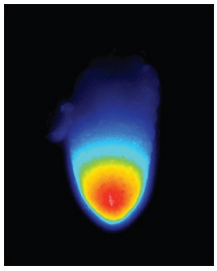
PLANT DEVELOPMENT

Wave-up call

Science **349**, 864–868 (2015)



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Strigolactones (SLs) are hormones composed of a tricyclic lactone (ABC-ring) and a butenolide group (D-ring) that are produced in the plant root. The plant SL receptor, the α/β hydrolase fold protein D14, mediates the hydrolysis of SL into ABC-ring and D-ring fragments. The secretion of SLs in the soil enables communication with symbiotic mycorrhizal fungi. The dormant root parasitic weed *Striga hermonthica* also detects SL in the soil, triggering it to undergo seed germination through activation of ethylene biosynthesis. However, there is a significant temporal gap between initial SL reception and *Striga* germination. To determine the temporal dynamics of SL perception during *Striga* germination, Tsuchiya *et al.* designed two fluorescent probes called Yoshimulactone Green (YLG) and Yoshimulactone Green Double (YLGW), composed of fluorescein attached to one or two SL D-ring fragments, respectively, whose fluorescence emission is activated by recombinant D14. The authors screened YLG against a candidate group of *Striga* α/β hydrolase fold enzymes and found that a family of *Striga* HYPOSENSITIVE TO LIGHT (HTL) enzymes interacted with and hydrolyzed YLG, suggesting that they are *Striga* SL receptors. They detected fluorescence at the root tip of YLGW-treated *Striga* seeds with a progressive movement up the seed over a six-hour period. A second wave of fluorescence at around 24 hours was observed, coinciding with the initiation of germination. The authors defined the initial wave as the wake-up phase and the second wave as the elongation tide. Inhibition of protein translation prevented YLGW-mediated germination by slowing the propagation of the wake-up wave, whereas ethylene inhibition blocked germination by reducing the amplitude of the wave. Overall, the use of the YLGW probe provides some new insights about SL perception during germination, but further studies are needed to investigate what genetic and cellular changes occur during the wake-up phase that primes *Striga* for germination. *GM*

NUCLEOTIDE METABOLISM

Salvaging chemotherapy

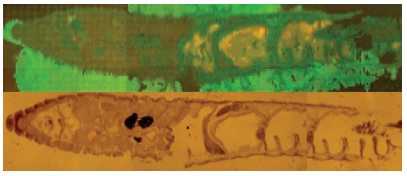
Nature **524**, 114–118 (2015)

DNA nucleotides are produced either by *de novo* biosynthesis or by salvage pathways that recycle nucleobases from catabolized nucleic acids. As the genome contains epigenetically modified cytosine bases, including 5-hydroxymethyl- and 5-formyl cytosine (5hmC and 5fC), it remains an open question whether these modified bases, when released as nucleosides (5hmdC and 5fdC respectively), affect subsequent DNA metabolism. Zauri *et al.* now reveal how spurious genomic incorporation of these epigenetic nucleosides is avoided. HPLC analysis of DNA from cell lines transfected with 5hmdC triphosphate (5hmdCTP) demonstrates that 5hmdC is tolerated by the DNA replication apparatus and incorporated into genomic DNA. Biochemical studies showed that genomic integrity is instead maintained by the nucleotide salvage pathway: two kinases involved in the biosynthesis of deoxycytidine triphosphates exclude the modified cytidines as substrates, thereby preventing the synthesis of their dNTPs. Cancer cell line profiling revealed that 5hmdC treatment generally had no adverse effects on cells, but was cytotoxic in cell lines that overexpressed cytidine deaminase (CDA), which converts cytosine nucleotides to their corresponding uracil derivatives. Perturbation of cellular CDA levels by shRNA knockdown or overexpression validated the link between CDA activity and 5hmdC cytotoxicity. The authors further showed *in vitro* that CDA converts 5hmdC and 5fdC to 5hmdU and 5fdU; these analogs, after phosphorylation and genomic incorporation, induce a DNA damage response, cell cycle arrest and cell death. To test the therapeutic potential of CDA-mediated activation of 5hmdC and 5fdC, the authors demonstrated in a mouse xenograft model that CDA expression facilitated tumor reduction under 5hmdC and 5fdC treatment. Through clarification of the metabolic fate of epigenetic cytosine modifications, the authors have, in parallel, identified a potential nucleotide therapeutic approach for certain cancers. *TLS*

CHEMICAL ECOLOGY

Washing out worms

Nat. Commun. **6**, 7869 (2015)



NAT. COMMUN.

Polyphenols, known to cause protein precipitation, are produced in abundance by plants, meaning that earthworms are likely to be subjected to particularly high concentrations of these compounds due to plant decomposition. Previous research has shown that earthworms prefer plant material with low amounts of polyphenols, suggesting the compounds do affect the worms. But how do they contend with these molecules to prevent their deleterious effects? Liebeke *et al.* used metabolomics to search for small molecules that might be involved. The authors performed imaging mass spectrometry of cryosectioned worms looking for highly abundant molecules that might interact directly with the polyphenols. They identified a peak corresponding to 2-hexyl-5-ethylfuran-3-sulfonate and several variants present in the earthworm gut. Though this molecule has been identified in worms before, its biological role had not been established. The authors found the molecule in the anterior part of the gut lumen, well positioned to interact with material eaten by the worm. The suite of compounds are unique to earthworms as compared to other species and were also found in all earthworms tested (14 species across three families), and their abundance varied across life stages, consistent with a physiological role unique to the earthworm habitat. *In vitro* studies established that the compounds are surfactants and can solubilize lipids in addition to protecting proteins from polyphenols. However, *in vivo* experiments showed that the compounds are produced in greater quantities in response to a high-polyphenol diet than to a control or high-fat diet, and are present in higher quantities in earthworms collected from sites with larger amounts of leaf litter, suggesting that their primary function is linked to polyphenols. The discovery of these 'drilodefensins' sets the stage for further research into their biosynthesis and the mechanism by which complexed polyphenols are removed from the gut. *CG*