THE MOLECULAR MOTOR OF PLASMODIUM PARASITES

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Gliding motility and host cell invasion by apicomplexan parasites (that include *Plasmodium* and *Toxoplasma*) are empowered by an actin-myosin motor located underneath the parasite plasma membrane. During cell invasion, the parasite trans-membrane protein TRAP (or other family members) connects the motor with the ligands on the host cell plasma membrane. The extra-cellular adhesive domains of TRAP bind to cellular receptors whereas its cytoplasmic tail (TRAP-tail) interacts with F-actin using aldolase as a bridge. We used a panel of mutant TRAP-tails to reveal the minimal aldolase-binding motif, and showed that it consists of a single tryptophan embedded in a short stretch of acidic amino acids. In spite of its simplicity, this motif is highly specific for aldolase as revealed by pull-down assays using the immobilized sequence and a total cell lysate. A similar motif is found in a subset of aldolase-binding proteins (ABPs) such as the erythrocyte band 3 and the glucose transporter GLUT4, as well as in other molecules not yet defined as ABPs. We show that one of them, the Wiskott-Aldrich Syndrome protein (WASp), binds to aldolase using the predicted motif. Furthermore, ABPs containing this motif (band 3, GLUT4, and WASp) compete with the TRAP-tail for the binding to the enzyme, and utilize analogous aldolase-anchoring residues. The interaction of this subset of ABPs with aldolase is competitively inhibited by the enzyme substrate (fructose-1,6-biphosphate) and products (dihydroxyacetone phosphate and glyceraldehyde 3-phosphate). We conclude that the aldolase-binding motif defined here is conserved in evolution, suggesting a broader-than-expected role for this enzyme in cellular physiology. We speculate that this new motif might recruit aldolase and associated glycolytic enzymes to subcellular sites where the generation of ATP is required, including the *Plasmodium* actin/myosin motor.