Translation Initiation Inhibitors for the Treatment of Malaria

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Principal investigator

Rivka Dikstein

Faculty of Biochemistry
Department of Biomolecular Sciences

Overview

Malaria, caused by Plasmodium falciparum, remains a leading global health burden with growing drug resistance threatening current therapies. This technology introduces small-molecule inhibitors (i14G1s) that disrupt the interaction between translation initiation factors eIF1 and eIF4G1, a critical step in mRNA translation. Short-term treatment of P. falciparum with i14G1s was shown to inhibit parasite growth and block translation initiation, highlighting a novel therapeutic strategy that exploits the parasiteâ€™s translational machinery.

Applications

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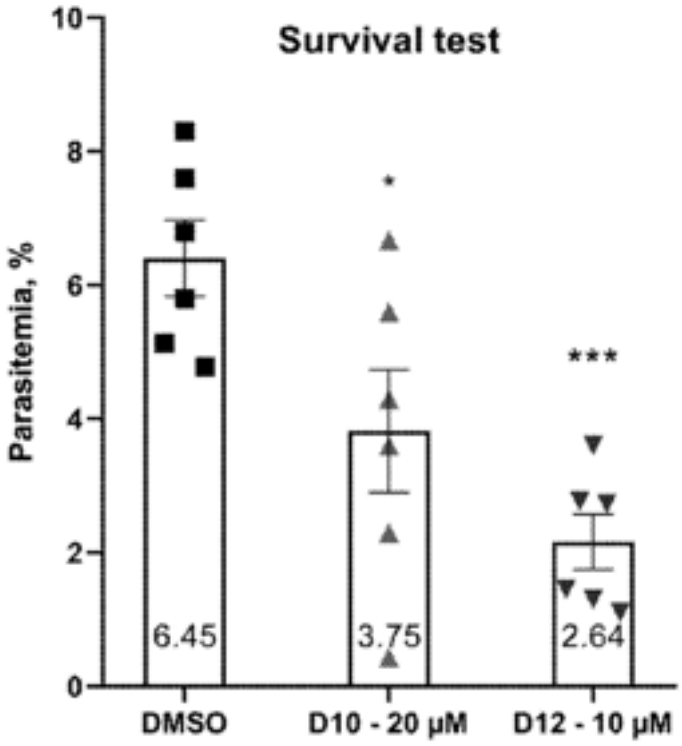

P. falciparum treated with i14G1-10 (20 ÂµM) or i14G1-12 (10 ÂµM) showed 42% and 69% reduced parasitemia after 24 h.

Differentiation

- Novel mechanism: first in-class inhibitors of eIF1â€“eIF4G1 interaction
- Direct parasite targeting: blocks growth and translation
- Resistance bypass: acts on a non-traditional pathway
- Screening platform: HTS-identified, enabling optimization

Development Stage

Small-molecule inhibitors (i14G1s) were identified through screening of 100,000 compounds and validated to specifically disrupt eIF1â€“eIF4G1 interactions.
Mechanistic studies confirm inhibition of translation initiation in human cells, and short-term treatment of P. falciparum demonstrated suppression of parasite growth.Â

References

Sehrawat et al, PNAS, 2022 [1]