Giardia genome unlocked

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Giardia lamblia, one of the most common human parasites in the United States, causes more than 20,000 intestinal infections a year, often through contact with contaminated drinking or swimming water. In the September 28 issue of *Science*, an international team led by researchers at the MBL (Marine Biological Laboratory) describe the complete genome (genetic sequence) of *Giardia,* which could lead to the development of new drugs to combat this persistent infection, called giardiasis.

“Even though there are treatments now available, a number of people get chronic giardiasis, which is difficult to eliminate. So there is interest in new treatments,” says Hilary Morrison, Ph.D., of the MBL’s Josephine Bay Paul Center for Comparative Molecular Biology and Evolution, the first author on the paper.

The *Giardia* parasite lives in the human intestine in a swimming and feeding form called a trophozoite, which is eventually expelled through the stools. Outside the body, *Giardia* takes the form of a highly infectious cyst that can live for weeks in water, soil, food, or on other surfaces.

Giardiasis is most common among children, especially those who are exposed to diaper changing. Swimmers, hikers, campers and others who drink untreated water are also prone to the infection (hence the nickname "backpacker's disease" or "beaver fever"), as are international travelers. Common symptoms include diarrhea, nausea, stomach cramps and gas, and usually persist two to six weeks. Because the parasite clings

to intestinal cells that absorb fats and nutrients, giardiasis can lead to severe complications such as poor nutrient absorption and weight loss.

“Although not life threatening, *Giardia* is a rather fastidious parasite and quite important from an economical viewpoint worldwide and in the United States, where it constitutes the major cause of diarrheal disease in children in daycare centers,” says Mitchell Sogin, Ph.D., director of the Josephine Bay Paul Center and leader of the *Giardia study*.

Analysis of the *Giardia* genome revealed several unusual proteins that are promising drug targets, Morrison says. “These proteins are different enough from human proteins that if you affect them with a drug, it’s not going to affect the human counterparts,” she says. “Drugs can be devised that will interfere with the parasite’s ability to replicate, or to move or bind in the small intestine, or to exist at all.”

The MBL team also investigated the evolutionary history of this ancient parasite. *Giardia* is a single-celled eukaryote, meaning its cell has a nucleus, as do the cells of humans and most other multicellular organisms. But the *Giardia* genome is compact compared to other eukaryotes, with simplified machinery for several basic processes, such as DNA replication and RNA processing. If the *Giardia* genome had originally been complex and experienced gene loss over evolutionary time, Morrison says, one would expect to see parts of the machinery intact and parts missing. This, however, wasn’t the case. “It looks like the genome was just simpler to begin with,” she says. The authors hypothesize that *Giardia* diverged from other eukaryotes more than a billion years ago.

“We embarked upon this genome project because of its importance to human health and suggestions from earlier molecular analyses that *Giardia* represents a very early-diverging lineage in the evolutionary history of eukaryotes,” Sogin says. “*Giardia’s* genome content and

architecture support these theories about the parasite's ancestral character."

Another important finding, Sogin says, is that the genes that allow *Giardia* to evade the human immune response are organized differently than in other parasites. In the host intestine, *Giardia* eludes an immune system attack by shifting the proteins it displays on its surfaces. The genes for these surface proteins are scattered throughout the *Giardia* genome rather than found in clusters, as in other parasites.

Source: Marine Biological Laboratory