IN BRIEF

BIOTECHNOLOGY

Identifying and validating targets with CRISPR–Cas

Two new papers describe the incorporation of the CRISPR–Cas9 (clustered regularly interspaced short palindromic repeats–Cas9) gene editing system into drug target identification and validation protocols. Kasap *et al.* have developed a methodology that combines high-throughput sequencing followed by CRISPR–Cas9 gene editing to identify mutations that arise in drug-resistant clones of cancer cell lines. Transcriptome sequence reads were analysed to identify mutations in expressed genes that were present in ispinesib-resistant cells but not in parental cells. These mutations were then introduced into other cell lines using the CRISPR–Cas9 system to confirm that these mutations confer drug resistance. They then successfully used this system to identify mutations that confer resistance to an unrelated compound, YM155. The study by Smurnyy *et al.* used a similar approach to identify mutations that cause resistance to 6-thioguanine and triptolide. Forward genetic screens in cancer cell lines identified the genes encoding hypoxanthine-guanine phosphoribosyltransferase (HGPRT) and TFIIH basal transcription factor complex helicase XPB subunit (ERCC3) as causing resistance to 6-thioguanine and triptolide, respectively. Mutations were then introduced into these two genes using the CRISPR–Cas9 system. Point mutations in ERCC3 recapitulated the resistance phenotype when introduced into wild-type cancer cells. The CRISPR–Cas9 system could become an important part of an integrated approach to target validation in mammalian cells.

ORIGINAL RESEARCH PAPERS Kasap, C. *et al.* DrugTargetSeqR: a genomics- and CRISPR-Cas9-based method to analyze drug targets. *Nature Chem. Biol.* http://dx.doi.org/10.1038/nchembio.1551 (2014) | Smurnyy, Y. *et al.* DNA sequencing and CRISPR-Cas9 gene editing for target validation in mammalian cells. *Nature Chem. Biol.* http://dx.doi.org/10.1038/nchembio.1550 (2014)

MALARIA

New target for vaccine development

A protein involved in parasite egress, *Plasmodium falciparum* schizont egress antigen-1 (PfSEA-1), has been identified and could be used as an antigen in antimalarial vaccines. Antibodies to PfSEA-1 were found in individuals who were naturally resistant to *P. falciparum* infection, and vaccination of mice using recombinant PfSEA-1 prolonged survival after *Plasmodium berghi* infection. PfSEA-1 has a role in the emergence of parasites from red blood cells, whereas the four other parasite antigens that currently dominate malarial vaccine development target the entrance of the parasite into host tissue. PfSEA-1 could therefore be used with these other parasite antigens to develop vaccines that affect both parasite entry and exit.

ORIGINAL RESEARCH PAPER Raj, D. K. *et al.* Antibodies to PfSEA-1 block parasite egress from RBCs and protect against malaria infection. *Science* **344**, 871–877 (2014)

MOOD DISORDERS

microRNA in depression and treatment response

A microRNA, miR-1202, is downregulated in the brains of individuals with major depressive disorder. Patients who responded to treatment with antidepressants had lower levels of miR-1202 at baseline than did non-responders, and expression of miR-1202 increased during the course of treatment in antidepressant-responsive patients. miR-1202 regulates glutamate receptor 4 expression, which could explain these observations. miR-1202 could be a target for treating depression, or used as a biomarker to predict response.

ORIGINAL RESEARCH PAPER Lopez, J. P. *et al.* miR-1202 is a primate-specific and brain-enriched microRNA involved in major depression and antidepressant treatment. *Nature Med.* http://dx.doi.org/10.1038/nm.3582 (2014)