New genomics technique could improve treatment and control of malaria

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Credit: CDC

Single-cell genomics could provide new insight into the biology of Malaria parasites, including their virulence and levels of drug resistance, to ultimately improve treatment and control of the disease, according to new research funded by the Wellcome Trust and the National Institutes of Health.

The findings are revealed in a study by researchers at the Texas Biomedical Research Institute and published today in the journal *Genome Research*.

Malaria infections commonly contain complex mixtures of Plasmodium parasites which cause the disease. These mixtures, known as multiple genotype infections (MGI's), can alter the impact of the infection due to parasites competing with one another and can drive the spread of drug resistance. MGI's are extremely common in regions with high levels of malaria infection but their biology is poorly understood.

"Up to 70 per cent of infections in sub-Saharan Africa are MGI's and we currently don't know how many genotypes are present and whether parasites come from a single mosquito bite or multiple mosquito bites" says Shalini Nair, first author on the paper.

Current genome sequencing techniques involve the chemical disintegration of samples of red blood cells from infected patients to obtain parasite DNA, which are then sequenced. This grouped sequencing cannot account for variations between individual parasites found in cells.

Single cell genomics allows the separation and isolation of cells to extract and sequence individual parasite DNA and determine any differences between the parasites within an infection.

"Current sequencing techniques really limit our understanding of malaria parasite biology" says Dr. Ian Cheeseman, who led the study. "It's like trying to understand human genetics by making DNA from everyone in a village at once. The data is all jumbled up, but what we really want is information from individuals."

The team used methods of single cell-sorting and whole genome

amplification to separate out individual cells and amplify their DNA for sequencing directly from infected red blood cells. The use of single-cell genomics allows sequencing of individual parasites directly from a patient's blood.

The technique allows a comprehensive description of the composition of MGIs, and will reveal information on the strength of an infection and the development of drug-resistance, which can inform disease control interventions.

Though the technology is currently too expensive and demanding for routine use in the clinic, as the technology matures the applications for understanding malaria biology are vast.

Dr Michael Dunn, Head of Genetics and Molecular Sciences at the Wellcome Trust said: "Malaria remains one of the biggest killers in the world today despite decades of control efforts. Any insight into the fundamental genetics and overall biology of the disease is valuable to improve future interventions and reduce rates of infection and mortality".

Two forms of malaria parasites were sequenced in the study; *Plasmodium falciparum* (responsible for up to 700,000 deaths per year) and *Plasmodium vivax* (responsible for 20 million infections per year).

More information: Nair S et al. (2014) *Genome Research*. "Single-cell genomics for dissection of complex malaria infections". www.genome.org/cgi/content/abstract/gr.168286.113

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