PLANT STRESS RESPONSES

Mechanism of pathogen-induced cap-independent translation in plants

> … the R-motif is an IRES

In response to different types of stress, relevant stress response mRNAs are selectively translated while translation initiation of most mRNAs in the cell is inhibited. Whereas this process is fairly well understood in animals, the corresponding mechanisms in plants are less clear. Wang et al. now report elucidating the mechanism of the translational response in plants to pattern-triggered immunity (PTI; a form of plant innate immunity).

The authors have previously identified a purine-rich element — the 'R-motif' — in the 5′ leader sequence of mRNAs encoding immunity proteins. The R-motif regulates their translation through interaction with poly(A)-binding proteins (PABPs); however, the mechanism of PTI-induced translation reprogramming remains unknown.

Whereas canonical translation initiation depends on the m^7G 'cap' at the mRNA 5′ end, translation of stress response mRNAs is typically cap-independent. Infection of plants with the bacterial epitope elf18 resulted in mRNA decapping, which was compromised in plants deficient in decapping enzymes. Nine R-motifs containing immunity mRNAs, including *TBF1*, became especially sensitive to elf18-induced decapping.

Credit: Sahil Ghosh/EyeEm/Getty

The authors hypothesized that the R-motif functions as an internal ribosome entry site (IRES) to mediate cap-independent translation of defense mRNAs during PTI. Mutating any of the R-motifs in the *TBF1* 5′ leader sequence decreased cap-independent translation of luciferase reporter mRNAs, supporting the notion that the R-motif is an IRES.

RNA probes containing *TBF1* R-motifs interacted with purified PABP8, and the interactions increased following elf18 treatment. When co-expressed in plants, PABP8 greatly increased translation of reporter transcripts with wild-type, but not mutant, R-motifs; conversely, in *pabp* mutant protoplasts, R-motif-reporter translation was compromised. Thus, PABP–R-motif interaction enhances cap-independent translation.

PABPs are known to interact with eukaryotic translation initiation factor 4 G (eIF4G) and facilitate canonical translation initiation. In addition to eIF4G, plants express a specific eIF4G isomer, eIFiso4G (encoded by two redundant genes, *eifiso4g1* and *eifiso4g2*), and the authors showed that this isomer also interacts with PABPs. Without PTI signalling, translation of R-motif-containing reporters increased in *eif4g* mutant plants, but decreased in *eifiso4g1 eifiso4g2* mutant plants. By contrast, translation of an mRNA lacking R-motifs decreased in the *eif4g* plants, but not in the *eifiso4g1 eifiso4g2* plants. Furthermore, the *eifiso4g1 eifiso4g2* plants failed to increase reporter translation in response to elf18 treatment. Thus, eIF4G and eIFiso4G may be negative and positive regulators of R-motif-mediated translation, respectively, and eIFiso4G specifically functions in R-motif-dependent translation.

To determine the roles of PABPs and eIFiso4G in basal immunity and in PTI, the different mutant plants were inoculated with a *Pseudomonas syringae* strain (to test basal immunity) or subjected to elf18 treatment (PTI). The results showed that eIFiso4G, in association with PABPs, both affects basal immunity and induces PTI.

Finally, MAP kinase 3 (MPK3) and MPK6 (MPK3/6) are essential regulators of PTI. Depletion of both kinases compromised elf18-induced translation of different R-motif-containing reporters. MPK3/6 phosphorylated PABP8 and eIFiso4G, enhanced their association with R-motifs and reporter translation, and were necessary for elf18-triggered PTI. Furthermore, MPK3/6 phosphorylated eIF4G and inhibited canonical translation.

In summary, following microbial infection, MPK3/6 turn off cap-dependent translation by inducing mRNA decapping and inhibiting eIF4G, while inducing R-motif-dependent translation by enhancing PABP and eIFiso4G activities. The result of this shift is the reprogramming of the infected plant cell translatome. As the R-motif is prevalent in stress response mRNAs in various organisms (including in humans), it will be interesting to study whether R-motifs mediate different translational stress responses in other higher eukaryotes.

Eytan Zlotorynski

ORIGINAL ARTICLE Wang, J. et al. PABP/purine-rich motif as an initiation module for cap-independent translation in pattern-triggered immunity. *Cell* https://doi.org/10.1016/j.cell.2022.06.037 (2022)