Deciphering the molecular mechanism of a novel cryptosporidiosis therapy

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Cryptosporidiosis is a diarrheal disease affecting humans and mammals, caused by microscopic protozoan parasites of the genus Cryptosporidium, within the phylum Apicomplexa. Among the several species infecting humans, Cryptosporidium hominis is human-specific, whereas Cryptosporidium parvum is the most common zoonotic species. Recent global health reports have recognised Cryptosporidium species as one of the most lethal pathogens affecting malnourished infants and young children. The disease ranks among the top three diarrheal pathogens in terms of disability-adjusted life years (DALYs) lost. In Sweden, cryptosporidiosis has been a notifiable human disease since 2004. There is an urgent need in developing novel compounds against cryptosporidiosis to expand the unique FDA-approved therapeutic. We have developed experimental drug candidates targeting essential, non-redundant metabolic pathways in the parasite. After years of optimising compounds, the lead compounds have demonstrated an extraordinary preventive and curative efficacy against infection in both in vitro and in vivo infection models. However, their molecular targets remain unidentified. To address this, we employ an affinity-based protein labelling and structural homology analysis and molecular docking. These approaches aim to elucidate the identification of target and the molecular mechanisms of action of the lead compounds against cryptosporidiosis.