

Genomic fluke close-up

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Parasitic flukes have been a leading source of food-borne infections, sparking fear and wreaking havoc on human public health, and contributed to more than 3 billion in animal agricultural losses per year in the U.S. alone.

They typically infect the [small intestine](#) or liver, causing severe illness and death, with symptoms including fever, pain, diarrhea and malaise during the acute phase of the illness, and chronic disease as well. In their [vertebrate hosts](#), they live, mate, and multiply.

Scientists have long been interested in better understanding these parasites, in order to alleviate their toll on human and animal health.

Now, a group led by Makedonka Mitreva at Washington University in St. Louis has recently performed the largest comparative genomic analysis of fluke species to date, including *Fp. Buski* and *Fa. Hepatica* and *Fa. gigantica*. It has made the genomes of all three human-infecting flukes widely available for the scientific community, and provided a better understanding of their evolutionary history, diversity, and adaptation to different hosts. Ultimately, the research team hopes their study provides a strong foundation to develop improved medical interventions, treatments and diagnosis.

The study was published in the advanced online edition of *Molecular Biology and Evolution*.

To perform their work, they used Ugandan cattle liver and Vietnamese

pig intestines as sources, and sequenced and assembled two new nuclear and two mitochondrial genomes (subcellular organelles only maternally inherited) of *Fp. buski* and *Fa. gigantica*. The size of the nuclear genomes were 748 Mb and 1.13 Gb respectively. Despite these differences in size, these genomes contained about the same number of protein coding genes, from about 11,000-12,500.

"This suggested to us that the relatively larger Fasciola genomes did not evolve through whole-genome duplications, but rather, are interspersed with many repetitive elements, such as DNA transposons and LINEs," said corresponding author Dr. Mitreva. "Our data lead to the hypothesis that TE-mediated genomic changes likely have contributed to the increased adaptive capacity of Fasciola spp. to new habitats and [host species](#) after their divergence from Fasciolopsis.

Next, the group performed a comparative genome analysis to better understand the [genome](#) evolution of fasciolid flukes. Molecular dating showed that the split between the Fasciolopsis genera and Fasciola took place around 88.1 Ma during the late Cretaceous period.

Their data supports that Fasciolidae may have originated in ancient African elephants and later expanded into Eurasian herbivores. From there, as the family diversified, [host](#) shifts occurred in both hosts, and organ habitats from the small intestine to the liver between 65 Ma and 55.9 Ma.

"Interestingly, this was during the same [time period](#) as the Cretaceous-Paleogene mass extinction, and the profound climatic and ecological changes that occurred during this period may have contributed to the adaptive radiation of these flukes to new niches," said Mitreva.

The more recent divergence between *Fa. hepatica* and *Fa. gigantica* occurred around 5.3 Ma, where their hosts of *Fa. hepatica* were

elephants, while *Fa. gigantica* originated in an African ruminant close to modern-day cows.

Next, to better understand the genes involved in medically important flukes, they performed a large-scale gene comparison among 8 different trematode species that have had their genomes sequenced. Gene families of interest that were identified include excretory and secretory proteins important for adaptation, including cathepsins, which are used to break down tissue and blood for nutrition and help evade the host immune system. Important cell signaling molecules found especially in sensing organs, the G protein-coupled receptors, were shown to have undergone positive selection to help flukes adapt to new ecological niches.

"This comparative analysis provides novel insight into the biology and evolution of Fasciolidae and other fluke families of medical importance," said Mitreva. "The genomic resources that these studies have provided should enhance development of novel interventions and diagnosis, and underpin genomic epidemiologic investigation of new disease outbreaks, virulence and drug resistance.

Provided by Oxford University Press

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