

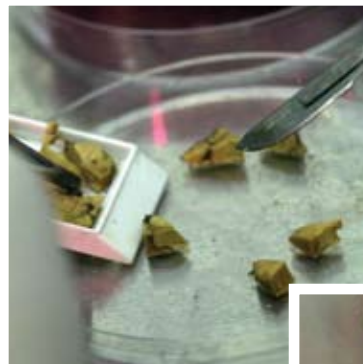
Comparative Pathogenomics of Epidemiologically and Genetically Diverse Strains of *Mycobacterium avium* subspecies *paratuberculosis*

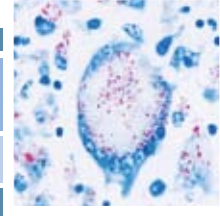
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■ Johne's disease, a chronic intestinal disease of ruminants, imposes a \$1.5 billion economic burden on the U.S. agricultural industry annually.

Johne's disease (JD) is a chronic intestinal disease of ruminants, including domestic and wild species, caused by *Mycobacterium avium* subspecies *paratuberculosis* (MAP). It has been estimated that at least 40 percent of herds in the United States with more than 300 animals per herd are infected. JD has also been predicted to impose an economic burden of \$1.5 billion annually to the U.S. agricultural industry. Furthermore, JD has been implicated as a possible etiological agent of Crohn's disease in humans. Despite considerable research efforts, prevention and control strategies of JD remain problematic.

MAP persistently infects and survives within host cells called macrophages. Currently, there are no reports on the behavior of diverse clinical isolates of *M. paratuberculosis* within a host/host cell (macrophage). Scientists believe that this critical piece of evidence is important to understanding the complex mechanisms underlying the virulence of this economically important animal pathogen.





Comparative gene expression of clinical isolates of MAP in a bovine monocyte-derived macrophage environment was studied. Selective capture of transcribed sequences was employed to identify the genes expressed

by a MAP strain (MAP6) isolated from a Crohn's disease patient. cDNA libraries were created from macrophages exposed to MAP.

Results suggest that the bovine and the human MAP isolates lead to anti-inflammatory and anti-invasive pathways in the macrophage environment whereas, in sheep, the MAP leads to a more pro-inflammatory pathway. Thus, the infecting strain genotype may play a role in polarizing the host immune responses and dictate the outcomes in this economically important disease.

The data collected for this study enabled scientists to write a successful proposal to USDA for \$350,000 to study genotype-specific host pathogen interactions. These studies will significantly increase our understanding of the early molecular events involved in the pathogenesis of JD, enabling scientists to design intervention strategies such as vaccines and early diagnostic tests.



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