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Julie Tottey, Gilles Lalmanach. Functional characterisation of cysteine cathepsins as new virulence factors in the apicomplexan parasite *Cryptosporidium parvum*. Journées d'Animation Scientifique de la Fédération de Recherche en Infectiologie (FéRI), Fédération de Recherche en Infectiologie (FéRI), Jul 2023, Tours (France), France. hal-04395670

**HAL Id: hal-04395670**

**<https://hal.science/hal-04395670>**

Submitted on 15 Jan 2024

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## Session 2: Virulence mechanisms and host-pathogen adaptation

### Title: Functional characterisation of cysteine cathepsins as new virulence factors in the apicomplexan parasite *Cryptosporidium parvum*

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#### Abstract :

*Cryptosporidium parvum* is an apicomplexan parasite responsible for a zoonotic disease affecting both human health and livestock. The parasite is transmitted through the fecal–oral route and develops in ileal epithelial cells. The resulting enteric disease leads to watery diarrhoea that can be life-threatening in individuals with an immature or a compromised immune system. The only approved treatments against cryptosporidiosis have limited efficacy in the total clearance of the parasite. Improving our understanding of the parasite biology and host-pathogen interactions, as well as identifying new drug targets, are key steps towards the development of much needed effective control strategies.

Cysteine proteases play key roles in the pathogenesis of protozoan parasites, including cell or tissue penetration, hydrolysis of host or parasite proteins, and evasion or modulation of the host immune response, making them attractive chemotherapeutic and vaccine targets. For instance, papain-like proteases (clan CA, family C1) from protozoan parasites responsible for human or bovine trypanosomiasis (cruzipain, congopain<sup>1</sup>) and malaria (falcipains<sup>2</sup>) are already well characterised as druggable targets based on *in vitro* and *in vivo* models.

Genes encoding cathepsin L-like proteases (clan CA, family C1) have been reported in the genome of *C. parvum*, but only one (*ie.* cryptopain-1) has been analysed biochemically<sup>3</sup> to date. By combining our knowledge and expertise from the parasitology and protease biochemistry areas, we propose to detect cysteine protease-dependent activities throughout the *C. parvum* life cycle and characterise new cryptopain-like proteases in order to improve our understanding of their biological functions and identify novel targets for chemotherapy.

**Keywords :** *Cryptosporidium parvum*, Apicomplexa, cysteine cathepsins

#### References :

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