X-RAY STRUCTURE OF *OSTERTAGIA OSTERTAGI* ASP-1 PROVIDES DETAILED INSIGHTS IN DIMERIZATION MECHANISM AND PROTEIN CYCLIZATION

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CAP superfamily proteins (a.k.a. SCP/TAPS proteins) constitute an extremely diverse family of proteins in organisms spanning the entire animal kingdom. Even though CAP proteins such as the activation-associated secreted proteins (ASPs) are known to be involved in host-parasite interactions and are among the most abundant proteins in the excretome/secretome of numerous parasitic nematodes, their exact function(s) remain(s) elusive. Given the current issues caused by anthelmintic resistance, novel routes in parasite control are highly necessary, the most promising of which may be vaccination-based. ASPs are promising vaccine candidates in several parasitic nematode species, including *Ostertagia ostertagi*, one of the most prevalent and pathogenic gastro-intestinal parasites in cattle. However, the aforementioned lack of functional (and structural) information precludes the development of protective recombinant ASP vaccines. In this frame, we provide high-resolution crystallographic data of recombinantly produced ASP-1 from *O. ostertagi* (*Oo*-ASP-1).

Besides confirming the overall CAP superfamily topological hallmarks for *Oo*-ASP-1, i.e. the presence of the N-terminal CAP domain and the C-terminal cysteine-rich domain, we delve deeper in the 3D-structure of this abundantly secreted protein and elaborate on its highly peculiar traits. In agreement to its biologically relevant quaternary structure, i.e. exclusively as a dimer, inspection of the structure revealed the *Oo*-ASP-1 dimer as being maintained through a single intermolecular disulphide bridge, stabilizing an unusually small interaction surface. Moreover, unlike any other CAP superfamily member described to date, an additional intramolecular disulphide bridge links the N- and C-termini, thereby yielding a cyclic molecule. Whereas cyclization of the molecule may render it more resistant to proteolysis, *in vivo* dimerization of *Oo*-ASP-1 may be crucial in its function.

Apart from providing a brief overview on CAP superfamily proteins and ASPs in particular, the findings presented here and their importance in future developments in the field of vaccine-based helminth control will be discussed.