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DEFENSE OF THE DOCTORAL

DISSERTATION

"A Role for Basigin in Toxoplasma gondii Invasion"

by

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Cell Biology, Neuroscience and Physiology Program

DMV 2013, University of Tehran, Faculty of Veterinary Medicine

Thesis Advisor:

Dr. George Yap, Ph.D.
Department of Medicine

Friday, April 1st, 2022
10.00 A.M.
Cancer Center G1196

https://rutgers.zoom.us/j/94128447768?pwd=T1dZV1J4RmpBR3JqMnQyNW80N2s3Zz09

Meeting ID: 941 2844 7768
Password: 998157

ABSTRACT

Toxoplasma gondii is an apicomplexan parasite that causes extensive necrotic lesions in the central nervous system (CNS) of immunocompromised patients resulting in life-threatening encephalitis. Recent studies reveal that *T. gondii* has a high tropism for astrocytes, the most abundant glial cell in the brain, among neural cells. Astrocytes perform a wide range of functions influencing how the CNS deals with infections and injuries. The process by which *T. gondii* attaches and invades these host cell surface receptor(s) is unknown. Our laboratory obtained proteomic data indicating that *T. gondii* engages with members of the BASIGIN (BSG) receptor family. This thesis hypothesizes that invasion of astrocytes by *T. gondii* is mediated by attachment of the parasite to certain members of the BSG family. This study found that primary astrocytes express two members of BSG immunoglobulin family: basigin and embigin. Antibody blockade of either basigin or embigin caused a significant reduction of parasite infectivity in astrocytes. The role of basigin during *T. gondii* invasion was determined in a mouse astrocytic cell line (C8-D30) with exclusive expression of basigin. CRISPR-mediated deletion of basigin in these cells resulted in decreased *T. gondii* infectivity. *T. gondii* replication and invasion efficiency were not altered by basigin deficiency, but parasite attachment to astrocytes was markedly reduced. Finally, a proteomic screen was performed to identify parasite antigens that interact with basigin. This screen identified several *T. gondii* proteins including, Toxoplasma-encoded cyclophilins, the protein 14-3-3 and protein disulfide isomerase (TgPDI) as putative basigin-ligands. We validated TgPDI as a genuine basigin-binding ligand and demonstrated that inhibition of the parasite's enzymatic activity abrogated attachment to host cells. Finally, mutagenesis of the active site of TgPDI resulted in loss of basigin binding. These studies identify a novel host receptor-parasite ligand pair that is critical for *T. gondii* infection of astrocytes.