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# IN BRIEF

## PARASITE PHYSIOLOGY

### RIFINs promote rosette formation during malaria

Rosetting — the formation of clusters in which uninfected red blood cells (RBCs) aggregate around a central *Plasmodium falciparum*-infected RBC (iRBC) — promotes RBC sequestration in the microvasculature and is associated with severe malaria. The *P. falciparum* erythrocyte membrane protein 1 (PfEMP1) mediates the formation of rosettes with blood group O RBCs but not with group A RBCs, suggesting that another *P. falciparum* protein might participate in rosette formation. Now, Goel *et al.* show that *P. falciparum*-encoded repetitive interspersed families of polypeptides (RIFINs) are expressed on the surface of iRBCs and that RIFIN-specific antibodies disrupt group A rosettes, but not group O rosettes. Furthermore, transfection of parasites that were selected for their low ability to form rosettes with a RIFIN-encoding *rif* gene resulted in rosette formation with group A RBCs and led to their *in vivo* sequestration in the microvasculature of infected rats. These data suggest that *P. falciparum* uses PfEMP1 to form rosettes with group O RBCs and RIFINs to form rosettes with group A RBCs.

**ORIGINAL RESEARCH PAPER** Goel, S. *et al.* RIFINs are adhesins implicated in severe *Plasmodium falciparum* malaria. *Nature Med.* http://dx.doi.org/10.1038/nm.3812 (2015)

## VIRAL PATHOGENESIS

### HCV RNA acts as a miR-122 sponge

The liver-specific microRNA-122 (miR-122) represses translation by associating with Argonaute and binding to cellular mRNAs (ceRNAs). Notably, replication of hepatitis C virus (HCV) requires binding of miR-122 to viral genomic RNA. Now, Luna *et al.* show that extensive binding of miR-122 to the viral RNA results in reduced binding of miR-122 to ceRNAs, which leads to functional de-repression of its endogenous mRNA targets in HCV-infected cells. To test the hypothesis that HCV RNA acts as a sponge that sequesters miR-122 away from its cellular targets, the authors modified the miR-122-binding sites in the viral RNA to bind miR-15. Indeed, infection with this viral variant resulted in de-repression of miR-15 ceRNAs, whereas miR-122 targets were unaffected. These data suggest that HCV modifies the functions of infected cells by sequestering a key host microRNA.

**ORIGINAL RESEARCH PAPER** Luna, J. M. *et al.* Hepatitis C virus RNA functionally sequesters miR-122. *Cell* **160**, 1099–1110 (2015)

## VIRAL INFECTION

### CRISPR–Cas9 defence against HIV-1

The CRISPR–Cas system is a defence mechanism that uses guide RNAs (gRNAs) and Cas nucleases to bind to complementary sequences in invading DNA and degrade them. Liao *et al.* transfected human cell lines with Cas9 and with gRNAs targeting the long terminal repeats (LTRs) of HIV-1, which led to reduced infection of these cells by HIV-1, compared with wild-type cells. Similarly, CRISPR–Cas9 transfection into cell lines with integrated virus reduced the levels of proviral DNA. Furthermore, human T cell lines engineered to stably express Cas9 and LTR-specific gRNAs maintained a low level of viral infection even 14 days post-infection with HIV-1. Finally, the authors showed that CRISPR–Cas9 efficiently reduced virus production in primary human cells, demonstrating that expression of the CRISPR–Cas9 system in humans confers protection against HIV-1 infection.

**ORIGINAL RESEARCH PAPER** Liao, H.-K. *et al.* Use of the CRISPR-Cas9 system as an intracellular defense against HIV-1 infection in human cells. *Nature Commun.* http://dx.doi.org/10.1038/ncomms7413 (2015)



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