PROJECT SUMMARY

Diseases caused by parasitic species of the genus, *Perkinsus*, in bivalve mollusks are world wide problems. The parasite, *Perkinsus marinus* (Dermo) is one of the two important protozoan parasites causing severe mortality in the American (eastern) oyster, *Crassostrea virginica*, on the US east and Gulf coasts since the 1950s. Previously, no information existed on lipid metabolism and biosynthesis in this parasite, although its host is an ecologically and economically important aquatic species. Via a previous NSF award important information has been obtained concerning lipid metabolism in *P. marinus* in relation to its host. *P. marinus* is similar to *Plasmodium* spp. in phospholipid synthesis and can acquire and metabolize exogenous lipids to constitutive lipid components as can most of the studied parasitic protozoans. The meront stage of this parasite, however, differs from all of the other parasitic protozoans, which rely on their host for essential lipids, by its ability to synthesize a range of saturated and unsaturated fatty acids, including the essential fatty acid, arachidonic acid (AA). The ability of *P. marinus* to synthesize AA is novel. No other parasitic protozoans have been reported to have such a capability. Within the host, however, the parasite appears to use host fatty acids rather than synthesizing its own. Also, for development from meronts to prezoosporangia, the parasite seems to require host lipids. Several questions arise from these findings: (1) does the meront stage of *P. marinus* have two trophic metabolic phases, host-associated and host-disassociated; (2) what pathway(s) does the parasite use for AA synthesis; (2) are the parasites' fatty acid (FA) synthetic activities regulated by temperature and salinity, the two important factors that control the infection development and progression in the host; (4) is the parasites' FA biosynthetic capability related to the mechanisms for disease transmission; (5) for development from meronts to prezoosporangia, does the parasite require host lipids; and (6) is AA a virulence factor and does AA have other physiological functions in addition to being an essential membrane component? To answer these questions, it will be determined: (1) whether the meront stage has two divergent metabolic pathways or meronts retain their synthetic capability within the host, (2) the pathway(s) used by meronts for AA synthesis and identify and clone the gene(s) responsible for desaturation activity, (3) effects of temperature and salinity on the fatty acid biosynthetic activity of the parasite, (4) how long meronts remain viable and infective in a lipid-free environment, (5) lipid requirements for meronts to develop to prezoosporangia, and (6) whether meronts can produce prostaglandins (PGs), which have potential pathogenic effects on the host, from AA. The results will not only lead to an in-depth understanding of the significance of *de novo* lipid and FA synthesis in *P. marinus* and its relationship to the parasite's development, life cycle completion, disease transmission and pathogenesis of the host, but will also build a basis for future studies on the molecular mechanisms underlying the host-parasite interaction and identification of factors that regulate host-parasite relationship in lipid metabolism. If it is shown that *P. marinus* meronts have two trophic metabolic phases, then *P. marinus*-oyster system may be an ideal model for investigating host-parasite relationships in lipid metabolism and the underlying mechanisms that trigger and regulate the "on" and "off" of fatty acid synthesis system of the parasite. If it is proven that host-associated *P. marinus* meronts retain fatty acid synthesis capability, *P. marinus* would be a useful model for development of drugs targeting lipid metabolic pathways. Lipid biosynthetic pathways are currently being investigated as potential drug targets in several protozoan parasites of humans including *Plasmodium* and *Trypanosoma* species. Additionally, via this project, opportunities will be provided to graduate, undergraduate, and high school students to receive hands-on research experience and training in marine science in general and lipid biochemistry, molecular genetics, and parasitology in particular.