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Researchers identify new leprosy bacterium

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A new species of bacterium that causes leprosy has been identified through intensive genetic analysis of a pair of lethal infections, a research team reports in the December issue of the *American Journal of Clinical Pathology*.

All cases of leprosy, an ancient disease that still maims and kills in the developing world, previously had been thought to be caused by a single species of bacterium, said lead author Xiang-Yang Han, M.D., Ph.D., associate professor in Laboratory Medicine at The University of Texas M. D. Anderson Cancer Center.

"We have identified a second species of leprosy mycobacterium, and in identifying this killing organism we've better defined the disease that it causes, diffuse lepromatous leprosy (DLL)." Han said. DLL occurs mainly in Mexico and the Caribbean.

There are hundreds of thousands of new cases of leprosy worldwide each year, but the disease is rare in the United States, with 100-200 new cases annually, mostly among immigrants. Leprosy initially attacks skin and nerve cells. It can be successfully treated with antibiotics in its early and intermediate stages.

R. Geetha Nair, M.D., a physician with Maricopa Integrated Health System in Phoenix, contacted Han in 2007 for help confirming a possible leprosy diagnosis in a patient who died that February.

The patient, a 53-year-old man originally from Mexico, was admitted

that month for treatment of extensive leg wounds. While undergoing antibiotic treatment and additional diagnostic testing the next day, he was stricken with high fever and shock. He died after 10 days in intensive care.

Analysis of autopsied tissue at the Phoenix hospital suggested a diagnosis of diffuse lepromatous leprosy, a form first described in Mexico in 1852. Han said DLL uniquely attacks a patient's skin vasculature, blocking or impeding blood flow. This leads to extensive skin death at late stage and may cause secondary infection and fatal shock. The DLL bacterium had never been studied.

The research team also analyzed samples from a similar lethal case of a 31-year-old man in 2002 with so much skin damage that he was first admitted to a hospital burn unit.

Telltale fingerprint points to new species

Han and M. D. Anderson colleagues diagnose infections in cancer patients. Han developed in 2002 a way to identify unusual bacteria by analyzing small but significant differences in the 16S ribosomal RNA gene. "This is like a fingerprint analysis to solve crimes," Han said. He has discovered and named several new bacterial species that cause unusual infections.

Across a group of bacteria called mycobacteria, the 16S rRNA gene is 93 to 100 percent identical. There are 110 species of mycobacteria, with those causing tuberculosis and leprosy the best known. Sequencing the 16S rRNA gene is a fast and accurate way to identify mycobacteria, which usually grow slowly, Han noted. Accurate identification improves patient care decisions.

Han and colleagues compared the lethal bacterium's 16S rRNA gene and

five other genes to other mycobacteria. They found that the bacterium had the most in common with *Mycobacterium leprae*, previously thought to be the sole cause of leprosy.

Yet there were also significant differences with *M. leprae*. The lethal bacterium's 16S rRNA gene sequence differed by 2.1 percent. "That may sound like a small difference, but to anyone familiar with mycobacteria, it's huge," Han said. In all previously studied *M. leprae* strains, no variation in the 16S rRNA gene had been noted at all.

Analysis of the other five genes turned up more differences. The researchers named the new species Mycobacterium lepromatosis. They have since confirmed *M. lepromatosis* as the cause of two lethal cases of DLL in Singapore.

What's next for *M. lepromatosis*

The team is working to better understand the bacterium and how it causes DLL. They are attempting to sequence the entire *M. lepromatosis* genome and looking for ways to grow the organism in the lab. Neither leprosy mycobacteria can be cultured because over millions of years they lost genes necessary to survive outside their hosts, a process called reductive evolution.

One of the puzzles of leprosy is that M leprae strains collected worldwide are virtually identical, while the clinical features of the disease and its severity vary greatly both geographically and from person to person. Evidence suggests that individual host immune factors play the key role in determining how the disease progresses.

The authors conclude that the new species *M lepromatosis* could account for some of this geographical and individual variation.

Source: University of Texas M. D. Anderson Cancer Center