


ML Tonkin*, M Roques*, MH Lamarque, M Puginier, D Douguet, J Crawford, ML Lebrun, MJ Boulanger (2011) Host cell invasion by Apicomplexan parasites: insights from the co-structure of AMA1 with a RON2 peptide. Science 333: 463-7. [Chosen as the top biochemistry paper in this issue of Science and co-published with Perspective: “Revealing a Parasite’s Invasive Trick” (Baum and Cowman)]


* These authors contributed equally
Abstract
Parasites of phylum Apicomplexa cause devastating diseases on a global scale. *Toxoplasma gondii*, the etiological agent of toxoplasmosis, and *Plasmodium falciparum*, the most virulent agent of human malaria, have the most substantial effects on human health and are the most widely studied. The success of these parasites is due in part to a sophisticated molecular arsenal that supports a variety of novel biological processes including a unique form of host cell invasion. Accessing the protective environment of the host cell is paramount to parasite survival and mediated through an active invasion process: the parasite propels itself through a circumferential ring known as the moving junction (MJ) formed between its apical tip and the host cell membrane. The MJ ring is comprised of a parasite surface protein (AMA1) that engages a protein secreted by the parasite into the host cell and presented on the host cell surface (RON2). Thus, through an intriguing mechanism the parasite provides both receptor and ligand to enable host cell invasion. Prior to the studies described herein, the characterization of the AMA1-RON2 association was limited to low-resolution experiments that provided little insight into the functional and architectural details of this crucial binary complex. Towards elucidating the mechanism of AMA1-RON2 dependent invasion, I first structurally characterized *T. gondii* AMA1 bound to the corresponding binding region of RON2; analysis of the AMA1-RON2 interface along with biophysical data revealed an intimate association likely capable of withstanding the shearing forces generated as the parasite dives through the constricted MJ ring. To investigate the role of the AMA1-RON2 complex across genera, species and life-cycle stages, I next characterized the AMA1-RON2 complex from a distantly related genus within Apicomplexa (*Plasmodium*; *Plasmodium falciparum*) and from a divergent pairing within *T. gondii*. By combining structural, biophysical and biological data, I was able to generate a detailed model describing the role of AMA1 and RON2 in MJ dependent invasion, which is currently supporting efforts to develop novel vaccines and cross-reactive small molecule therapies.

Awards, Scholarships, Fellowships
Charles S. Humphrey Graduate Student Award (2013–2014)
President’s Research Scholarship (2013–2014)
NSERC Alexander Graham Bell Canada Graduate Scholarship - CGS D3 (2011–2014)
Ventura Neale Trust Endowed PEO Scholar Award (2012–2013) [One of 8 Endowed PEO Scholar Awards from Canada and the USA]
Charles S. Humphrey Graduate Student Award (2012–2013)
President’s Research Scholarship (2012–2013)
Lindau Award; Canadian Student Health Research Forum (2011) [Recognition of research with greatest novelty and potential, nomination to attend 2014 Nobel Laureate Meeting in Lindau, and selection as the Lindau Lecturer for the 2015 CSHRF]
Julie Payette NSERC Research Scholarship (2010–2011) [Most prestigious Master’s level NSERC scholarship awarded to the top 24 applicants]
Mrs. Annie Greskiw Graduate Award (2010–2011)
President’s Research Scholarship (2010–2011)
UVic Graduate Fellowship (2009–2010)
Howard E. Petch Research Scholarship (2009–2010)

Presentations
ML Tonkin, JR Beck, PJ Bradley, MJ Boulanger (2014) Structural characterization of the ISP proteins critical for replication of the apicomplexan parasite *Toxoplasma gondii*. **19th Annual University of Victoria Biochemistry and Microbiology Graduate Student Symposium**, Victoria, BC. [First Place Talk Award]
ML Tonkin, SA Arredondo, BC Loveless, JJ Serpa, KAT Makepeace, N Sundar, E T. gondii AMA1-bound to the corresponding binding region of RON2; analysis of the AMA1-RON2 interface along with biophysical data revealed an intimate association likely capable of withstanding the shearing forces generated as the parasite dives through the constricted MJ ring. To investigate the role of the AMA1-RON2 complex across genera, species and life-cycle stages, I next characterized the AMA1-RON2 complex from a distantly related genus within Apicomplexa (*Plasmodium*; *Plasmodium falciparum*) and from a divergent pairing within *T. gondii*. By combining structural, biophysical and biological data, I was able to generate a detailed model describing the role of AMA1 and RON2 in MJ dependent invasion, which is currently supporting efforts to develop novel vaccines and cross-reactive small molecule therapies.

Publications