論文の内容の要旨

論文題目　Functional analysis of Rab7D small GTPase of *Entamoeba histolytica*
(赤痢アメーバ原虫における低分子量 GTPase Rab7D の機能解析)

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Entamoeba histolytica, the causative agent of amebiasis, is a human intestinal parasite that has several virulence-associated mechanisms, including motility, adhesion, vesicular trafficking, trogocytosis, and phagocytosis. EhRab7D, a small GTPase previously identified from isolated phagosomes, was hypothesized to have function in trogocytosis (internalization of the prey by nibbling) and phagocytosis, and thus in pathogenic mechanisms. To characterize the biological role of EhRab7D, overexpression and gene silencing *E. histolytica* strains were established, and assays for trogocytosis, phagocytosis, pinocytosis, motility, cellular adhesion, as well as RNA seq analysis, were performed using these strains. EhRab7D interacting proteins were identified using GST-EhRab7D in affinity purification then *in silico* analysis of EhRab7D protein and prediction of its secondary structure were also performed to discover its unique features among EhRab7 isotypes. The results showed that EhRab7D regulates actin-related processes including negatively regulates trogocytosis, phagocytosis and pinocytosis; in contrast, it positively regulates motility and cellular adhesion. Furthermore, *in silico* analysis of EhRab7D identified a unique acidic amino acid stretch composing the natural

disordered region in the carboxyl terminus. In addition, amino acid substitutions within the previously identified effector binding surface of mammalian Rab7 were identified, suggesting they may be involved in the binding to unique effectors and biological functions. Affinity purification showed 11 actin-related proteins interact with EhRab7D-GDP including Arp2/3, that previously known to interact with human WASP and Scar1 through the acidic region. Altogether, EhRab7D is involved in actin-associated cytoskeleton-related processes in GDP dependent manner, while their specific mechanisms remained elusive.