Title: Towards the Structure Based Design of Broad Spectrum Anti-Apicomplexan Drugs

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Abstract:

Apicomplexan parasites are responsible for several diseases including malaria, toxoplasmosis and cryptosporidiosis. Drug administration remains the preferred treatment strategy for most of these diseases. However, the emergence of resistance in all available therapies necessitates the urgent discovery of novel drug-scaffolds targeting unique parasite proteins and pathways.

Inhibition of cell division by using tubulin targeting, antimitotic compounds has been the most successful strategy for cancer treatment up to now. Implementing a similar strategy to arrest parasite replication using apicomplexan tubulin specific inhibitors offers a completely new and attractive avenue towards anti-apicomplexan drug discovery. However, this strategy has not been explored sufficiently mainly due to the lack of biochemical and structural knowledge on apicomplexan tubulins. In this talk I will present a very first structural description of apicomplexan tubulin drug-binding sites together with the comparison to their mammalian counterparts. Utilizing this structural information, we are developing novel anti-tubulin drugs specific for protozoan parasites. My presentation will highlight how this structural knowledge is enabling the rational development of specific and broad-spectrum anti- apicomplexan drugs.