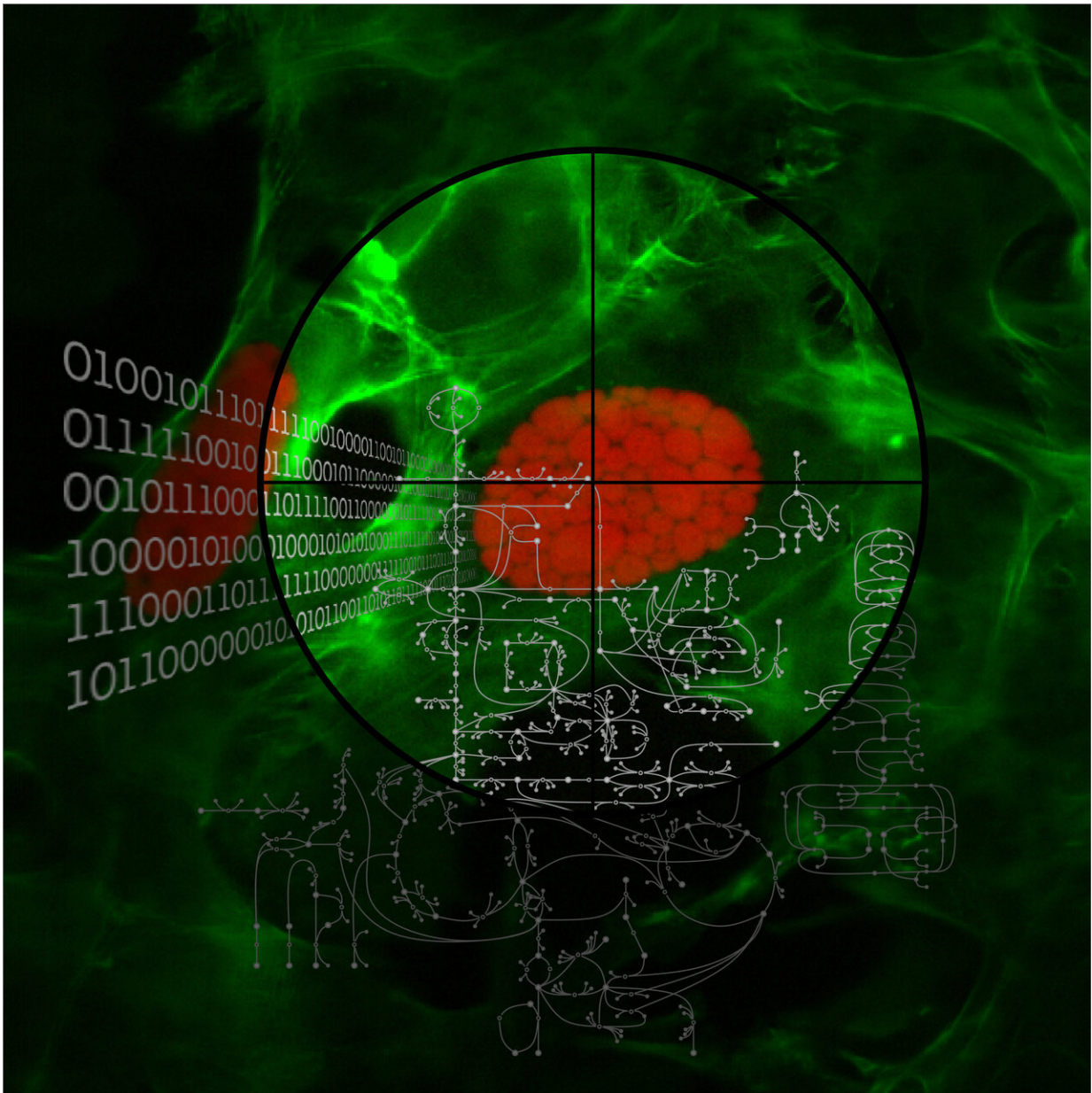


Gene deletion study identifies many new targets in malaria pathogen

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The researchers specifically removed over 1,300 individual genes in the malaria parasite Plasmodium (in red, host cells in green) and were thus able to identify many new targets in the pathogen. Credit: Institut für Zellbiologie, Universität Bern

Despite great efforts in medicine and science, more than 400,000 people worldwide are still dying of malaria. The infectious disease is transmitted by the bite of mosquitoes infected with the malaria parasite Plasmodium. The genome of the parasite is relatively small with about 5,000 genes. In contrast to human cells, Plasmodium parasites only have a single copy of each individual gene. If one removes a gene from the entire genome of the parasite, this leads therefore directly to a change in the phenotype of the parasite.

An [international consortium](#) led by Professors Volker Heussler from the Institute of Cell Biology (ICB) at the University of Bern and Oliver Billker from the Umeå University in Sweden and formerly at the Sanger Institute in Great Britain has taken advantage of this fact. The researchers carried out a genome-wide gene deletion study on [malaria parasites](#): They specifically removed over 1,300 individual [genes](#), observed the effects during the entire life cycle of the parasite and were thus able to identify many new targets in the pathogen. The study was published in *Cell*.

Individual genetic codes accelerate research by decades

The researchers used a malaria mouse model established at the Institute of Cell Biology at the University of Bern. Each of the 1,300 parasite genes was replaced by an individual genetic code to analyze how the

removal of the individual genes affects the parasite. The use of individual codes allows researchers to study many parasites simultaneously and thus drastically shortens the time of their analysis.

After three years of research, the consortium succeeded in systematically screening the genome of the parasite in all life cycle stages. "The deletion screen carried out jointly with the Sanger Institute enabled us to identify hundreds of targets, particularly in the parasite's metabolism," said Rebecca Stanway from the ICB, one of the lead authors of this study.

Model calculations extend experimental findings

To analyze the large number of identified metabolic genes, the Berne researchers have joined forces with Professor Vassily Hatzimanikatis of the EPFL in Lausanne and Professor Dominique Soldati-Favre of the University of Geneva to form the "MalarX" consortium, which is financially supported by the Swiss National Science Foundation. Using data of the malaria genome screen, the group at EPFL has calculated models that show essential metabolic pathways of the parasite. "Thanks to these models, it is now possible to predict which of the previously unexplored genes are vital for the parasite and are therefore suitable targets for malaria control," adds [model](#) expert Anush Chiappino-Pepe from the EPFL in Lausanne.

Some of these predictions were then experimentally confirmed by the Bern researchers in close collaboration with the group of Prof. Chris Janse at the University of Leiden in the Netherlands.

"The genome-wide screen with the corresponding metabolic models represents a breakthrough in malaria research," said Magali Roques of the team in Bern. "Our results will support many malaria researchers worldwide. They can now concentrate on essential parasite genes and

thus develop efficient drugs and vaccines against various stages of the parasite's life," added Dr. Ellen Bushell, former scientist at the Sanger Institute.

More information: *Cell* (2019). [DOI: 10.1016/j.cell.2019.10.030](https://doi.org/10.1016/j.cell.2019.10.030)

Provided by University of Bern

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