Credit: PhotoAlto/Sandro Di Carlo Darsa

selected miRNAs. Together, these observations indicate that 3′US represses tumour suppressor genes, which occurs in trans, through miRNA-mediated silencing in ceRNA networks. The key role of these trans effects was confirmed by mathematical modelling.

In summary, pervasive 3′US, which occurs in many cancers, modulates tumour suppressor ceRNA networks and interferes with the ability of ceRNAs to bind and sequester miRNAs, resulting in increased miRNA-mediated silencing of their ceRNA tumour suppressor partners. Overall, this work highlights the emerging importance of ceRNA networks in regulating tumour suppressors.

Paulina Strzyz

ORIGINAL ARTICLE Park, H. J. et al. 3′ UTR shortening represses tumor-suppressor genes in trans by disrupting ceRNA crosstalk. *Nat. Genet.* **50**, 783–789 (2018)

FURTHER READING Anastasiadou, E., Jacob, L. S. & Slack, F. J. Non-coding RNA networks in cancer. *Nat. Rev. Cancer* **18**, 5–18 (2018) | Lee, Y.-R., Chen, M. & Pandolfi, P. P. The functions and regulation of the PTEN tumour suppressor: new modes and prospects. *Nat. Rev. Mol. Cell Biol.* https://doi.org/10.1038/s41580-018-0015-0 (2018)

is regulated by the ER-associated transcription factor Opi1, which interacts with PA and thus senses cellular levels of PA. When PA levels are low, Opi1 translocates from the ER to the nucleus to repress the expression of phospholipid metabolic genes. Here, the authors find that the PA-rich surface of nuclear lipid droplets can sequester Opi1 and thereby modulate its transcriptional activity through negative feedback control.

Thus, the yeast INM is metabolically active and produces lipid droplets that can sequester a transcription factor that regulates lipid metabolism. Whether the metabolic function of the INM is conserved between yeast and humans remains to be determined. It will also be interesting to study whether nuclear lipid droplets can store other nuclear proteins and thus have a broader role in regulating nuclear function.

Kim Baumann

ORIGINAL ARTICLE Romanauska, A. & Köhler, A. The inner nuclear membrane is a metabolically active territory that generates nuclear lipid droplets. *Cell* https://doi.org/10.1016/j.cell.2018.05.047 (2018)

MICRORNA

Parasitic interference

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Cotesia vestalis is a parasitic wasp, which lays its eggs in larvae of the moth *Plutella xylostella*. With its eggs the wasp releases into the host the symbiotic polydnavirus *C. vestalis* bracovirus (CvBV) and embryonic cells called teratocytes. Wang et al. now show that the teratocytes and CvBV introduce microRNAs (miRNAs) that can delay larval growth.

The authors took advantage of the recently sequenced genomes of *C. vestalis* and *P. xylostella* to identify *C. vestalis* miRNAs and assess their roles in parasitism. They produced small nuclear RNA libraries from teratocytes and larvae of *C. vestalis* and identified >150 miRNAs.

Twenty of the teratocyte-expressed miRNAs were encoded by the CvBV provirus (the first polydnavirus miRNAs to be described). Analysis of the expression of several CvBV-encoded miRNAs in *P. xylostella* larvae at different times after egg deposition showed that they were expressed and indicated that they emerge through both viral infection and expression in teratocytes.

Whereas viral infection could directly deliver miRNAs to host cells, transmission of teratocyte-expressed miRNAs to host cells was suggested to be mediated by extracellular vesicles such as exosomes. Following co-culturing of teratocytes with Pxem_ZJU cells, which is an established *P. xylostella* cell line, teratocyte-produced exosomes were indeed taken by Pxem_ZJU cells.

Twenty teratocyte-expressed miRNAs — especially miR-375-3p and miR-281-3p, which are also endogenously expressed in *P. xylostella* — were more abundant in Pxem_ZJU cells co-cultured with teratocytes than in control cells. Moreover, in haemocytes collected from parasitized *P. xylostella*, most of the miR-281-3p and miR-375-3p miRNAs were of *C. vestalis* origin. Thus, miRNAs released from teratocytes were taken up by the parasitized larvae.

Almost 100 *P. xylostella* genes were predicted to be targets of the most abundant miRNAs expressed in teratocytes and/or encoded by CvBV. One of the prominent targets was ecdysone receptor (*EcR*), which was predicted to be targeted by Cve-miR-281-3p (encoded by the *C. vestalis* genome) and Cve-miR-novel22-5p (encoded by the CvBV genome).

P. xylostella larvae parasitized by *C. vestalis* exhibit pronounced size reduction and inhibition of metamorphosis. Analysis by dual-luciferase reporter assays supported the targeting of *EcR* by Cve-miR-281-3p and Cve-miR-novel22-5p, and injection of mimics (agomirs) of either miRNA into larvae inhibited EcR expression. As EcR mediates the response to the moulting hormone ecdysone in insects, its inhibition by Cve-miR-281-3p and Cve-miR-novel22-5p could explain the growth delays of parasitized larvae.

In summary, *C. vestalis*-derived miRNAs of both CvBV and teratocyte origin — some of which target the same *P. xylostella* genes — are expressed in host tissues and can contribute to the developmental delays observed in parasitized larvae, at least partly by inhibiting EcR. This could guarantee the availability of host resources for wasp development. As the relationship between the miR-281 family and *EcR* is conserved in butterflies and moths, other parasites are likely to employ the same strategy.

Eytan Zlotorynski

ORIGINAL ARTICLE Wang, Z. Z. et al. Parasitic insect-derived miRNAs modulate host development. *Nat. Commun.* **9**, 2205 (2018)