3):799–807. doi:10.1093/jxb/ert474.
24. Baena-Gonzalez E, Rolland F, Thevelein JM, Sheen J. A central integrator of transcription networks in plant stress and energy signalling [J]. Nature. 2007;448(7156):938–942. doi:10.1038/nature06069.
25. Peng Y, Chen L, Li S, Zhang Y, Xu R, Liu Z, Liu W, Kong J, Huang X, Wang Y, et al. BRI1 and BAK1 interact with G proteins and regulate sugar-responsive growth and development in Arabidopsis [J]. Nat Commun. 2018;9(1):1522. doi:10.1038/s41467-018-03884-8.
26. Urano D, Phan N, Jones JC, Yang J, Huang J, Grigston J, Taylor JP, Jones AM. Endocytosis of the seven-transmembrane RGS1 protein activates G-protein-coupled signalling in Arabidopsis [J]. Nat Cell Biol. 2012;14(10):1079–1088. doi:10.1038/ncb2568.
27. Kose HB. Structural studies on the A. Thaliana heterotrimeric G-protein: understanding the mechanism of α subunit [J]. Biophys J. 2014;106(2):50a–51a. doi:10.1016/j.bpj.2013.11.361.
28. Roy Choudhury S, Pandey S. Phosphatidic acid binding inhibits RGS1 activity to affect specific signaling pathways in Arabidopsis[J]. Plant J Cell Mol Biol. 2017;90(3):466. doi:10.1111/tpj.13503.
29. Wu X, Fleming A, Ricketts T, Pavel M, Virgin H, Menzies FM, Rubinsztein DC. Autophagy regulates Notch degradation and modulates stem cell development and neurogenesis. Nat Commun. 2016;7:10533. doi:10.1038/ncomms10533.