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## VIEWPOINT

## Sugars, senescence, and ageing in plants and heterotrophic organisms

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### Abstract

**Although an involvement of metabolic signals in the regulation of plant senescence has been demonstrated in a range of studies, the exact signalling pathways remain largely unresolved. For leaves, evidence supports a role of sugar accumulation in the initiation and/or acceleration of senescence. However, regulation of senescence or ageing may respond to different metabolic signals in heterotrophic plant organs and heterotrophic organisms. In animals and yeast, dietary restriction results in increased lifespan. In this article, the metabolic regulation of leaf senescence is compared with the effects of dietary restriction. Similarities and differences in the signalling pathways are discussed, including the role of autophagy, TOR (target of rapamycin), Sir2 (silent information regulator-2), and SnRK1 (sucrose non-fermenting-1-related protein kinase-1).**

### Evidence for an involvement of sugars in the regulation of leaf senescence

Leaf senescence is a plastic process that can be triggered by a variety of external and internal factors (Buchanan-Wollaston *et al.*, 2003). Senescence reduces photosynthetic carbon fixation, but is important for the recycling of nitrogen and other nutrients, for example, resulting in increased grain protein (Uauy *et al.*, 2006). Due to its position at the crossroads of carbon and nitrogen metabo-

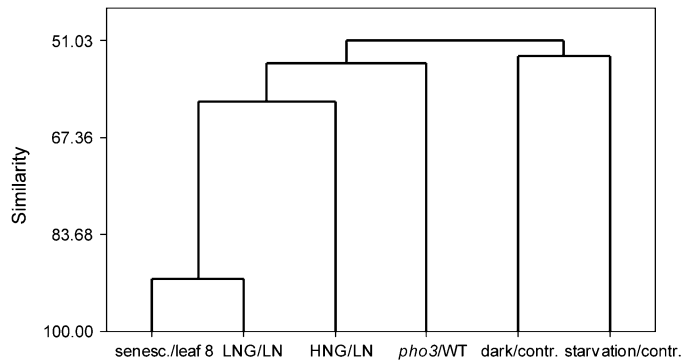
lism, senescence is regulated by carbon and nitrogen signals. Increasing evidence suggests a role for hexose accumulation in ageing leaves as a signal for either senescence initiation or acceleration in annual plants (Masclaux *et al.*, 2000; Moore *et al.*, 2003; Masclaux-Daubresse *et al.*, 2005; Parrott *et al.*, 2005, 2007; Pourtau *et al.*, 2006; Wingler and Roitsch, 2008).

Recently, the role of sugar accumulation or starvation in leaf senescence has been critically evaluated by van Doorn (2008). This author has pointed out that little is known about sugar concentrations and senescence regulation in different tissues and cells. While we agree with the view that sugars may not always be the direct cause of leaf senescence, sufficient evidence supports the notion that sugar signalling plays a role in senescence regulation in a complex network with a variety of other signals, for example, resulting from biotic or abiotic stress (Wingler and Roitsch, 2008).

In addition to sugar accumulation, dark treatment induces leaf yellowing. This treatment can result in starvation, but is also likely to signal via light signalling pathways. It is not surprising that expression of genes involved in downstream processes, such as proteolysis, overlap between senescence initiated by different treatments that result in sugar accumulation or starvation. The senescence-specific cysteine protease gene *SAG12* has been shown to be induced (Pourtau *et al.*, 2006; Parrott *et al.*, 2007) or repressed (Noh and Amasino, 1999) by sugars during senescence, but the behaviour of single genes, which may respond after senescence has been initiated, cannot necessarily tell us whether senescence is sugar- or starvation-induced. Comparison of overall changes of the transcriptome (Buchanan-Wollaston, 2005; Wingler and Roitsch, 2008) is a better way of testing whether senescence is regulated by starvation, darkness or sugar accumulation.

To compare different treatments, microarray results for experiments using the *Arabidopsis* Affymetrix ATH1 array were clustered (Fig. 1). Global changes in response to glucose treatment (Pourtau *et al.*, 2006) clustered closely with changes during developmental leaf senescence (Schmid *et al.*, 2005) when glucose was supplied to intact plants in combination with low nitrogen supply, but less closely in combination with high nitrogen supply, a treatment that does not induce visible senescence. Accumulation of sugars due to a mutation in the *SUC2* sucrose transporter gene (*pho3* mutant; Lloyd and Zakhleniuk, 2004) clustered with the experiments in which glucose was supplied externally. Interestingly, gene expression changes during dark-induced senescence (Lin and Wu, 2004) did not cluster with developmental senescence, but with the effect of starvation in

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**Fig. 1.** Clustering of Affymetrix ATH1 data for different treatments. Signal ratios between treatments calculated for all array elements were clustered using the average linkage method and the correlation coefficient distance measure. ‘senesc./leaf 8’, Ratio between senescent leaves and leaf 8 (Schmid *et al.*, 2005); ‘LNG/LN’, ratio between growth on low nitrogen medium plus glucose and low nitrogen medium without sugar (Pourtau *et al.*, 2006); ‘HNG/LN’, ratio between growth on high nitrogen medium plus glucose and low nitrogen medium without sugar (Pourtau *et al.*, 2006); ‘*pho3*/WT’, ratio between the sugar-accumulating *pho3* mutant and wild type (Lloyd and Zakhleniuk, 2004); ‘dark/contr.’, ratio between plants kept in the dark for 5 d and controls grown under 8 h days (Lin and Wu, 2004); ‘starvation/contr.’, ratio between cell cultures starved of sucrose for 48 h and controls before starvation (Contento *et al.*, 2004).

cell cultures (Contento *et al.*, 2004). This supports the view that high sugar/low nitrogen conditions and not starvation and/or dark trigger changes in gene expression that are characteristic of developmental leaf senescence.

Changes in gene expression induced by steam girdling of barley leaves (Parrott *et al.*, 2007), which results in internal sugar accumulation, demonstrate that this regulation is not restricted to *Arabidopsis* leaves. However, in contrast to leaves, senescence or senescence-like symptoms (including enhanced proteolysis) are delayed by sugar feeding in isolated heterotrophic plant tissues such as root tips (James *et al.*, 1993), suggesting that different signalling responses are triggered by the carbohydrate status of auto- and heterotrophic plant tissues. To understand such differences fully, a systematic comparison of the transcriptomic responses of plant cell cultures, dark-incubated leaves and different types of heterotrophic tissues to carbohydrate status would be beneficial.

#### *The role of autophagy in the metabolic regulation of leaf senescence*

Autophagy is an evolutionarily conserved process contributing to the degradation of macromolecules in animals, yeasts, and plants. In animals and yeasts, autophagy is a regulated process for the removal of damaged proteins and organelles. In plants, autophagy has been shown to occur during sucrose starvation, nitrogen deficiency, and senescence (Bassham *et al.*, 2006). Recently, it has been

demonstrated that autophagy is required for the senescence-dependent degradation of Rubisco (Ishida *et al.*, 2008). Mutations in autophagy genes can, however, result in accelerated rather than delayed senescence (Thompson *et al.*, 2005), suggesting that autophagy is essential for nutrient remobilization before the onset of visible senescence and, possibly, for waste removal as in animals. While autophagy is generally considered to be induced by sugar starvation, statistical analysis using MapMan (Usadel *et al.*, 2005) to identify gene ontologies that respond differently to a treatment than the remaining genes on the array indicates that expression of autophagy genes is not only induced by senescence, dark treatment, and starvation, but also by treatment with glucose in the presence of low nitrogen (see Supplementary Table S1 at *JXB* online). By contrast, glucose does not induce autophagy genes in the presence of high nitrogen supply. Together with the observation that mutants in autophagy genes are hypersensitive to nitrogen deficiency as well as carbon starvation (Thompson *et al.*, 2005), this indicates that the carbon/nitrogen balance may play an important role in the induction of autophagy. Although autophagy was induced in all treatments resulting in senescence, which autophagy genes were induced varied between the different treatments (see Supplementary Table S2 at *JXB* online).

Another interesting link between carbon availability, senescence, and autophagy has recently been established by Baena-González *et al.* (2007). This work has demonstrated that the protein kinase SnRK1 (sucrose non-fermenting-1-related protein kinase-1) is involved in the signalling response to carbon depletion. Overexpression of *KIN10*, encoding the catalytic subunit of SnRK1, increased the expression of normally sugar-repressed genes involved in catabolic pathways and also led to the induction of autophagy genes. Interestingly, *KIN10*-overexpressing plants showed delayed flowering and senescence. This is consistent with the view that increased carbon availability and not starvation is involved in the initiation of senescence.

#### *Parallels between the metabolic regulation of leaf senescence and the effect of dietary restriction on ageing in heterotrophic organisms*

Parallels can be drawn between the metabolic regulation of leaf senescence and the extension of life span by dietary restriction in heterotrophic organisms. While leaf senescence can be monitored as a decline in chlorophyll or photosynthetic function, ageing in heterotrophic organisms is usually a demographic measure, i.e. based on the change in the fraction of individuals alive over time. Although it is more difficult to determine the exact time at which a leaf is dead, senescence usually results in the death of a leaf and can also be monitored as leaf longevity.

Dietary restriction, for example, by dilution of growth media or reduced availability of food, has been shown to extend life span in a large range of organisms, including yeasts, invertebrates, and mammals (reviewed by Mair and

Dillin, 2008). Some of the regulatory pathways may be conserved between plants and heterotrophic organisms. For example, SnRK1 is related to Snf1 (sucrose non-fermenting-1) in yeast and AMPK (AMP-activated protein kinase) in animals. In addition to the plant SnRK1 (Baena-González *et al.*, 2007), Snf1 (Bitterman *et al.*, 2003) and AMPK (Mair and Dillin, 2008) have been linked to extended life span and dietary restriction.

When energy supply is low, AMPK inhibits processes, such as protein synthesis, by the inhibition of TOR (target of rapamycin). Reduced TOR signalling can result in increased life span (Mair and Dillin, 2008). This suggests a complicated web of interactions between proteins involved in co-ordinating energy status, sugar content, nitrogen availability, cell fate, and longevity. However, the existence of a similar web of interaction remains to be demonstrated in plants (Baena-González and Sheen, 2008). Conditional silencing of the *Arabidopsis* TOR kinase induced early leaf yellowing, chlorophyll degradation, and accumulation of high soluble sugar concentrations. In the same plants, the activity of enzyme markers for nitrogen remobilization was increased, indicating that, in plants, TOR is needed to restrain senescence and nutrient recycling (Deprost *et al.*, 2007).

In addition to the proposed function of reduced TOR signalling in extended life span in response to dietary restriction, it is now well known that, in animals and yeasts, decreased nutrient availability can stimulate autophagy in part by the inhibition of TOR signalling (Finkel *et al.*, 2007). In *Caenorhabditis elegans*, RNAi inhibition of autophagy genes, in turn, prevented the extension of life span by TOR inhibition or dietary restriction (Hansen *et al.*, 2008). However, the role of autophagy in animals is complex in the sense that it constitutes a stress adaptation that avoids cell death and suppresses apoptosis, whereas, in other circumstances, it constitutes an alternative cell-death pathway (Maiuri *et al.*, 2007). A parallel can be seen in plants, where, despite the role of autophagy in senescence, mutants in autophagy show accelerated senescence and cell death (Thompson *et al.*, 2005). Further characterization of *Arabidopsis* mutants in autophagy genes could shed more light on the interaction between carbon supply, TOR signalling, and leaf longevity in plants.

Another possible parallel between the regulation of leaf senescence and the effect of dietary restriction on ageing is the involvement of the NAD/NADH ratio. The *Arabidopsis* onset of leaf death5 (*old5*) mutant that shows early senescence has recently been identified as a mutant in quinolinate synthase, an enzyme required for the *de novo* synthesis of NAD (Schippers *et al.*, 2008). In heterotrophic organisms, Sir2 (silent information regulator-2), an NAD-dependent histone deacetylase, is involved in life-span extension in response to dietary restriction. In yeast, low glucose supply has been suggested to extend life span by reducing the NADH concentration and thereby activating Sir2 (Lin *et al.* 2004). Less is known about the role of Sir2 in plants, but it has been shown that down-regulation of the rice Sir2 orthologue results in premature cell death re-

sembling the hypersensitive response to pathogens (Huang *et al.*, 2007).

While, in yeasts, ageing can be delayed by decreased glucose supply (Bitterman *et al.*, 2003), similar to the proposed role of hexose signalling in leaf senescence, dietary restriction in *Drosophila* is more responsive to reduced protein or amino acid rather than to reduced sugar supply (Mair *et al.*, 2005; Lee *et al.*, 2008). This is opposite to the effect of nitrogen on plants, where high nitrogen supply inhibits the senescence-inducing effect of glucose (Pourtau *et al.*, 2006). In conclusion, although the molecular processes involved in the regulation of senescence/ageing in response to metabolic signals may be conserved, the signals which they respond to may have diversified reflecting the metabolic requirement (autotrophic/heterotrophic, inorganic/organic nitrogen supply) of different organisms.

## Supplementary data

Supplementary data can be found at *JXB* online.

**Supplementary Table S1.** Statistical analysis of changes in the expression of autophagy genes in *Arabidopsis* in response to different treatments.

**Supplementary Table S2.** Changes in the expression of autophagy genes in *Arabidopsis* in response to different treatments.

## References

- Baena-González E, Rolland F, Thevelein JM, Sheen J.** 2007. A central integrator of transcription networks in plant stress and energy signalling. *Nature* **448**, 938–943.
- Baena-González E, Sheen J.** 2008. Convergent energy and stress signaling. *Trends in Plant Science* **13**, 474–482.
- Bassham DC, Laporte M, Marty F, Moriyasu Y, Ohsumi Y, Olsen LJ, Yoshimoto K.** 2006. Autophagy in development and stress responses of plants. *Autophagy* **2**, 2–11.
- Bitterman KJ, Medvedik O, Sinclair DA.** 2003. Longevity regulation in *Saccharomyces cerevisiae*: linking metabolism, genome stability, and heterochromatin. *Microbiology and Molecular Biology Reviews* **67**, 376–399.
- Buchanan-Wollaston V, Earl S, Harrison E, Mathas E, Navabpour S, Page T, Pink D.** 2003. The molecular analysis of leaf senescence: a genomics approach. *Plant Biotechnology Journal* **1**, 3–22.
- Buchanan-Wollaston V, Page T, Harrison E, et al.** 2005. Comparative transcriptome analysis reveals significant differences in gene expression and signalling pathways between developmental and dark/starvation-induced senescence in *Arabidopsis*. *The Plant Journal* **42**, 567–585.
- Contento AL, Kim S-J, Bassham DC.** 2004. Transcriptome profiling of the response of *Arabidopsis* suspension culture cells to Suc starvation. *Plant Physiology* **135**, 2330–2347.
- Deprost D, Yao L, Sormani R, Moreau M, Leterreux G, Nicolai M, Bedu M, Robaglia C, Meyer C.** 2007. The *Arabidopsis*

TOR kinase links plant growth, yield, stress resistance and mRNA translation. *EMBO Reports* **8**, 864–870.

**Finkel T, Serrano M, Blasco MA.** 2007. The common biology of cancer and ageing. *Nature* **448**, 767–774.

**Hansen M, Chandra A, Mitic LL, Onken B, Driscoll M, Kenyon C.** 2008. A role for autophagy in the extension of life span by dietary restriction in *C. elegans*. *PLoS Genetics* **4**, e24.

**Huang L, Sun Q, Qin F, Li C, Zhao Y, Zhou D-X.** 2007. Down-regulation of a *SILENT INFORMATION REGULATOR2*-related histone deacetylase gene, *OsSRT1*, induces DNA fragmentation and cell death in rice. *Plant Physiology* **144**, 1508–1519.

**Ishida H, Yoshimoto K, Izumi M, Reisen D, Yano Y, Makino A, Ohsumi Y, Hanson MR, Mae T.** 2008. Mobilization of Rubisco and stroma-localized fluorescent proteins of chloroplasts to the vacuole by an *ATG* gene-dependent autophagic process. *Plant Physiology* **148**, 142–155.

**James F, Broquisse R, Pradet A, Raymond P.** 1993. Changes in proteolytic activities in glucose-starved maize root tips: regulation by sugars. *Plant Physiology and Biochemistry* **31**, 845–856.

**Lee KP, Simpson SJ, Clissold FJ, Brooks R, Ballard JWO, Taylor PW, Soran N, Raubenheimer D.** 2008. Life span and reproduction in *Drosophila*: new insights from nutritional geometry. *Proceedings of the National Academy of Sciences, USA* **105**, 2498–2503.

**Lin J-F, Wu S-H.** 2004. Molecular events in senescing *Arabidopsis* leaves. *The Plant Journal* **39**, 612–628.

**Lin S-J, Ford E, Haigis M, Liszt G, Guarente L.** 2004. Calorie restriction extends yeast life span by lowering the level of NADH. *Genes and Development* **18**, 12–16.

**Lloyd JC, Zakhleniuk OV.** 2004. Responses of primary and secondary metabolism to sugar accumulation revealed by microarray expression analysis of the *Arabidopsis* mutant, *pho3*. *Journal of Experimental Botany* **55**, 1221–1230.

**Mair W, Dillin A.** 2008. Aging and survival: the genetics of life span extension by dietary restriction. *Annual Review of Biochemistry* **77**, 727–754.

**Mair W, Piper MDW, Partridge L.** 2005. Calories do not explain extension of life span by dietary restriction in *Drosophila*. *PLoS Biology* **3**, 1305–1311.

**Maiuri MC, Zalckvar E, Kimchi A, Kroemer G.** 2007. Self-eating and self-killing: crosstalk between autophagy and apoptosis. *Nature Reviews Molecular Biology* **8**, 741–752.

**Masclaux C, Valadier MH, Brugière N, Morot-Gaudry JF, Hirel B.** 2000. Characterization of the sink/source transition in tobacco (*Nicotiana tabacum* L.) shoots in relation to nitrogen management and leaf senescence. *Planta* **211**, 510–518.

**Masclaux-Daubresse C, Carrayol E, Valadier MH.** 2005. The two nitrogen mobilisation- and senescence-associated GS1 and GDH genes are controlled by C and N metabolites. *Planta* **221**, 580–588.

**Moore B, Zhou L, Rolland F, Hall Q, Cheng W-H, Liu Y-X, Hwang I, Jones T, Sheen J.** 2003. Role of the *Arabidopsis* glucose sensor HXK1 in nutrient, light, and hormonal signaling. *Science* **300**, 332–336.

**Noh YS, Amasino RM.** 1999. Identification of a promoter region responsible for the senescence-specific expression of *SAG12*. *Plant Molecular Biology* **41**, 181–194.

**Parrott DL, McInerney K, Feller U, Fischer AM.** 2007. Steam-girdling of barley (*Hordeum vulgare*) leaves leads to carbohydrate accumulation and accelerated leaf senescence, facilitating transcriptomic analysis of senescence-associated genes. *New Phytologist* **176**, 56–69.

**Parrott D, Yang L, Shama L, Fischer AM.** 2005. Senescence is accelerated, and several proteases are induced by carbon 'feast' conditions in barley (*Hordeum vulgare* L.) leaves. *Planta* **222**, 989–1000.

**Pourtau N, Jennings R, Pelzer E, Pallas J, Wingler A.** 2006. Effect of sugar-induced senescence on gene expression and implications for the regulation of senescence in *Arabidopsis*. *Planta* **224**, 556–568.

**Schippers JHM, Nunes-Nesi A, Apetrei R, Hille J, Fernie AR, Dijkwel PP.** 2008. The *Arabidopsis* onset of leaf death5 mutation of quinolinate synthase affects nicotinamide adenine dinucleotide biosynthesis and causes early ageing. *The Plant Cell* **20**, 2909–2925.

**Schmid M, Davison TS, Henz SR, Pape UJ, Demar M, Vingron M, Schölkopf B, Weigel D, Lohmann JU.** 2005. A gene expression map of *Arabidopsis thaliana* development. *Nature Genetics* **37**, 501–506.

**Thompson AR, Doelling JH, Suttangkakul A, Vierstra RD.** 2005. Autophagic nutrient recycling in *Arabidopsis* directed by the ATG8 and ATG12 conjugation pathways. *Plant Physiology* **138**, 2097–2110.

**Uauy C, Distelfeld A, Fahima T, Blechl A, Dubcovsky J.** 2006. A NAC gene regulating senescence improves grain protein, zinc, and iron content in wheat. *Science* **314**, 1298–1301.

**Usadel B, Nagel A, Thimm O, et al.** 2005. Extension of the visualization tool MapMan to allow statistical analysis of arrays, display of corresponding genes, and comparison with known responses. *Plant Physiology* **138**, 1195–1204.

**van Doorn WG.** 2008. Is the onset of senescence in leaf cells of intact plants due to low or high sugar? *Journal of Experimental Botany* **59**, 1963–1972.

**Wingler A, Roitsch T.** 2008. Metabolic regulation of leaf senescence: interactions of sugar signalling with biotic and abiotic stress responses. *Plant Biology* **10**, 50–62.