Membrane Biogenesis in the Intracellular Parasite *Toxoplasma gondii* and its Significance as a Chemotherapeutic Target

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T. gondii is an obligate intracellular parasite that causes infections in immuno-compromised individuals. Our focus is to measure the capacity of the parasite for autonomous membrane biogenesis needed for its successful replication with the eventual aim to render the parasite uniquely susceptible to the compounds disrupting its lipid metabolism. Our data provide the evidence of *de novo* phospholipid synthesis in *T. gondii* demonstrative of PtdSer, PtdEtn, PtdCho and PtdIns. *T. gondii* lacks the PtdEtn methylation pathway to synthesize PtdCho indicating it is a choline auxotroph. Dimethylethanolamine, a choline analog, dramatically interfered with the PtdCho metabolism of *T. gondii* and caused a marked inhibition of its growth within human fibroblasts. These finding reveal how the selective inhibition of PtdCho synthesis by Dimethylethanolamine is a powerful approach to arresting parasite growth.

Examination of PtdSer metabolism demonstrates that free *T. gondii* secretes a soluble PSD (PtdSer decarboxylase) that can decarboxylate the exogenous liposomal PtdSer to PtdEtn. Quantitatively, axenic *T. gondii* can secrete up to 20% of its PSD pool in 2 hrs at 37°C. Either depletion of parasite ATP or intracellular calcium or reduction in temperature to 4°C inhibits the PSD secretion. The *Tg*PSD cDNA encodes a 337-aa protein with a putative 22-aa secretory-signal peptide at its N-terminus. The *Tg*PSD gene can functionally complement an *S. cerevisiae* mutant devoid of PSD activity. These findings demonstrate extremely novel features of the parasite enzyme, since neither soluble nor secreted forms of PSD have been previously described for any organism.