CASE STUDY

New Hope for Malaria Treatment: Hijacking the Parasite's Protein Factory

The challenge

Malaria continues to be a leading cause of death in many developing countries. The parasite that causes it, *Plasmodium falciparum*, is becoming increasingly resistant to current medicines. To outpace resistance, scientists must find drugs that work in completely new ways.

The solution

Using the MX1 and MX2 beamlines at the Australian Synchrotron, researchers identified a completely novel approach: targeting the malaria parasite's protein production machinery through a strategy known as reaction hijacking. Two molecules were central to this breakthrough:

- ML471 locks onto tyrosine-tRNA synthetase in *P. falciparum*, blocking it from producing proteins essential for survival.
- DACM, a natural product from soil bacteria, targets a different enzyme (aspartyl-tRNA synthetase) in a similarly precise way.

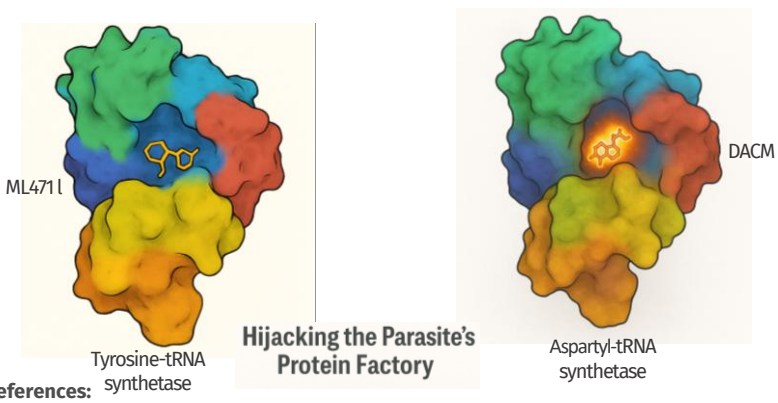
High-resolution crystal structures obtained at the MX beamlines showed exactly how both drugs bind to parasite enzymes but not to human equivalents. This selectivity is key to developing new antimalarials that are both effective and safe.

The impact

The discovery opens a completely new avenue for antimalarial drug development—one that bypasses current mechanisms of resistance. ML471, in particular, demonstrated single-dose effectiveness in mouse models, highlighting its promise as a next-generation therapy.

This work also reinforces the importance of synchrotron techniques in tackling global health challenges. By revealing molecular details with atomic-level precision, MX1 and MX2 played a critical role in identifying and validating new drug targets.

The research was a global collaboration involving ANSTO, the University of Melbourne, Monash University, Griffith University, and international partners like the ICGEB (New Delhi), Takeda Pharmaceuticals (USA), and Medicines for Malaria Venture (MMV) etc.



References:
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Ketprasit N et al. bioRxiv, 2025. DOI: https://doi.org/10.1101/2025.03.20.644283

Research Priority

ANSTO capability/instrument

MX1/MX2 Beamlines
Macromolecular Crystallography
Australian Synchrotron

Collaborators/Client

University of Melbourne

ANSTO-Australian Synchrotron
Griffith University
CSIRO
Monash University
University of Basel
Takeda
ICGEB
Columbia University Medical Center
University of Pretoria
Federal University of São Paulo
Columbia University Medical Center
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UN Sustainable Development Goals

3-Good Health & Well-Being

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