Schistosome Parasites Linked to Deadly Bladder Cancer

Researchers at GW's School of Medicine and Health Sciences (SMHS) have identified a gene that enables the parasite Schistosoma haematobium to establish a foothold in its human host, which ultimately may lead to a devastating form of bladder cancer.

Schistosomes, or helminth worms, are waterborne parasites that can cause chronic inflammation and fibrosis in the liver, symptoms that may migrate to the bladder, causing inflammation, granulomas, and eventually, bladder cancer. The worm is responsible for two-thirds of the world’s 200 million to 400 million cases of human schistosomiasis, resulting in an estimated 280,000 deaths per year.

In the July issue of the journal Hepatology, researchers from SMHS describe how they demonstrated the role of the metastasis-associated protein-1 (MTA1) gene in the proliferation of schistosomes. They infected two strains of mice with schistosome cercariae, a larval stage of the parasite. One group of mice, wild-type, had an intact MTA1 gene in their DNA. The other mice, MTA1-/-, lacked that gene, but were otherwise genetically normal. MTA1 is a crucial gene that controls the process of chromatin remodeling of cytokines, including those responsible for inflammation. By using the mice that lacked the gene, investigators were able to compare their reaction to parasite infestation to that of the normal, wild-type mice.

At various stages after infection, blood from the portal circulatory system of the liver was analyzed for worms and parasite eggs. "At the 12th week of infection, we found that the wild-type mice had severe granulomatous lesions in the liver," says lead author Sujit Nair, Ph.D., assistant research professor in SMHS’s Department of Biochemistry and Molecular Biology. "Their worm count was very high. In the mice that did not have the gene, however, there were neither worms nor eggs that we could collect from the portal perfusion."

From these results, the researchers concluded that absence of the MTA1 gene does not compromise the mice's susceptibility to the parasite infection, but it does limit the survival or maturation of schistosomes in the host, and possibly egg release and deposition.

Senior author Rakesh Kumar, Ph.D., professor and Catharine Birch & William McCormick Chair of Biochemistry and Molecular Biology, explains that expression of MTA1, a nuclear protein, regulates the expression of inflammatory cytokines that are produced by Th1 and Th2 cells of the immune response. By increasing the expression of MTA1 in the wild-type mice, the parasite "hijacks" the gene, "which in turn allows it to up-regulate pro-inflammatory cytokines, and these pro-inflammatory cytokines in turn will provide a favorable atmosphere for the pathogens to grow and cause a persistent inflammation," he says. "It's the persistent inflammation over time that we believe can lead to cancer."