Cryptosporidium Remodels Host Microvilli Through an Exported Virulence Factor

The intestinal parasite Cryptosporidium is a leading cause of diarrhoeal disease, contributing to early childhood morbidity and mortality. Like other members of the phylum Apicomplexa, Cryptosporidium has secretory organelles containing proteins that are exported into host cells following parasite invasion. For Cryptosporidium, the identity and function of the vast majority of these proteins is unknown. Using a bioinformatics approach, we first identified a putative host-exported protein with serine repeats, which we epitope tagged at the endogenous locus. With a combination of super-resolution and expansion microscopy we discovered that this protein localises to the parasite's secretory dense granule organelles prior to host-cell invasion, and then within the host microvilli following invasion. To determine the function of this MicroVilli Protein (MVP) we used yeast-2-hybrid screening, detecting interacting partner EBP50; a scaffold protein known to facilitate F-actin recruitment and control microvilli dynamics. Microvilli elongation is commonly seen in Cryptosporidium infected epithelial cells, but the mechanism for this was previously unknown. Parasites deficient in MVP have moderately attenuated growth yet show a complete lack of elongated host microvilli during infection. It is known that the Escherichia coli virulence factor MAP also interacts with EBP50, driving cell surface membrane protrusions and displacement of the NH3 sodium transporter contributing to diarrhoeal symptoms. While MVP has C-terminal homology with MAP, there does not appear to be evidence of a horizontal transfer event. This suggests a convergent evolution between bacteria and parasite that may contribute to diarrhoeal symptoms during infection.