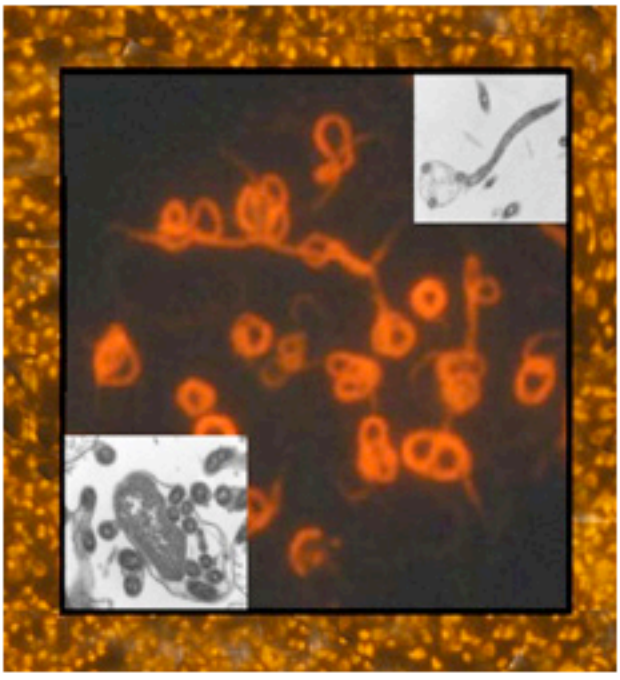
Margulis and colleagues' spirochete research may point to new Lyme treatment



In *Proceedings of the National Academy of Sciences*, Distinguished Professor Lynn Margulis, Geosciences, UMass Amherst advanced and former students James MacAllister and Andrew Wier and their colleagues in Norway and Canada, report new details about the life history of the spirochete bacterium, *Borelia burgdorferi*, which causes Lyme disease. Their study leads them to suggest that clinical trials of the antibiotic Tigecycline are warranted. This drug potentially provides a treatment regimen for people with Lyme disease that has worked, so far only in the laboratory, to destroy spirochetes, they point out.

The study represents a lifetime of work by medical microbiologist Oystein Brorson and his pathologist cousin, Sverre-Henning Brorson of Oslo, Norway, says Margulis, a winner of the Darwin and Wallace Medal from the Linnean Society of London. She recently returned to campus from a year as Eastman Professor at Balliol College, Oxford University.

B. burgdorferi spirochetes take up residence in tissues of people bitten by ticks that carry the bacteria in their guts and inject them via saliva. The spirochetes' most familiar form is an agile, spiral-shaped swimmer associated with acute symptoms of Lyme disease and rapid reproduction of the bacteria. But as Margulis explains, these bacteria can "go underground" and persist for years by entering a self-protective, quiescent stage known as a spirochete round-body (RB) propagule. In this state, they better resist what scientists call "unfavorable environmental conditions" such as starvation, desiccation and exposure to antibiotics such as penicillin and deoxycillin. Chronic Lyme disease symptoms correlate with the continuous presence of reversible RB propagules in patients' moist tissues.

What the Brorsons' work shows is that, unlike other antibiotics, Tygecycline administered at the correct dosage and timing destroys the bacterium even when it has protected itself in this quiescent stage. Other antibiotics, if they do anything at all, simply cause *B. burgdorferi* to enter its RB propagule state and wait out the treatment. "Tigecycline is, so far, the only known antibiotic that destroys the Lyme disease spirochete in both the growing and the quiescent RB stages of its life history" Margulis notes.

She and her students are interested in spirochetes, in particular two individuals found embedded in ancient (15 million-year-old) amber and their RB propagules, because of the Serial Endosymbiosis Theory of the evolution of nucleated cells. It posits that animal, plant, fungal and other cells with nuclei evolved by symbiotic merger of two types of bacteria, at least: A spirochete (belonging to the eubacterium group) that reversibly develops RB propagules in response to changing conditions, and *Thermoplasma*, from the archaebacterium group, a sulfide-gas-making microbe that lives in nearly boiling and very acidic waters (more acid than our stomachs). In their PNAS paper, the authors state that "chronic spirochete infections in humans when seen in their ecological-evolutionary context are examples of symbioses that have evolved over geologic time."

Image: Persistent quiescent Lyme disease spirochete (*Borrelia burgdorferi*) round bodies (RBs) may endure for years. They stain red as seen with here with a fluorescence microscope (scale bar = 8 micrometers). One RB is seen at very high magnification with an electron microscope (EM) thin section in the lower left inset). After incubation in a favorable supportive blood serum growth medium for over one month the RBs develop into normal helical swimmer spirochetes as seen in the EM photo of the upper right inset (bar = 1 micrometer). (Photo courtesy of Oystein and Sverre-Henning Brorson)

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