NovelBiotechnology

E. coli – from human stool to biotech tool

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WHITEPAPER

Undeniably, *E. coli* is the most unsung hero of biotechnology.

Biochemists and geneticists have torn it apart and studied its components, helping us unravel the mysteries of life at the molecular level (and making it the most well-characterized organism on the planet along the way). Countless graduate students have poked and prodded it on their way to advanced degrees. Pharmaceutical companies have – and continue to – use it as a host organism to manufacture drugs (like insulin). It has been coaxed to produce industrially important chemicals and enzymes at commercial scale. It is also used to manufacture plasmid DNA – everything from the small-scale plasmid preps on the lab bench, to large GMP-grade manufacturing runs for plasmids used in the manufacture of cell and gene therapies, vaccines, and RNA therapeutics.

But why does *E. coli* have this place of prominence?

Many scientists have devoted their careers to engineering *E. coli*. They can speak at length about the best methods for engineering the organism, wax eloquent about its metabolic capabilities, and can enumerate the applications of the bacterium in fields as diverse as industrial chemicals, bio-produced fragrances, or pharmaceuticals. Yet if you ask them why this organism rose to prominence instead of one of a vast number of other prokaryotic species on our planet, you will usually be met with a blank stare.

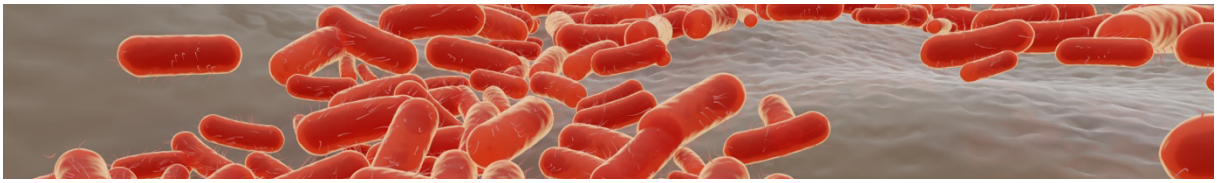
If you find yourself equally puzzled by that question, then this multi-part series is for you.

In this series we will explore the legacy of this unlikely hero, and will also consider – with all due respect to *E. coli* – why it is high time to add additional bacterial species to the biotechnology toolbox.

E. coli's storied career comes from a very messy beginning (quite literally). *E. coli* was first described by the pediatrician Theodor Escherich (the "E" in *E. coli*) in 1885. Theodor, who was studying the bacterial colonization of the gastrointestinal tract, managed to isolate a bacterial strain from fecal samples from human infants, and christened this newfound organism as *Bacterium coli commune*. In doing so, he simultaneously kicked off the study of the human intestinal microbiome and identified an organism that would play an essential role in the development of genetics, molecular biology, and biotechnology.

We now know that the human gut is home to a large variety of bacterial species, but most members of the gut microbiome are extremely fastidious and difficult to cultivate outside the body. In contrast, *B. coli commune* was easily isolated from stool samples and cultured in the laboratory, happily growing in a variety of simple media formulations (for those unfamiliar with *E. coli* cultivation, the most common growth media formulations still in use to this day are little more than broths composed of water, table salt, yeast extract, and soluble animal protein – essentially the broth present in a bowl of ramen noodles).

The name of the organism was changed to the now familiar *E. coli* in the 1919 edition of *Manual of Tropical Medicine,* where the authors reassigned *B. coli commune* to a newly created genus – *Escherichia* – in homage to the work of Theodor Escherich. While Theodor was the first to report on the isolation of the strain, he was certainly not the last. Many other scientists around the world were also examining the stool samples of patients with hopes of unraveling the causes of a variety of human diseases. They too managed to isolate their own strains of *E. coli* – some of which would eventually earn a rightful place in the biotech hall of fame.



K-12 STRAIN

Anyone who has worked with *E. coli* has probably heard of the K-12 strain of *E. coli*, and if they haven't heard of it, they have likely worked with one of its ancestors. The K-12 strain of *E. coli* is the progenitor of commonly employed strains such as W3110, MG1665, DH5α, and DH10b – popular strains for research, molecular cloning, and production of recombinant proteins and bio-based chemicals. K-12 was isolated from the feces of a diphtheria patient in Palo Alto, California in 1922. In 1925, this strain was deposited into the strain collection at Stanford University's Department of Bacteriology and Experimental Pathology, where it was quickly adopted by instructors in the bacteriology teaching labs as a model *E. coli* strain. From there the K-12 strain managed to play a critical role in the education and research endeavors of many bacteriologists, and due to its familiarity among scientists, was a pragmatic choice for a model system for many seminal experiments that are still taught in textbooks today.

B STRAIN

In a similar vein, the B strain of *E. coli* is thought to be derived from a strain isolated from the feces of a patient recovering from dysentery in Paris, France sometime around 1918, and was deposited into the strain collection at the Pasteur Institute. From there the B strain was disseminated among prominent scientists of the day, and (like the K-12 strain) helped lay the groundwork for our modern understanding of genetics and molecular biology, and played a pivotal role in the birth of the biotech industry. Derivatives of this strain, such as the BL21 and BL21(DE3) strains, are popularly used in research settings for production of recombinant proteins (a gene mutation in a prominent *E. coli* protease reduces proteolytic activity and protects recombinant proteins being produced in these strains from degradation).

While the K-12 and B lineages are definitely the most famous collection of strains, countless other strains of *E. coli* have been isolated from the gut of mammals and deposited in strain collections around the world. This would include some *E. coli* strains that have acquired genes that convert them from commensal organisms (those that live in harmony with their host) to pathogens.

As an interesting side note, it seems that laboratory strains of *E. coli* have forsaken their humble roots, as studies have shown that after decades of propagation and manipulation in the laboratory, K-12 derivatives have lost their ability to colonize the mammalian gut.

In our next installments of this series, we will look at a number of key moments that served to further galvanize *E. coli's* status in the biotech industry. If you enjoyed this article, I have relied on a number of other excellent articles on the subject, and I would point the interested reader to the references section below for additional details.

REFRENCES

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