Title:	Transient State Kinetics of Plasmodium falciparum Apicoplast DNA Polymerase Suggests the Involvement of Accessory Factors for Efficient and Accurate DNA Synthesis.
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Abstract:	Plasmodium, the causative agent of malaria, belongs to the phylum Apicomplexa. Most apicomplexans, including Plasmodium, contain an essential nonphotosynthetic plastid called the apicoplast that harbors its own genome that is replicated by a dedicated organellar replisome. This replisome employs a single DNA polymerase (apPol), which is expected to perform both replicative and translesion synthesis. Unlike other replicative polymerases, no processivity factor for apPol has been identified. While preliminary structural and biochemical studies have provided an overall characterization of apPol, the kinetic mechanism of apPol's activity remains unknown. We have used transient state methods to determine the kinetics of replicative and translesion synthesis by apPol and show that apPol has low processivity and efficiency while copying undamaged DNA. Moreover, while apPol can bypass oxidatively damaged lesions, the bypass is error-prone. Taken together, our results raise the following question—how does a polymerase with low processivity, efficiency, and fidelity (for translesion synthesis) faithfully replicate the apicoplast organellar DNA within the hostile environment of the human host? We hypothesize that interactions with putative components of the apicoplast replisome and/or an as-yet-undiscovered processivity factor transform apPol into an efficient and accurate enzyme
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