

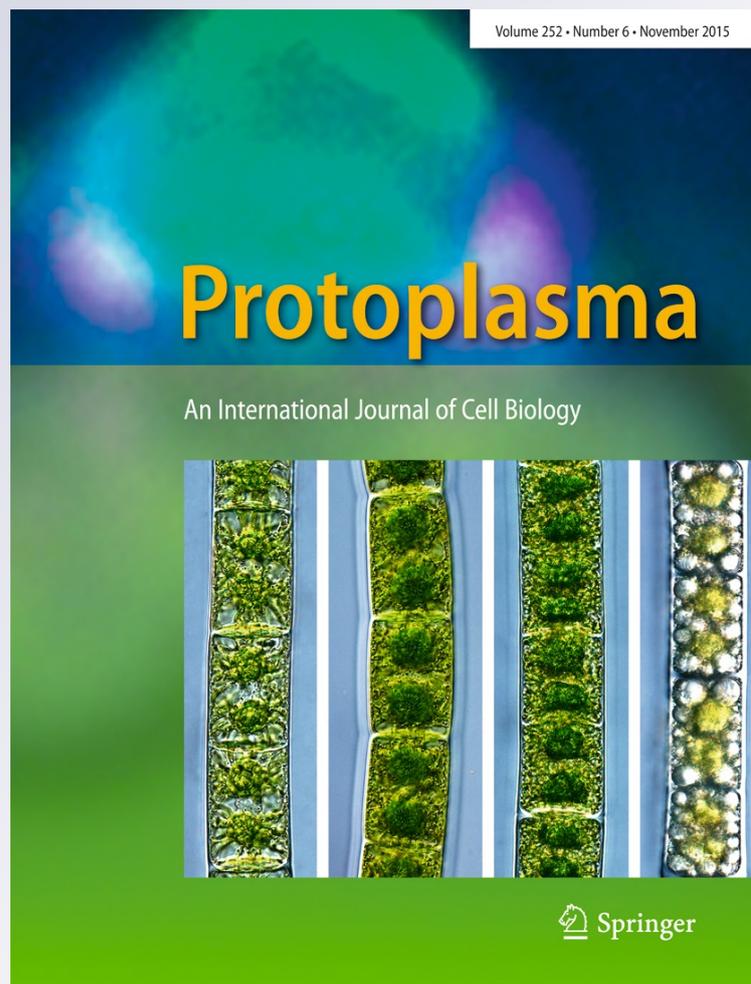
Turn of the screw—helicases everywhere

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Like any other form of tradition, biological inheritance requires stability. It is the unique structure of the double helix that rendered DNA an ideal molecule to convey genetic tradition. However, when tradition should come into life, stability has to be made more fluid from time to time. In case of DNA, this job is played by unique molecular motors, the helicases, able to unwind nucleic acids using the chemical energy of ATP as a fuel. Whether DNA has to be copied, recombined during meiosis, or opened up to read out the encoded information during transcription, helicases are always involved. What is often overlooked is that many helicases are also acting in RNA-dependent processes—they splice mRNA, they process rRNA, or they assist the initiation of translation. It seems that some of them can even perform different jobs, depending on context and localisation. Although nucleases are canonically searched in the nucleus, they can also shift from the nucleus into the cytoplasm. Two contributions from the current issue highlight the importance of these versatile and somewhat promiscuous proteins in quite different organisms—the parasite *Plasmodium* and the Angiosperm rice. They also emphasize the impact of helicases for both medical and agricultural applications.

The work by Tajedin et al. (2015) in the current issue was motivated by the question how *Plasmodium falciparum*, the causing agent of malaria, can acquire drug resistance. In addition to generic mechanisms such as drug export or degradation, mutations in the DNA repair machinery have been

identified as important factor. Several repair pathways converge on the TFIIH (transcription factor II H) complex, which has to be recruited to the site of DNA damage. The helicase XPD (from *Xeroderma pigmentosum* disease, a human disorder arising from a mutation in this gene), as the central component of this complex, seems to play no role for the initiation of transcription, which may be the reason why this gene can accumulate mutations without impairing viability of the pathogen too substantially. To exert its function in repair, XPD has to interact with a second protein, p44, leading to the question whether it might also interact with other partners in other functional contexts. Using the *Plasmodium* standard strain 3D7, addressed also in the malaria genome project, the authors conduct a study on the molecular function of the *P. falciparum* homologue of XPD and its interaction partner, p44, based on recombinantly expressed proteins. They show the enzymatic activities and the interactions in vitro, confirm a DNA helicase activity, and also define the relevant domains by truncation constructs. When they follow the expression and localisation in vivo, they see colocalisation in the nucleus during the blood stage. However, the two proteins are found in the cytoplasm during the trophozoite and schizont stages, and p44 is also found in two different high molecular weight protein complexes. These findings indicate functional diversity, depending on the developmental stage of the cell, and at the same time open the potential to identify novel drug targets to combat this important disease.

Whether this second, still unknown, function of the XPD helicase is related to RNA processing remains to be elucidated. *Plasmodium* definitely is endowed with a different type of helicase of the so called UAP56 group, which works as RNA-dependent ATPase, and can bind to RNA and act as a RNA helicase. The UAP56 helicases are phylogenetically related to the eukaryotic initiation factor 4A and also able to move between nucleus and cytoplasm. The mammalian

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homologue has been shown to work in splicing and mRNA transport to the cytoplasm. The contribution by Tuteja et al. (2015) in the current issue investigates now the rice homologue of the UAP56 helicase type. They show that the transcripts for this protein accumulate in response to salt stress (probably mediated by the phytohormone abscisic acid). Similarly to the *Plasmodium* work, they use recombinant protein to characterize the molecular function in vitro and demonstrate that the rice UAP56 homologue can bind RNA, and unwind it by cleaving ATP. What comes as a certain surprise is the finding that the same protein can also unwind DNA (even at about a twofold higher affinity compared to RNA) and even can move into two directions (3' to 5' and 5' to 3') along its substrate. As found for the *Plasmodium* XPD, this helicase seems to exert multiple functions, depending on its localisation. The functional shift is apparently linked with the response to salinity stress, one of the major constraints in agriculture, which will become even more accentuated by climate change. This represents not only a second example

for the technological impact of a dual-function helicase, but is also conceptually interesting: changes in subcellular localisation of a protein might be a mechanism, by which a cell can achieve different functions using the same protein, which again is a nice example for the parsimony of nature.

Conflict of interest The author declares that he has no competing interests.

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