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NEWSRELEASE

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Study Discovers Novel Pathway for Parasite Invasion and Dissemination

NEWARK, N.J.—Parasites known as apicomplexans are responsible for widespread infections, including malaria and toxoplasmosis, in human and animal populations. While most other intracellular pathogens get into our cells first by a process known as phagocytosis or "cellular eating," apicomplexans are well-known exceptions because they infect their host cells by active invasion at the cell's membrane surface. Now, researchers in the Center for Immunity and Inflammation at Rutgers New Jersey Medical School describe a novel hybrid invasion pathway that starts with the host cell eating the *Toxoplasma* parasite which, in turn, escapes to form its own vacuolar niche. This study will be published this week in the journal *Proceedings of the National Academy of Sciences*.

In humans, toxoplasmosis—initiated by ingestion of contaminated food and water—quickly spreads throughout the body. To fight off the infection, the immune system generates a specific type of response called type 1 immunity which kills most of the invading parasites and prevents overgrowth and death of the host. An important cell that senses the parasite and alerts the rest of the immune system is the professional phagocyte—cells that protect the body from infections—known as dendritic cells and macrophages. Phagocytes however, are also co-opted by the parasite using these immune cells to ferry infectious stages into the eyes and brain where the parasite remains hidden. In patients whose immune response becomes weakened by AIDS or chemotherapy, reactivation of the parasite infection in the brain can lead to fatal encephalitis.

The team of scientists led by George Yap, an associate professor of medicine at Rutgers, investigated the differences between virulent and avirulent strains of the parasite in how they infected phagocytic cells known as macrophages. Yanlin Zhao, a research associate in the Yap lab, found that virulent strains infected cells via the classical pathway of invasion at the cell surface. However, avirulent strains were surprisingly gobbled up by macrophages, where they soon ended up in lysosomes, the cellular compartment where phagocytosed material are normally digested and degraded. Instead of dying inside lysosomes, the parasite initiated invasion and established a structure known as a moving junction. Escaping through the moving junction, the parasite establishes its vacuolar niche inside the macrophage where it can acquire nutrients and divide. The researchers suggest that their findings represent a new pathway for parasite invasion, which they named phagosome-to-vacuole-invasion or PTVI.

The PTVI pathway of *Toxoplasma* infection of phagocytic cells may be important for the ability of avirulent strains to induce a stronger immune response, which enhances their dissemination to tissue sites—such as the eyes, brain and placenta—and ultimately their increasing prevalence in nature. Future work will determine what phagocytic receptors are involved in PTVI and what

parasite genes were lost during the evolution of virulent strains. Andrew Marple, an MD/PhD student at NJMS as well as collaborator at Oxford University and Dartmouth, also contributed to the published work.

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Founded in 1954, **Rutgers New Jersey Medical School** is the oldest school of medicine in the state. Today it is part of Rutgers, The State University of New Jersey and graduates approximately 170 physicians a year. Dedicated to excellence in education, research, clinical care and community outreach, the medical school comprises 22 academic departments and works with several healthcare partners, including its principal teaching hospital, The University Hospital. Its faculty consists of numerous world-renowned scientists and many of the region's "top doctors." New Jersey Medical School hosts more than 50 centers and institutes, including the Public Health Research Institute Center, the Global Tuberculosis Institute and the Neurological Institute of New Jersey. For more information please visit: njms.rutgers.edu