

Publication

A novel multiple-stage antimalarial agent that inhibits protein synthesis

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There is an urgent need for new drugs to treat malaria, with broad therapeutic potential and novel modes of action, to widen the scope of treatment and to overcome emerging drug resistance. Here we describe the discovery of DDD107498, a compound with a potent and novel spectrum of antimalarial activity against multiple life-cycle stages of the Plasmodium parasite, with good pharmacokinetic properties and an acceptable safety profile. DDD107498 demonstrates potential to address a variety of clinical needs, including single-dose treatment, transmission blocking and chemoprotection. DDD107498 was developed from a screening programme against blood-stage malaria parasites; its molecular target has been identified as translation elongation factor 2 (eEF2), which is responsible for the GTP-dependent translocation of the ribosome along messenger RNA, and is essential for protein synthesis. This discovery of eEF2 as a viable antimalarial drug target opens up new possibilities for drug discovery.

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