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William R. Jacobs, Jr., Ph.D., studied math at the University of Pittsburgh and microbial genetics at Edinboro State University, and completed his graduate studies at the University of Alabama in Birmingham, where he investigated leprosy. There he was introduced to bacteriophages (viruses that infect bacteria), which have since become invaluable tools in his research. Dr. Jacobs moved to Einstein in 1985 to become a postdoc with Barry Bloom, who was studying *Mycobacterium tuberculosis*.

In 1987, Dr. Jacobs set up his own lab at Einstein and began to isolate mycobacterial phages from the dirt in his backyard. His phage collection has grown over the years, thanks to high school students in his summer *Phage Phinders* program. Dr. Jacobs uses these phages to genetically manipulate mycobacteria. In the mid-1980s, he joined a circular piece of DNA (a plasmid) from *E. coli* to DNA from a mycobacterial phage to make a genetic tool he named "the shuttle phasmid." Because this hybrid DNA can replicate itself as a plasmid in *E. coli* and as a phage in *Mycobacterium*, it can shuttle genes from one to the other, including genes that have been inserted into *E. coli* in the lab. Investigators around the world now routinely use shuttle phasmids to knock out mycobacterial genes.

A series of breakthroughs followed, including the isolation in 1990 of a mutant of rapidly growing (and therefore research-friendly) strain of *Mycobacterium* that was amenable to genetic manipulation, the expression of foreign proteins in the vaccine known as bacille Calmette-Guérin in 1991, and the incorporation of a luciferase gene into *Mycobacterium* in 1992. Luciferase is the firefly enzyme that generates bursts of light. By using the shuttle phasmid to transfer the gene into *Mycobacterium*, Dr. Jacobs developed a way to screen antimicrobial drugs rapidly: luminescence indicates that *Mycobacterium* is still alive, whereas no luminescence shows that a drug has done its job.

The Jacobs group also has isolated a mutant whose mycolic acids have shorter than normal carbon chains, which helps explain the basis for the key diagnostic test used to identify mycobacteria for the last 125 years. Dr. Jacobs is now working to devise a safer and more effective vaccine using attenuated *M. tuberculosis* and other attenuated mycobacteria.