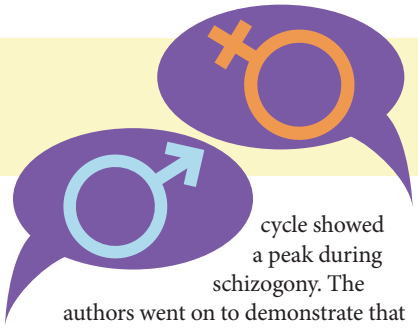
PARASITE BIOLOGY

Let's talk about sex



> *P. falciparum* uses the release of extracellular vesicles as a social mechanism of sensing a hostile host environment and triggering sexual differentiation.

Eukaryotic cells release a range of extracellular vesicles of varying sizes that have important roles in intercellular communication and which in some cases have been shown to be involved in host–pathogen interactions. Two new studies now show that the release of extracellular vesicles by *Plasmodium falciparum*-infected red blood cells (RBCs) is involved in active cell–cell communication to promote sexual differentiation.

Neta Regev-Rudzki, Danny Wilson *et al.* observed through co-culture experiments that plasmid-based drug resistance and fluorescent protein markers could be transferred between RBCs infected with ring-stage *P. falciparum*, and transwell assays confirmed that this DNA-dependent transfer of information did not require cell–cell contact. Culture medium that had been conditioned with *P. falciparum*-infected RBCs was fractionated by density gradient centrifugation, and the fraction responsible for plasmid transfer activity was analysed by atomic force microscopy and cryo-transmission electron microscopy, revealing the presence of spherical exosome-like microvesicles of ~70 nm in diameter. The authors found that the release of these exosome-like vesicles from infected RBCs increased the differentiation of *P. falciparum* gametocytes.

At 100–400 nm in diameter, the vesicles released from *P. falciparum*-infected RBCs that were characterized in the second study, by Pierre-Yves Mantel *et al.*, were larger than those identified by Regev-Rudzki, Wilson *et al.* and are referred to as RMVs (microvesicles released from RBCs). Using mass spectrometry-based proteomic profiling of RMVs purified from conditioned medium, the authors found that in addition to proteins characteristic of RBCs, RMVs contained more than 30 parasite proteins, particularly proteins associated with the Maurer's cleft. Analysis of the timing of RMV release during the *P. falciparum* life cycle showed a peak during schizogony. The authors went on to demonstrate that RMVs are immunostimulatory and that, in agreement with the results from Regev-Rudzki, Wilson *et al.*, they stimulate gametocytogenesis when taken up by RBCs.

Clearly, there are many details still to work out, but these studies indicate that exosome-like microvesicles and RMVs both have a part to play in cell–cell communication in *P. falciparum* populations. Both sets of authors suggest that *P. falciparum* uses the release of extracellular vesicles as a social mechanism of sensing a hostile host environment and triggering sexual differentiation.

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ORIGINAL RESEARCH PAPERS Regev-Rudzki, N. *et al.* Cell-cell communication between malaria-infected red blood cells via exosome-like vesicles. *Cell* **153**, 1120–1133 (2013) | Mantel, P.-Y. *et al.* Malaria-infected erythrocyte-derived microvesicles mediate cellular communication within the parasite population and with the host immune system. *Cell Host Microbe* **13**, 521–534 (2013)